VET. Toxicology

All things are poison and nothing without poison. ***'All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy.'***

VET. Toxicology

ϖ INTRODUCTION

- Toxicology
- derived **from Greek word Toxicon**
- **Which means poison**
- **defined literally as ‘’the study of poisons’’**
- thus it defined scientifically as **the study of the harmful effects of poisons on living organisms**

including their

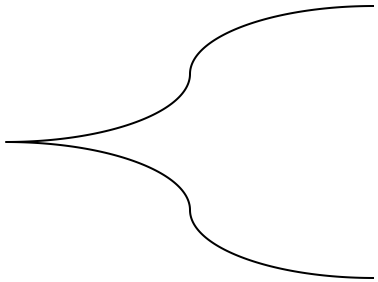
- **chemical properties**
- **biological effects.**
- **<u>Diagnosis</u> and <u>treatment</u> of organisms that are affected by poisons**

Cond,

- **These adverse effects may occur in many forms, ranging from immediate death to slight changes not realized until months or years later.**
- **may occur at various levels within the body, such as an organ, a type of cell, or a specific biochemical (from the molecular**

Cond’

Poison



Solid
liquid
gas

- **Are all substances toxic?**
- **All are toxic to some quantifiable degree**
- **Sugar has an LD_{50} of 30,000 mg/kg**
- **ethanol has an LD_{50} of only 13,700 mg/kg**
- **Even water has a recognized LD_{50} of**

Basic terminologies and definitions related to Toxicology

Poison – any solid, liquid or gas (present in any state) either oral or topical route can interfere with life process of the organism.

Toxicant (xenobiotics). An alternative term for poison.

***Toxin*. A poison that originates from biological processes**

- **Mycotoxins (fungal toxins)**
- **Zootoxins (animal toxins)**
- **Phytotoxins(plants).**

- ***Toxicity*. The quantity or amount of a poison that causes a toxic effects**

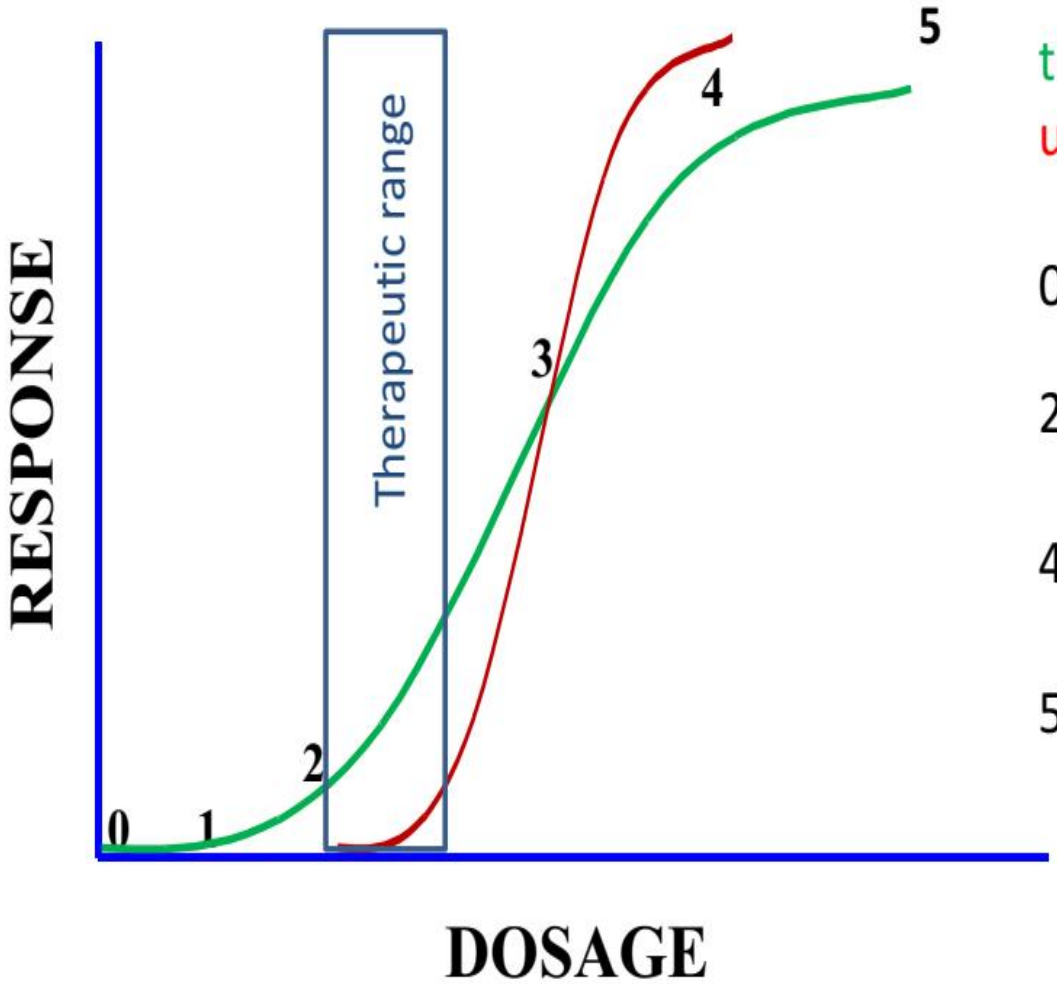
Cond’

- ***Toxicosis*. A disease state that results from exposure to a poison.**
- ***Dose*. The amount of toxicant that is received per animal.**
- **Dosage*. The amount of toxicant per unit of animal mass or weight. Can be expressed as the amount of toxicant per unit of Mass or Weight per unit of time or by the length and frequency of exposure .**

eg 1. 2 mg/kg/day.

eg 2. 2.5 mg/kg/day for 2 years

Dose-Response Relationship



therapeutic effects
undesired/unwanted effects

0-1 NOAEL (No Observable Effect Level)

2-3 Linear Range

4 Maximum Response

5 Plateau

cond’

- ***Threshold dose*** - The highest dose of a toxicant at which toxic effects are not observed
- LD (lethal Dose) the lowest dose of toxicant which causes lethalty or death in animals during observation time
- LD50(Lethal dose50): The dose of a drug that produces death in 50% of the animal population tested or The dose at which 50% of the animals die during some period of observation
- (mg/kg.wt)

The lower the LD50 dose, the more toxic

Cond,

LC_{50}= The concentration of a chemical in an environment (generally air or water) which produces death in 50% of an exposed population of test animals in a specified time frame

expressed as milligrams of substance per liter of air or water (or as ppm)

Cond,

- ppm (**part per million)**

Chemical concentration in toxicology generally expressed in ppm

- **ppm= 1 mg/1 kg**
- **For H_2O at STP (standard temperature [23°C] and**

Cond’

Which means that

1 liter of water = 1 kg

1 mg / kg = 1 ppm

1 mg / liter = 1 ppm

Generally

- **1ppm=1 mg/1 kg =1mg/1000g = 1mg/10^3 g = 1mg /10^6mg = 0.0001%**

cond

Rule to convert ppm to a % and % to ppm

- to convert ppm to a % move the decimal point 4 places to the left
- to convert the percentage to ppm move the decimal point 4 places to the right.

Ex. 124PPM = 0.0124%

0.5% = 5000 PPM

Sub discipline of toxicology

- **toxicology a multi -disciplinary science and subdivided**

- **Clinical toxicology: deals with the effects of poisons on living things**
- **Developmental - effects of poisons on the developing organs**
- **Nutritional : studies toxic effect on foodstuff**
- **Ecotoxicology: deals the fate and effects of poisons on ecosystems**

Cond,

- **Forensic t- studies unlawful use of toxic agents & their detection for judicial purposes**
- **Reproductive t- studies the occurrence of adverse effects on reproductive systems of an animal**

- **Sources of poisoning**

Can be categorized

1. natural source

- **grass and plants grown on soils rich in toxic minerals**

2. man made poisoning

- **Accidentally- through contamination of feed and water**
- **Intentionaly- unlawful or criminal**

cond’

Depending on

The agent used

Dose toxicity

Route

frequency toxicity

duration of exposure toxicity

Symptoms

acute

sub acute

chronic

Cond’

Acute toxicity: results from exposure to relatively high dose of a compound over a short period(few days)

- Symptoms are more sever & death is rapid

- **Subacute toxicity** appearance of a mild form of toxic symptoms following repeated administration to relatively low doses of poisons for at least 90 ds

- symptoms develop gradually

- **Chronic toxicity**: mild form of toxicity syndrome following long term repeated

Cond’

- **Classification of poisons/ toxicant**

poisons classified based on

- **Sources (plant , bacteria, fungal, snakes)**
- **Physical state (solid, liquids, gas)**
- **Physical characteristics (inflammable , explosive**
- **chemical characterstics- (inorganic, organic)**
- **Uses (insecticides , Acaricides)**
- **Target organs**
- **biological effects**
- **Toxic potential**

Target organ	Toxicants
Respiratory	Nitrate, Co, chlorate cyanide
Nervous	Barbiturates, NaCl
Kidneys	CCl4, Mycotoxins
GIT	Arsenic, NaCl
Heart	Cardiac glycosides
Skeleton	Lead, fluorine, selenium

Based on toxic potential	
Extremely toxic	< 1mg/kg
Highly toxic	1-50mg/kg
moderately toxic	50-500mg/kg
Slightly toxic	0.5-5g/kg
practicaly non toxic	5-15g/kg
relatively harmless	>15g/kg

Sampling and processing of samples

- If a known toxin is suspected, a specific analysis should always be requested—laboratories cannot just “check for poisoning.” A complete description of clinical and epidemiologic findings may help differentiate poisoning from infectious diseases that can simulate poisoning.

Cont...

- The most critical samples to be collected are generally stomach contents, liver, kidney, whole blood, plasma/serum, and urine, but exceptions exist, such as cerebral tissue for cholinesterase analysis. For some investigations, the diagnosis requires analysis of feed or water. If there is doubt about sample submission procedures, the laboratory should be contacted.

Guidelines for Submitting Samples for Toxicologic Examination

Suspected Poison or Analysis	Specimen Required	Comments
Ammonia	Whole blood or serum	Frozen
	Urine	Frozen
	Rumen contents	Frozen (or may add 1–2 drops saturated $HgCl_3$)
Anticoagulants (warfarin and related compounds)	Whole blood	Heparin or EDTA
	Liver	Refrigerated
	Feed	
	Stomach contents	
Arsenic	Liver	
	Kidney	
	Urine	
	Ingesta	
	Feed	
Chlorates	Stomach contents	Frozen, in airtight container

Guidelines for Submitting Samples for Toxicologic Examination

Suspected Poison or Analysis	Specimen Required	Comments
	Feed	
Chlorinated hydrocarbons	Cerebrum Ingesta Body fat Liver Kidney	Use only glass containers Avoid contamination Refrigerated or frozen
Cholinesterase	Serum Cerebrum	Frozen
Copper (and Ni, Fe, Co, Cr, and Tl)	Kidney Liver Serum Feed Whole blood Feces	

Guidelines for Submitting Samples for Toxicologic Examination

Suspected Poison or Analysis	Specimen Required	Comments
	Liver, kidney	
Nitrate	Forage Water Body fluids (eg, aqueous humor)	Refrigerated
Organophosphates (and carbamates)	Feed Ingesta Urine	Also send urine, blood, and stomach contents from clinically normal animals
Oxalates	Fresh forage Kidney	Do not macerate; freeze Fixed in formalin
Phenols	Gastric or rumen contents	In airtight container
Polychlorinated (and polybrominated) biphenyls	Fat Cerebrum	

Guidelines for Submitting Samples for Toxicologic Examination

Suspected Poison or Analysis	Specimen Required	Comments
Rumen pH	Ingesta	Frozen
Selenium	Whole blood Feed Liver Hair clippings	Heparinized
Sodium (NaCl)	Brain Serum CSF Feed	Other half fixed in formalin
Sodium fluoroacetate (1080)	Stomach contents Liver	Frozen
Strychnine (and some other convulsants such as bromethalin)	Liver Kidney	

Guidelines for Submitting Samples for Toxicologic Examination

Suspected Poison or Analysis	Specimen Required	Comments
TDS (total dissolved solids)	Water	
Triaryl-PO_4	Ingesta Feed	
Urea	Feed	See Ammonia, above
Vitamin A (also D and E)	Liver Serum	Frozen
Vitamin D_3 (rodenticides)	Kidney	
Zinc	Liver Kidney Serum	Use "trace minerals" tubes
Zinc phosphide	Liver Gastric contents	Frozen

Cont...

- Tissues or fluids for chemical analysis should be as fresh as possible and kept refrigerated. For some analyses, freezing is critical to prevent degradation of volatile chemicals, and in rare instances a chemical preservative is required.
- If legal action is a possibility, all containers for shipment should be either sealed so that tampering can be detected or hand-carried to the laboratory and a receipt obtained. The chain of custody must be accurately

Cont...

- If feed or water is suspected as the source of poisoning, samples of these and any descriptive feed tag should accompany the tissue samples.
- If at all possible, a representative composite sample of the feed should be submitted from the suspect lot or shipment. In some instances, if an adequate amount of involved feed is available, some of it may be fed to experimental animals in an effort to

Toxicokinetics

- **The process of absorption, distribution, biotransformation and excretion of toxicant in relation to time**
- **‘ in other words how the substance gets in to the body and what happens to it the body**

Cond’

- **Exposure to toxicant(posisons)**
- **There are four primary routes of exposure to chemicals**
- **Injection**
- **Ingestion/oral**
- **Contact (topical)**
- **Inhalation**

• Injection Cond’

- **The route in which the entire amount exposed is absorbed.**
- **Chemicals may be injected**

- **IV- directly into vein**
- **IM- into muscle**
- **Sc- under the skin**
- **IP- within the membrane lining the organs of abdomen.**
- **IV the most rapid methods of introducing chemicals into the body**

Cond’

- Ingestion

- common route of exposure to toxic chemicals

- In the stomach, the chemical is mixed with food, acid, and gastric enzymes.

- Stomach contents can alter the toxicity of a substance by influencing its absorption or modifying its chemical structure.

Cond,

- Insoluble chemicals in the gastrointestinal fluids are generally excreted with little harm, unless if they are corrosive or irritating
- Soluble chemicals are absorbed through the lining in the gastrointestinal tract

⎫ transported through the portal vein in to the liver

Cond,

- **Inhalation**

- The **principal mode of entry for chemicals in the form of vapors, gases, mists, or particulates..**
- **Inhaled toxins can cause harm by irritating and destroying respiratory tissue or by being absorbed into the blood.**

Toxicity is Dependent on Route of Exposure

Often, if a toxicant undergoes first-pass metabolism, it will be less toxic if administered orally than IV.

More toxic ←

Less toxic

IV > Inhalation > IM/SC > Dermal > Oral

No first-pass metabolism

Directly into systemic circulation

First-pass metabolism

(metabolized in the liver first)

transportation of toxicant

- A process whereby chemicals (Toxicants) move into the body(target organs)
- Toxicants may pass through a membrane by passive or active diffusion

cond

1. Passive *transport* or diffusion

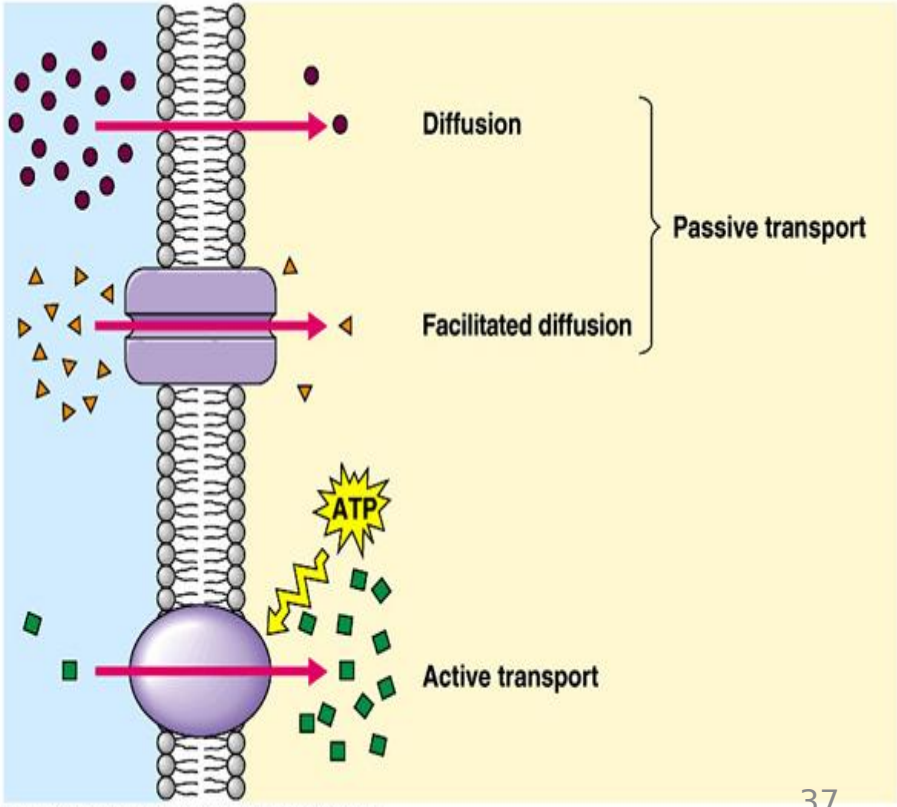
- simple diffusion (most toxicant cross membrane, small hydrophilic molecules permeate membranes through aqueous pores
- facilitating diffusic

• 2.Active transport-

Cell provides energy

For moving the toxic

across its membrane



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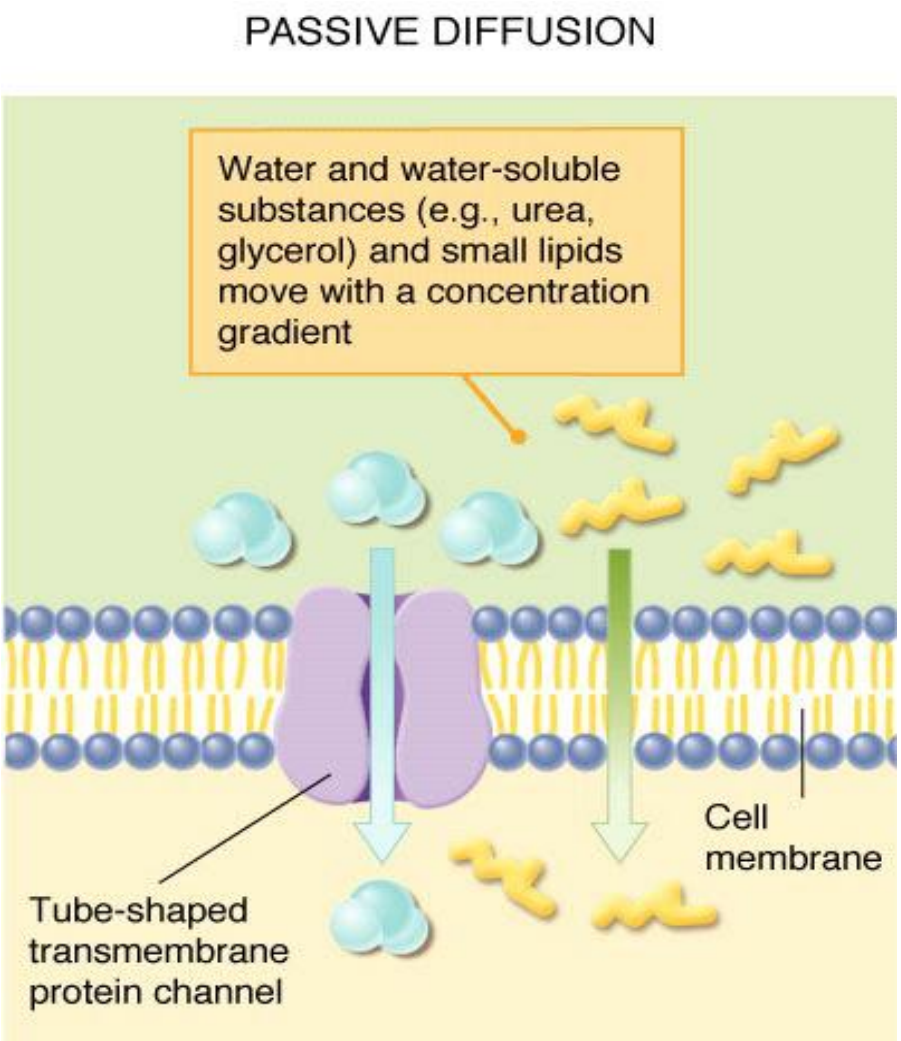
Cond’

- **Skin contact**

Chemicals can penetrate the skin

- by diffusion through the epidermis,
- entry into the sweat ducts
- entry along the hair follicles.

1) PASSIVE DIFFUSION



- It is defined as the difference in the drug concentration on either side of the membrane.
- Absorption of 90% of drugs.
- The driving force for this process is the concentration or electrochemical gradient.
- The process doesn’t

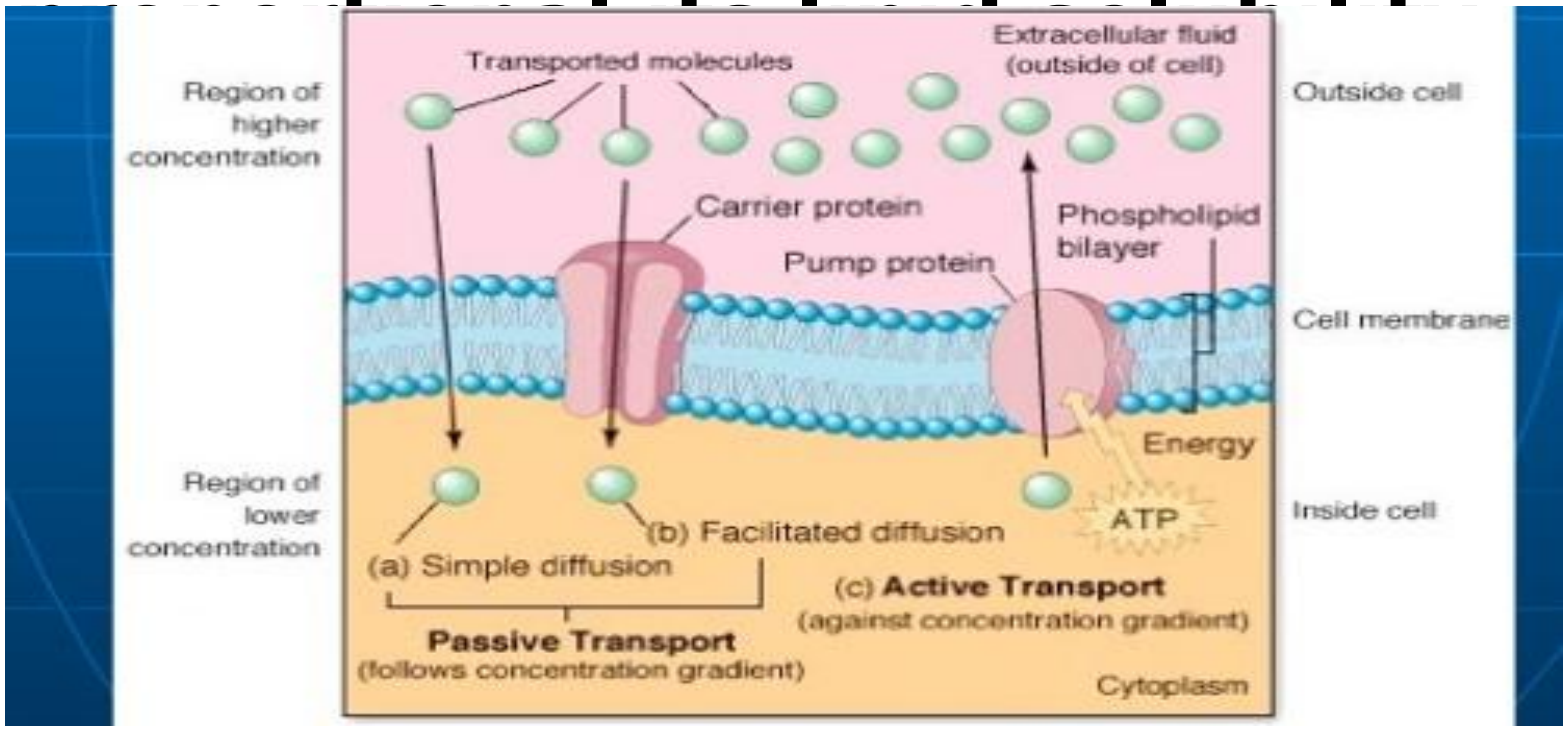
Factor affecting diffusion

a) Down hill transport
b) Greater the surface area & lesser the thickness of the membrane, faster the diffusion.
c) Equilibrium is attained when the concentration on either side of the membrane become equal.
d) Greater the membrane/ water partition coefficient of drug, faster the absorption. small hydrophilic pass through pores; larger molecules depends on lipid solubility
e) Ionized vs non-ionized(charged vs non- charged

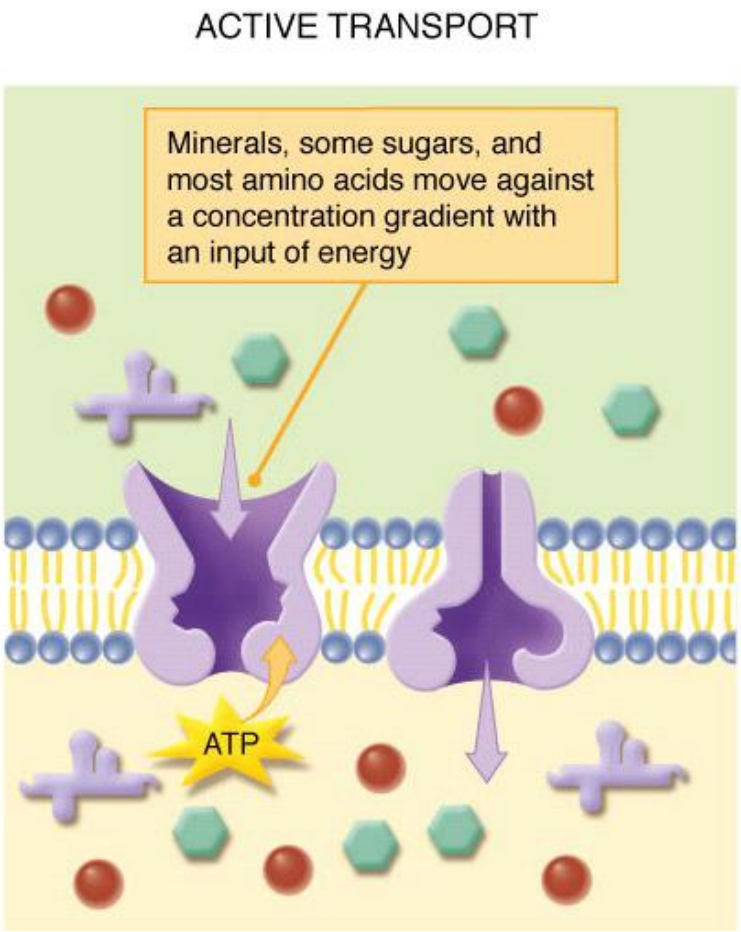
-lipid soluble to some extent

-Diffuse across lipid domain of membrane

-Rate of transportation



2) Active transport



- More important process than facilitated diffusion.
- The driving force is against the concentration gradient or uphill transport.
- Since the process is uphill, energy is required in the work done by the barrier.
- As the process requires expenditure of energy, it can be inhibited by metabolic poisons that

Cont,

- **DISTRIBUTION**

- **Following absorption xenobiotics are distributed throughout the body via blood stream at varying rates depending on a number of factors:**

- **The rate of distribution affected by**

1. **Physical & chemical properties of toxicant**

cond’

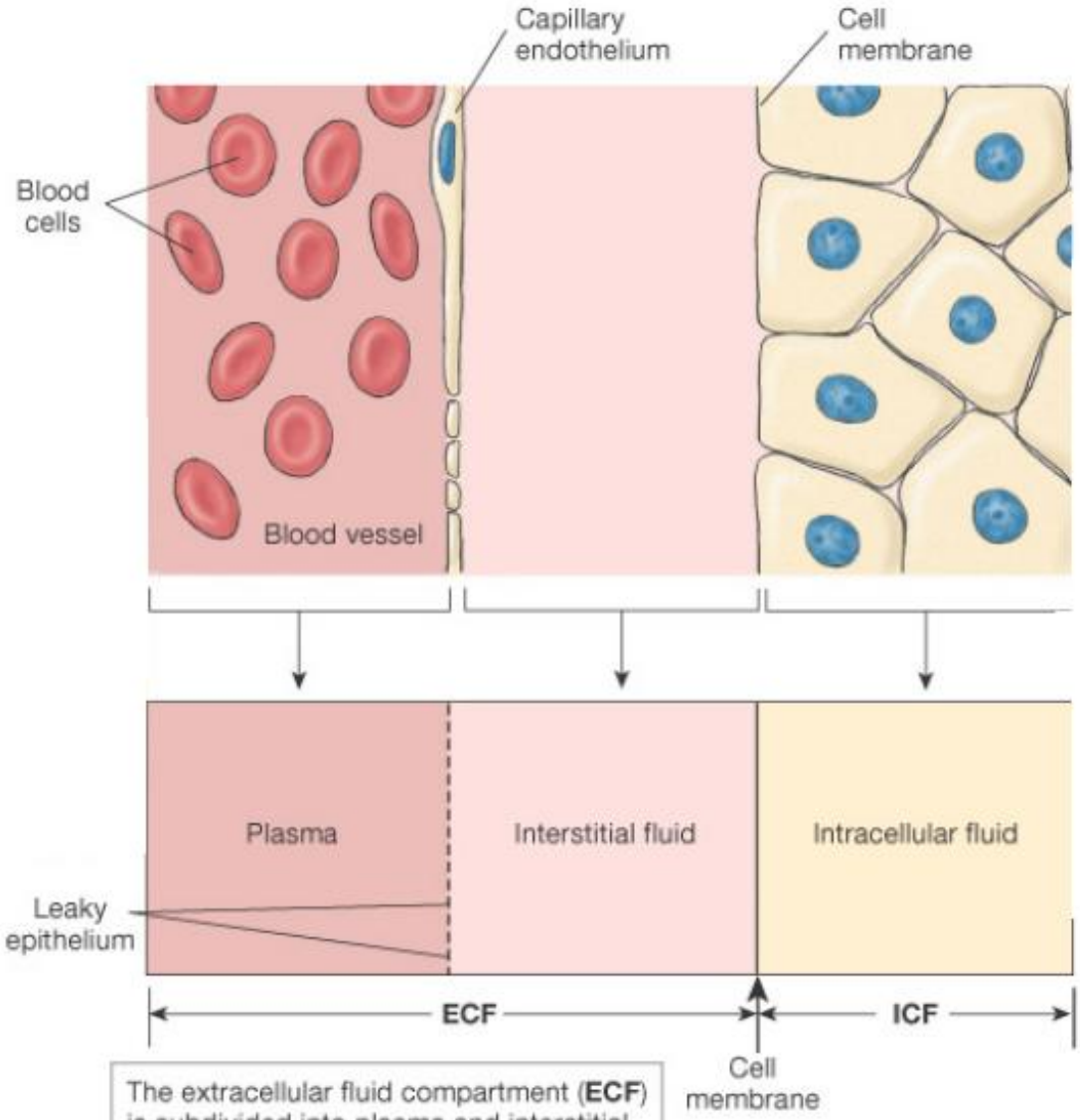
3. **Volume of blood flowing through tissue:**

(organ which receives high blood volume, will receive high quantity of toxicant)

4. **Tissue specificity of toxicant**

(Ex. Arsenic accumulates in the hair where as lead stored in bones.

Physical Barriers to Distribution



The extracellular fluid compartment (**ECF**) is subdivided into plasma and interstitial fluid. Material moving between cells and ECF must cross the cell membrane.

Distribution of toxicants

Distribution can be highly localized, restricted or disperse depending on:

1. Binding and dissolution into various storage sites (fat, liver, bone)
2. Permeability through membranes
3. Protein binding

If the toxicant accumulates at a site away from a toxic site of action, it is considered as a protective storage site

Effects of Storage on Toxicity

1. Reduces toxicity of some substances by taking toxic substances out of the sites of action.
2. Increases toxicity if: a)toxicity at storage site, b) displacement of one substance by another (e.g. bilirubin), loss of storage site.
3. Can produce chronic toxicity from prolonged exposure.

Cond,

Biotransformation: a Process that changes substances from hydrophobic to hydrophilic to aid in elimination

Purpose

1. facilitates excretion:

- **Converts lipophilic to hydrophilic compounds**

2. Detoxification/inactivation:

- **converts chemicals to less toxic forms**

Cond,

- Sites of b**iotransformation**

- **Liver: Primary site, Rich in enzymes(MFO- mixed enzyme function oxidases such as cytochrome P-450**
  - **Acts on endogenous(pigments, hormone) and exogenous(drugs toxin, food additives) compounds**
- **Extrahepatic metabolism sites**
  - **Intestinal wall**
  - **-Lungs, kidney, placenta, brain, skin, adrenal**

cond’

- **metabolism of xenobiotics tack places in two phases**
  - **phase I and phase II**

30 different enzymes are involved

- Phase I (non sythetic)reactions no new chemicals is produced., simply involves
- Hydrolysis, reduction and oxidation reaction

Cond’

Purpose Phase I (make the substance more soluble by addition of **polar functional groups (**OH, -NH_2, -SH or –COOH) **in a molecules.**

- However, there are xenobiotics(e.g acetaminophen and aflatoxin B1) for which the products of hepatic phase I metabolism are actually more toxic

Cond’

Phase II reaction (synthetic reaction)

- **Xenobiotics converted to more polar, hydroxylated derivatives.**
- **these derivatives are conjugated with molecules such as glucuronic acid, sulfate, or glutathione.**
- **become more water-soluble, and**

Excretion (elimination) is the final step in the disposition of a xenobiotic is excretion, whereby the xenobiotic or its metabolites are removed from the body via a number of different routes.

The following are the major ways through which poisons and their metabolites are excreted.

1. *Faecal excretion. Ingestion of a relatively insoluble poison (e.g., lead arsenate) is*

Cont...

3. Pulmonary excretion. Volatile poisons may be mainly excreted in the expired air, e.g., cyanide.

4. Urinary excretion. This is the most important pathway of the excretion of a poison. It is of great importance in detecting the pasture contamination with fluorides.

5. Milk and dermal excretion. Excretion can also take place through skin, e.g., arsenic, and in lactating animals in milk like DDT.

Mechanisms of action of poisons

1. Chemical injuries

   Acids , bases, proteins & lipids of the ell membrane are denature

2. Necrosis of epitheilal cells

   (highly metabolic active , such as hepatocytes, renal tubules, bone marrow and intestinal cells)

3. Inhibition of enzymes

   Denaturing- no more functional the animal will dies if there is no other alternatives

Cond’

4. functional effects on nervous system

- Block neurotrasmitters

5. Damaging the vascular system

- Toxicant oxidase Fe from Fe^{+2} to Fe^{+3}=

produce methemoglobin which can not transport oxygen Leads to tissue anoxia and then necrosis

Cond,

6.Immuno suppression

Reduce protein production(Antibodies)

Both **humeral** and cellular immunity affected due to reduction of antibodies by the action of xenobiotics

7.Developmental defect when acts on developed organ especially on the 3rd trimester of gestation

8. Carcinogenesis: damage of DNA leads to faulty DNA repairing and causes

Factors affecting the action of poisons

- Different factors affects the action of toxicants on target organs

1.Dose the action depends on the amount of substance absorbed into the blood stream

2. physical properties

- solid < powdered forms
- Finely powdered > coarse powders
- Gaseous > liquid > solid
- in aqueous solution< in oily medium

Cond’

3. chemical properties

- Red Phosphorus not toxic while yellow is toxic

4. Repeated exposure

- intensity depends whether the animal exposed to single or multiple doses

5.Route of exposure

Gaseous form more toxic when enter through respiratory route

6. Age: young and old animals are more sensitive

- Organ of detoxifying and metabolism not fully developed in young

Cond’

7. Sex:

- **Female more susceptible than male**
- **related to hormones**
- **e.g. castration increase susceptibility of male**
- **Administration of testosterone into female increase their resistance**

8. **species: effects of poison differ from spp to spp**
9. **Genetic variation: varies from population to population**
10. **disease: liver(cirrhosis), kidneys,**

Diagnosis of poisoning

- Diagnosis of poisoning in animals is not an easy task
- Never made with single observation
- For Dx of poisoning the following should be consider

- History
- Clinical symptoms
- necropsy
- Laboratory analysis

Cond’

- During History taking- question about
  - the change in location
  - applied chemicals to feeds
  - Application of insecticides, fertilizer , pesticide on grazing fields & presence of toxicant in the environment
- Clinical symptoms: examine for alteration of vital parametrs (RR, HR, Tem,) and function of other organs
- E.g Chlorinated hydrocarbones = hyperthermia

Cond’

- Necropsy:

⎫ considering lesion and lack of lesion

⎫ abnormal color of stomach and intestinal content

Laboratory analysis

Dx poisoning confirmed by hematological and biochemical tests

For this

serum ,whole blood, GIT content , bone, milk, feed , skin , hair and affected organs etc should be collected

Cond’

- Liver-200gm
- Kidney-200gm
- Stomach and intestinal content-500gm
- Skin and hair 10gm
- Feed = 2kg – upto 5 days
- Water = 2 Lt 5 days
- serum 3-5 ml
- Milk -100ml

Treatment of poisoning

- **Poisoning should take always as emergency cases**
- **Need to treat using specific antidotes**
- **To treat one must understand**

- **Toxicokinetics**
- **Toxicodynamics**
- **Action of antidotes**

Cont..

- Treatment of poisoning includes

1. **Removal of the source**

- **removal of animal from the area where poisons are present**

if it swallows

a. **Removal from GIT**

b. **Hastening the passage through bowl**

c. **Neutralization of the poisoning within the GIT**

Cont..

a. Removal of poisons from stomach

I . gastric lavage

- if ingestion is taken in preceding 2-4hrs
- Isotonic solution of NaCl, Sodium bicarbonate
- washing the stomach until the stomach is clear

II. Emetics(dog, cats, swine) in preceding2-3hrs

- done to empty the stomach by vomition

Cont..

b. hastening (speeding up) the passage through the bowl.

Orally: sodium sulphate for dogs & cats 1.0g/kg

100-200 g for large animals

c. Neutralization of the poisoning within the GIT

Using adsorbent agents like

- activated charcoal or neutralizing agents

2. **Elimination of poisons from the site of exposure**

Cond’

Ex. Washing the skin and eyes

3. Formation of **insoluble precipitate complex**

- **using agent that prevent dissolution of the toxicant by formation of insoluble complex**
- **Feeding calcium to form complex with oxalate**
- **Calcium oxalate can not be absorbed and removed with faces.**

Phytotoxicity

- Phytotoxicity :intoxication caused by toxic plants

- cause a variety of losses to the livestock industry
- are not palatable and are avoided if other forage is available.
- Poisonous plants can affect animals in many ways, including death, chronic illness and debilitation, decreased weight gain, abortion, birth defects, increased parturition interval, and photosensitization.

Cond’

- **Phytoepidemiology in Ethiopia**

- **Plant toxicities has significant impact to the Ethiopian livestock because of several reasons;**

I. The livestock management system

- **animals are reared in uncontrolled environment = get access to toxic plants**

II. Recurrent drought

- **results scarcity of animal feed.**

Most pasture plants are annuals (lasts for a year) while toxic

Cond’

III. Extensive grazing and deforestation

- **when grazing feed is compressed, animals search for grazing plants on newly opened uplands on hills which are toxic because it is likely to grow perennial toxic plants on lands of uncultivable areas like hills**

IV. Practice of herbal medication,

- **Herbal medications practices are based on frequent trial and error .on top of these most herbal medicines are toxic. So over dosage may result in toxicity.**

V. Lack of information on

Cond’

- **To decrease toxic plant hazards the following should be taken into consideration**
  - **Planned grazing during periods of high hazard,**
  - **Adequate fencing and weed control using herbicides,**
  - **Grazing least susceptible stock**
  - **Providing proper nutrition and water to minimize risks**

Cond’

¬ **Classification of phytotoxic plants.**

- Cynide poisoning (HCN / prussic acid)
- Nitrate poisoning
- Oxalate poisoning
- Plants causing photosensitivity
- Teratogenic plants

Cyanogenic plants poisoning (cyanide poisoning)

- **plants which contain hydrocyanic acid (prussic acid (HCN) or cyanogenic glycosides.**
- **one of the most common plant poisoning**
- **Starved and underfed animals are more prone for poisoning.**
- ***Species Affected:***
- **all species can be affected; *ruminants seem* to be affected more than monogastrics. Why?**
- **bacteria release HCN in ruminants, whereas monogastric animals (pigs and horses) are less susceptible due to destruction of the HCN by gastric acid.**

Cond’

- **Source of poising = ingestion of**
  - **sorghum (*Sorghum vulgare*)**
  - **Sudan grass (*Sorghum sudanesis)***
  - **Johnson grass*(sorghum halepense)***
  - **Sugarcane leaves/tops**
  - Hydrogen cyanide (HCN) is formed when the glycosides are hydrolyzed by enzymes (β-glycosideases) in plants or by rumen microorganisms:

HCN is concentrated in immature and seeds of the plant and the concentration decreases as the plants ages.

- **The plant material containing more than *20mg of HCN*/100gm is**

)

cond’

Scientific Name: *Sorghum vulgare*, **Common Name(s)**: *Sorghum (E), Mashila (Amharic)*

Sorghum sudanensis,
(Sudan grass)

Sorghum halepense,
(Johnson grass)

Cond’

- **The HCN or glycoside content of the plant is affected**

***1.* Nitrate level in the soil=**

- **High level of nitrogen and low phosphorus increase HCN content of the plant.**

2. Use of fertilizers and herbicides :

Nitrate fertilizers or herbicides like 2, 4, D enhance HCN content of the plant.

***3.* Drought, frosting, wilting,**

Cond’

4. Re-growth***:*** **re-growth sorghums accumulates high concentration of cyanide (30-40 heads of plants may kill 5-7 animals)**

5. **Age of plants –Young, green plants have the highest cyanide potential but this drops after pollination occurs and the seed sets**

6. Drying of the plants materials :reduce much of the

Cond’

- Toxicokinetics

- **HCN is rapidly absorbed from GIT after ingestion and from lungs through inhalation**
- **Detoxify into nontoxic metabolites (thiocyanate) in the liver by rhodanase enzyme system**
- **eliminated through urine and lungs(giving bitter almonds smell to the exhaled air)**

Mechanism of toxicity

- Cyanide combines with the cytochrome oxidase enzyme system blocking electron transport and energy production.
- absorbed it reacts with ferric iron (+3) in cytochrome oxidase in the mithochondria which halts cellular respiration.
- Oxyhemoglobin cannot release oxygen for electron transport in the cytochrome system since the cyanide – cytochrome oxidase will not function in electron transport.
- So oxygen cannot be utilized.
- Organs sensitive to O2 like the brain, heart, severely affected.

Cond’

- **Clinical signs**
- As cyanide is a potent, rapidly acting compound.
- Animals are usually found dead instantaneously. Initially there is excitement and generalized muscle tremor, animals jump, gasp for breath, and may have clonic convulsion due to anoxia.
- The pupils are dilated, mucous membrane are bright

- **Post-mortem Findings:**
  - **Bright red blood**
  - **epicardial haemorrhages,**
  - **"bitter almond" odour to rumen contents. Congestion and/or haemorrhage of abomasums, small intestine trachea and lungs.**
- **Diagnosis: - history of grazing the potential plant, clinical signs bright red colour of the mucous mm, post-mortem lesions, detection of HCN in a sample (feed, or stomach or rumen**

Cond’

- Dx. Any disease that induces sudden death may confuse with cyanogenic poisoning. *Anthrax, blackleg, bloat, hypomagnesemia, nitrite poisoning, fluoroacetate poisoning, lighting strike*.

poisoning with plant containing Nitrate/nitrite

- primary nutrient form of nitrogen in most soils
- Normal constituent of plants.
- In ruminant animals nitrate is converted to nitrite by bacteria in the rumen. Intern Nitrite is reduced to ammonia (NH_4) (when nitrate breakdown system is in balance no surplus accumulation of nitrites

Nitrate Reductase Nitrite Ammonia

protein

Blood urine

Cond’

- ***Nitrate poisoning*** **occurs when the nitrite level in the rumen exceeds the capacity of the microbes to convert it to ammonia. So ruminants are at higher risk.**

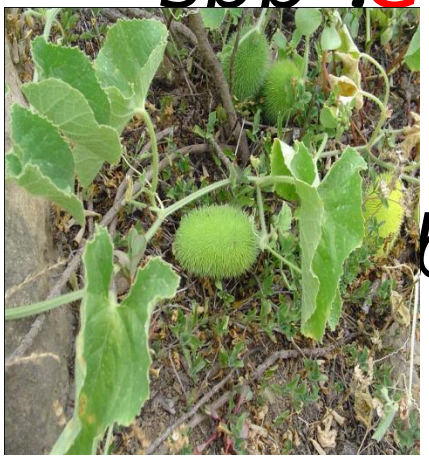
- **monogastric convert nitrate to nitrite in the intestine, closer to the end of the digestive tract, where there is less opportunity for the nitrites to be absorbed by the blood.**

- **this difference in the site of conversion that makes nitrate**

Cond’

- **Source**: *consumption of large amount*

oat hay, sorghum, corn, Sudan grass Amaranthus spp. (**“Aluma’’ A) , *Datura* spp (astenagir)** *solanium spp .Cucurbita, Rumx*



- *Amaranthus* *S.leagnofolium*

Toxicokinetics

Cond.

- rumen flora reduces nitrate to the much more toxic nitrite which normally is converted to ammonia and further utilized by the microorganisms.

- Nitrite is absorbed into the blood when the intake of nitrates and the production of nitrite exceed **Mechanism of toxicity**

- **nitrite is absorbed through the rumen wall into the bloodstream combine with haemoglobin methaemoglobin.**
- **When enough haemoglobin is converted to methaemoglobin the animal begins to suffer from oxygen starvation.**

Cond’

- **Clinical signs**
  - are **apparent when 40% of haemoglobin is changed into met- Hb**
  - **death occurs when 80% of the Hb is changed to met-Hb.**
  - **Nitrite poisoning is characterized by dyspnoea, gasping, rapid respiration, salivation and diarrhoea, colic, rapid but weak pulse, progressive development of cyanosis. Muscular weakness, ataxia, recumbency, convulsion**

Cond’

- **Post-mortem Findings:**
  - **Post mortem Findings are typical of met-Hb formation (dark brown blood with staining of tissues.**
  - **Mucous membranes are often cyanotic**
- **Diagnosis**
  - **history, clinical signs, laboratory confirmation of rumen nitrate/nitrite level, plasma**

cond’

- **Treatment**
  - Remove the **source**
  - **Therapy is directed toward conversion of met-Hb back to Hb**
  - **4% methylene blue solution i.v. at a dose of 4 to 15 mg/kg depending on the severity of toxicosis.**
  - **This drug is reduced in blood and body tissues to leucomethylene blue by another reductase enzyme.**
  - **The leucomethylene blue reduces met-Hb to Hb very rapidly.**
  - **Ruminal lavage with cold water**
  - **large oral doses of antibiotics such as penicillin to decrease microorganisms will help lessen the reduction of nitrate to nitrite**

Oxalate poisoning

- **Oxalic acid is an organic *dicarboxylic acid* (COOH-COOH),**
- **readily form insoluble salt with cation like calcium, magnesium but**
- **form soluble salt with sodium, potassium, and ammonium in water and poisonous for livestock.**
- **Insoluble oxalates passed through the digestive tract.**
- **Soluble oxalates may inter to the**

• cond

sources

Common sources of oxalates to livestock are plants which contain large amount of soluble oxalates (>10%): *rumex spp*., *oxalis spp*., *chenopodium spp*. *Beta vulgaris.* Oxalate content is highest in the leaves followed by the seeds with the lowest levels in the stems.

Cond’

Rumex

Chenopodium

Beta vulgaris
(Sugar beet)

Cond’

- ***Mechanism of action***

- **When ruminants consume oxalates, three consequences are possible:**
- **may be destroyed by rumen**
- **combine with free calcium in the rumen and be excreted in the faeces**
- **Be absorbed in the blood stream, to affect tissue and serum calcium,**
- **Oxalates are able to combine**

Cond’

- **results in a functional *hypocalcaemia manifested by tetany***
- **Oxalates may also crystallize in the vasculature and infiltrate vessels wall causing vascular necrosis and haemorrhage**
- **Insoluble calcium oxalate crystals cause renal tubular blockage and necrosis due to lodging calcium oxalate crystals in kidney tubules leading to anuria, uraemia leading**

Cond’

- **Clinical signs**
  - **Clinical signs may appear within 2-6 hours after ingestion of oxalate containing plants.**
  - **Slight to moderate colic, depression (dullness), muscular weakness**
  - **Irregular gait and head droops downward.**
  - **The animal may collapse and the**

Cond’

- **Diagnosis**
- **based on history, clinical signs and necropsy lesions**
- **(postmortem findings)**
- **Ascitis (hydrothorax), pale and swollen kidney confirmed by the finding of oxalate crystals in kidney**
- **Chemical analysis of blood revealing –*hypocalcaemia, h***
- **Low calcium *yperphosphatemia*in blood**
- **Increased phosphate level**

Cond’

- **Treatment**

- **Supply calcium and aid in elimination of the calcium oxalate**
- **Calcium borogluconate = IV may provide temporary relief but curative. (50-100 ml in sheep, 500 ml in cows, IV or SC)**
- **Providing di-calcium phosphate.**
- **saline –glucose solutions to produce diurisis**.

Poisoning by plant alkaloids

- **Different plants contain different alkaloids**
- **all have few properties in common**
- **Contain nitrogen in different forms**
- **act with different acid to form salts**
- **Bitter in taste**

cond’

I. Plants with Tropine alkaloids

- source

- Datura Stramonium (Jimsonweed, Thorn apple) = Astenagir, Badma Tebaki , Benji .commonly found in waste places
- Species Affected: Potentially all, cattle, sheep and goats are less sensitive than horses and poultry

Cond’

- **Target Organ(s)**: Nervous system
- Mechanism(s) of Toxic Action: Anticholinergic agent
- **Clinical Signs**: Restlessness, irritability, weakness, tachycardia, marked mydriasis, photophobia, dryness of the mucous membranes, and constipation. In severe cases, incoordination.
- **Post–mortem Findings**: Non–specific
- **Treatment**:
- Parasympathomimetics such as physostigmine are antidotal.
- Activated charcoal .
- Symptomatic and supportive

Cond’

II. Plants with Quinolizidine alkaloids

- Source: *Lupinus Spp* (Lupine, Blue bonnet)
- **Spp affected** : sheep & cattle
- **Target Organ(s)**: Nervous system
- **Toxic Action** are characterized

o –Lupinosis (a chronic liver disease): is due to a fungus infesting lupine stubble.

o – acute neurologic disease

Cond’

- **Clinical Signs:**
  - Sheep: Nervousness, depression, stiffness and reluctance to move, dyspnea, muscle twitching, loss of muscular control, convulsions, coma and death.
  - **Cattle**: Lupine is teratogenic if ingested between days 40 and 70 of pregnancy. Causes a skeletal malformation termed ‘crooked calf".
- **Post–mortem Findings**: Aside from the teratogenic effect, there are no characteristic gross or histological findings.
- **Treatment**: None

III.Plants With Pyridine Alkaloids

- Source: **Nicotiana Spp**

⎫ *N.attenuata*= wild tobacco

⎫ *N.trigonophylla*= wild tobacco

⎫ *N.tabaccum* =cultivated tobacco

⎫ *N.glauca*=tree tobacco

- active ingredient: **Nicotin**
- **Species Affected**: Potentially all
- **Target Organ(s)**: Nervous system, fetus

Cond’

- **Clinical Signs**: Excitement, shaking and twitching, staggering, weakness, and prostration followed by coma, paralysis and death.
- **Teratogenic Effect**: Swine; deformed limbs
- **Post-mortem Findings**: Non-specific
- **Treatment**: Symptomatic and supportive

Cond’

- Treatment =
  - no effective treatment
  - cottonseed products should be removed from the diet immediately.
  - A high intake of protein, calcium hydroxide, or iron salts appears to be protective in cattle

Plants causing photosensitivity

- **Photosensitivity is a condition in which animals become hypersensitive to solar rays in the presence of photo dynamic substances in the peripheral circulation or skin.**

Photo dynamic substances ⟷ ***UV light*** *(280–290nm)* **high energy com.**

- **forward and back ward reactions equally take place that means the high energy can return back to the ground state. energy will be releases in the process**
- **this energy can damage the epithelial cell membrane and leads for the formation of radicals. Then superoxide is formed which**

Photosensitization

- In cattle and horses, commonly will only affect the light colored hair and skin regions

Signs

- The skin becomes red, weepy and swollen.
- Swelling causes the ears to droop and eyelids to close.
- • There may be swelling under the jaws.
- • The animal may have difficulty breathing when there is extensive swelling around the nostrils and throat.

Signs

- • In the most severe cases the surface skin may
- crack, die and turn black. This dead skin may
- slough off.
- •There is intense irritation and pain. Animals will
- be agitated, scratch and rub against fixed
- objects, shake their head, seek shade and lose
- their appetite.
- Affected cattle will have a sharp drop in milk
- production.
- Cows with their udder affected will often kick at
- their belly and seek relief by standing in a dam

This ewe is suffering from photosensitisation

Diagnosis

- The location and appearance of skin damage and shade-seeking behaviour is characteristic of photosensitisation.
- The condition is diagnosed on the basis of clinical signs and access to toxic plants.

- Blood tests for liver function and post-mortem examination confirm photosensitisation due to liver

Treatment

First aid methods are aimed at removing the dietary cause and protecting from sunlight.

- Remove stock from the paddock where the trouble is occurring.
- Ideally, put affected stock in a darkened shed.
- Provide stock with water and cereal hay or lower quality pasture hay with no green colour.
- Anti-histamin
- Antibiotics

Cond’

- There are two types of photosensitivity

¬ ***Primary photosensitivity-*** due to plants with phytodynamic substances. *Hypericum and Fagopyrum* are the plants which contain hyperacin and fagopyrin which are the active principles respectively.

Black skinned animals and animals under shade do not suffer from the effect. Because the solar ray cannot penetrate

- Animals with light skin / light paches when exposed to bright sun light develop a syndrome of dermatitis. In sheep the ear, eyelid and perineum are swollen and also called big head. In cattle mostly the sides and back region are affected.

Cont...

- ***Secondary photosensitivity (hepatogenous)*** **–** ingestion of some substances lead to liver damage, obstructs the bile duct. So substances that are degraded in the liver or normally excreted in the bile remain in the circulation and reach in the periphery and initiate photosensitivity.

- Here there will be two syndromes

  Depression, anorexia, diarrhea and icterus, all related to liver damage and obstruction to the bile duct.

  The second is similar to the primary photosensitivity like dermatitis (cutaneous lesion). The most common secondary photosensitivity is phylloerythrin (chllorophill) degradiation in the bile. From the plants which cause this type *Lanthana camara* is the most important. It contains a chemical called Lantadine that damage the liver cells. So substances like

Hypericum

Fagopyrum

Lantana camara

Other poisoning plants

- Plants contain Ricin toxins
- Source; Ricinus Communis(Castor bean)= Gulo
- **Species Affected**: Potentially all
- **Target Organ(s)**: G.I. tract
- **Active Principle(s)**:
  - protein **Ricin**, one of the most toxic substances known. It is localized in the seeds.
  - Another toxic component is ricinin which causes seizures.

Recinus cominiu

Cond’

- **Mechanism(s) of Toxic Action**:
  - Ricin inhibits protein synthesis by damaging the 28s ribosomal subunit.
- **Clinical Signs**: severe gastroenteritis
- **Post–mortem Findings**: As for clinical Signs
- **Treatment**: Symptomatic and supportive

Cond’

- Cotton plant(Gossypol) poisoning

- **Source**: major toxic ingredient in the cotton plant (*Gossypium* spp)
- spp affected: All animals are susceptible, but monogastrics, immature ruminants, and poultry appear to be affected most frequently.
- **Target organs**: reproductive system, Liver, Hematologic tissues
- Active ingredient: gossypol

Gossypum(cotton)

– **Mechanisms of Toxicity** Cond’

gossypol causes gradual destruction of cardiac musculature.

– **Pulmonary effects** and **chronic dyspnea** are most likely secondary to cardiotoxicity.

– **Hepatotoxicity** can be a primary effect or secondary to congestive heart failure.

– **Hematologic effects** include increased RBC fragility, reduced oxygen–carrying capacity of blood.

Cond’

- **Reproductive effects**
  - reduced libido with decreased spermatogenesis
  - irregular cycling, luteolytic disruption of pregnancy,and direct embryotoxicity in females.
  - Green discoloration of egg yolks and decreased egg hatchability have been reported in poultry

Cond’

- **Clinical Findings**
- Signs of prolonged excess gossypol exposure in many animals are weight loss,weakness, anorexia, and increased susceptibility to stress.
- **Lesions:**
- **red-tinged fluid with fibrin clumps are frequently found in abdominal, thoracic, and pericardial cavities.**
- **Icterus and an enlarged, flabby, pale, streaked, and mottled heart with dilated ventricles and**

Cond’

- **Diagnosis: ba**sed on the following:

- **history of dietary exposure to cottonseed meal**
- **sudden death or chronic dyspnea, affecting multiple animals within a group;**
- **lesions consistent with the reported syndrome and associated cardiomyopathy and hepatopathy, with increased amounts of fluids in various body**

cond

- no response to antibiotic therapy; and
- Free gossypol at >100 mg/kg (100 ppm) of feed in the diet of pigs or young ruminants supports a presumptive diagnosis.
- Gossypol can accumulate in liver and kidney, which are additional specimens for postmortem analyses.
- In sheep, gossypol concentrations (free or bound) >10 ppm in the kidney and >20 ppm in the liver

ϖTOXICITY OF AGRO-CHEMICALS

- pesticides are any chemical or physical or biological agents that could kill or destroy unwanted plant or animal pests
- used to increase agricultural products.
- grouped as pesticides (insecticides, fungicides, herbicides rodenticides

Cond’

– **Insecticides**

- chemicals that are used to kill insects

broadly grouped as

- organophosphate
- Carbamates
- triazepentadienes (formamidines, e.g. amitraz),
- Organochlorines
- pyrethrins and pyrethroids, Rotenone

Cond’

Organophosphates and carbamates

- (ops) and (cms) commonly used as insecticides or pesticides in agriculture,
- used as parasiticides in veterinary medicine.
- Both types of chemicals produce their toxicity by inhibition of acetylcholinesterase (ACHE)

Cond’

- **Toxicokinetics**

- **entry into the body mainly through**
- **Oral (with contaminated feed/food)**
- **Dermal (when used as ectoparasiticides in the form of dust, dip, or oily solution).**

OPIs	**CmIs**
Diazinon	carbaryl
Sarin	dimetan
Coumaphos	Isolan
Coumapho	mesurol
Soman	Pyrolan
chlorothion	Zectran
Phorate	carbofuran
Malathion	
Dichlorvos	

Cond’

- **After absorption the chemical distributed in tissue throughout the body.**
- **OP insecticides may follow either activation or detoxification, or both.**
- **Activation implies that the metabolite is more toxic than the parent compound(, conversion of**

Cond’

- detoxification
- **Metabolite is less toxic than the parent compound**
- **Unlike OPs, most of CMs are metabolized to less toxic or non-toxic metabolites**
- **but some of the metabolites of CMs are quite toxic. e.g metabolites of carbofuran (3-hydroxycarbofuran and 3-ketocarbofuran**)
- **Activation and detoxification**

Cond’

- **Only few metabolites are excreted in the urine**
- **Residues of some OPs and CMs can also be detected in the feces, saliva, and milk.**

- ***Mechanism of Action***

- **OP and CM insecticides share common mode of insecticidal and toxicological action**
- **inhibit the enzyme AChE (an enzyme responsible for the destruction of the neurotransmitter**

Cond’

- **Clinical signs**
- **are due to over stimulation of the parasympathetic nervous system**
- **Most animal poisoning are manifested by**
- **vomiting, abdominal and chest pain, salivation, sweating, lacrimation, urination, diarrhea (SSLUD), lung edema, cyanosis and dyspnea**

Cond’

- **post mortem Lesions**

some of the common lesions are

- **haemoregic gastro-enterititis**
- **Pulmonary edema**
- **Degenerative changes in liver and kidneys**

- **Diagnosis**

- **history**
- **clinical**
- **post-mortem findings.**
- **It can be confirmed by determining the level of inhibition of AChE activity in blood from a live animal**

Cond’

- **Treatment**
  - **Gastric lavage**
  - **To stop further absorption of insecticides activated charcoal =dose 0.5 kg for sheep, 0.9kg for cattle**
  - **Washed with water if they are exposed to insecticides dermally.**

Cond’

- **Intravenous (IV) fluid therapy**
- **Atropine sulfate and /or pralidoxime (as Antidotal treatment)**
- **given at the dose of 0.5mg/kg IV for ruminants**
- **0. 2mg/kg iv for horse and small ruminant**
- **2 mg /kg iv for dogs.**
- **repeated at an interval of every hour until all hyper-secretary**

cond’

- **Organochlorine Insecticide**
  - known as chlorinated hydrocarbons
  - used as contact insecticide and ectoparasiticides
- are grouped into four classes.

1. Dichlorodiphenylethane (DDT, dicofol, perthane , methoxychlor and others)
2. Chlorinated cyclodienes (Aldrien, dieldrin, endrin, chlordane,endosulfan)
3. Hexachlorocyclohexane (lindane)
4. Miscellaneous groups (kepone,mirex, chlordecone)

Cond’

- ***Sources of poisoning***
  - Ingestion of contaminated feed
  - Inhalation or absorption from the skin during topical application
- ***Toxicokinetics***
  - **Ocl insecticides are water insoluble**
  - **Soluble in oils and organic solvents**

Cond’

- **Rapidly absorbed from the oily preparation through intact skin**
- **All the compounds penetrate easily through the skin and absorbed in the blood stream.**
- **Comes to liver , and degraded here to non toxic metabolites= come to intestine and get excreted through faeces**

cond,

- ***Mechanism of toxicity***
- They are neurotoxins.
- They interfere with normal function of the nerve membrane, Generally

1. Reducing the potassium transport through pores
2. Inactivating Na channel closure
3. Inhibiting NA^{+}-K^{+} and Ca^{2+}-Mg^{2+}ATPases

Cond’

- **Clinical findings**

- Toxicity causes initial stimulation of CNS followed by depression and death due respiratory failure.
- Generally the symptoms of poisoning due to CHC can be grouped into three

1. Behavioral symptoms (anxiety, aggressiveness, jumping over unseen object, madness
2. Neurological symptoms (hypersensitivity to external stimuli, girding of the teeth, spasm and twitching of the fore and hind quarter, hyperthermia)

Cond’

- **Post-mortem lesions**
  - **no specific symptoms in the nervous system of the affected animal.**
- **Hepatitis and nephrosis or necrosis of the liver may be observed**.
- Diagnosis
  - **Based on history, clinical and postmortem findings as well as analysis of feed and/or biological**

cond’

- Differential diagnosis
  - **Salt poisoning (absence hyperthermia, history)**
  - **Strychnine poisoning (absence of behavioral changes)**
  - **Lead poisoning (no abnormal posture)**

Cond’

- **Treatment**

- There is no specific antidote; treatment is only symptomatic and supportive.
- Remove the source of poisoning
- Anticonvulsants like barbiturate are helpful to control convulsion
- Activated charcoal(1-2kg /day for 2 weeks)may reduce the absorption of unabsorbed toxin
- Phenobarbital10mg/kg/day- to promote faster metabolism and excretion
- Small dose of atropine sulphate = to control the parasympathetic signs

Rodenticides

- agents which destroy the rodent pests (black rats -*Rattus rattus* and mice -*Mus musculus*),
- consume substantial quantity of pre-harvest, postharvest or stored grains
- also render the foodstuff unfit for consumption by soiling and contaminating with urine, faeces and pathogenic micro-organisms which are capable of infecting

Cond’

- Some of the most commonly employed rodenticides are
  - **α-Naphthyl thiourea (ANTU),**
  - **warfarins,**
  - **zinc phosphide,**
  - **fluoroacetate,**
  - **red squill and** others.

- **Aphla-naphthyl thiourea (ANTU)**

- **ANTU is odourless, colourless, and crystalline or powder**
- **rodenticide act on rats and mice .**
- **Dogs and cats can be affected.**

♣ ***Source of poisoning***

- **Accidental ingestion of baits prepared for rats**

- **Toxicity**
  - **Rats are highly susceptible, dogs, cats and pigs are more susceptible than other domestic animals.**
- **Mechanism of toxicity**
  - **ANTU interferes with uptake of O_2 from the pulmonary alveoli by producing extensive oedema of the lung.**
  - **This occurs due to *increased capillary permeability* and passage of fluid into airways. This leads to the formation of froth which**

- **Clinical signs**
  - **ANTU poisoning include vomiting, salivation, dyspnoea, tachycardia, anorexia, in-coordination, coughing, coma, convulsion and death.**
- **Postmortem findings**
  - **Cyanosis, dark coloured arterial blood**
  - **heavy and oedematous lung, presence of blood tinged fluid and froth in the bronchi, hydrothorax, hyperaemic**

Cond’

- **Diagnosis**
  - **History, clinical signs and postmortem findings. Gastric content and the vomitus are the most suitable specimens for analysis.**
- *DDX*
  - Urea poisoning, organophosphorus poisoning
- Treatment
  - Emetics or gastric lavage, sedatives like barbiturates, oxygen supplement
  - Competitive ANTU antagonists (1-ethyl-1-phenyl thiourea)

Cond’

- Warfarin
  - **Isolated from mouldy sweet clover. The warfarins are readily inactivated by the liver cytochrome system**
- *Source of poisoning*
  - **Ingestion of residue of rodenticide or baits intended for rodents**
  - **Pigs, dogs, and cats are often ingest warfarin poisoned rats or**

Cond’

- *Mechanism of toxicity*
  - interferes with normal function of vitamin K and causes coagulation defect.
- **Clinical signs**
  - After ingestion of warfarin the animal may show signs of bleeding around the gum, blood discharge through body orifices, haematoma under the skin and at joints, dyspnoea, weakness, shock and death.
- *PM*
  - Massive internal haemorrhage, blood in GIT, thorax, joints and pericardium,

Cond’

- **Diagnosis**
- History, clinical signs and postmortem findings. Laboratory evaluation of clotting and clotting factors.
- ***Treatment***
- Provide clotting factors by whole blood or plasma at the rate of 20ml/kg or 9ml/kg, respectively. Injection of viamin K, 5mg/kg for dogs and cats for three days,For large animals the dose is 0.5-

Cond’

•Zinc Phosphide (Zn_3P_2)

- *Source of poisoning*
- Ingestion of baits prepared for rats and malicious poisoning particularly to kill dogs or cats.
- *Mechanism of toxicity*
- irritant to the gut & produce severe gastroenteritis this may induce vomiting. The hydrolytic reaction of zinc phosphide with GIT content librates phosphine
- Zn_3P_2 H_2O $Zn^{2+} + PH_3$
- Zinc phosphide Zinc phosphine

- which is responsible for the wide spread cellular toxicity with necrosis of the GIT and

Cond’

- *Clinical signs*
- Anorexia, increase in rate and depth of respiration abdominal pain, bloat (ruminants), ataxia, weakness, dyspnoea, gasping, convulsion, coma and death in 4-48 hrs.
- *Postmortem*
- Pulmonary congestion and oedema, congestion of the liver and kidney, gastroenteritis,
- *Diagnosis*
- History, clinical signs and postmortem findings. Detection of zinc phosphide in stomach content.
- *Treatment*

⎫ There is no specific antidote but supportive and /or symptomatic may be given

⎫ Gastric lavage

⎫ Calcium borogluconate helpful

Herbicides

- **any compound that have the potential of either killing or damaging unwanted plants or weeds**
- **different herbicides exist**
- **most of them having relatively low toxicity (>1g/kg) .**
- **Mostly used herbicides**

Dipyridinium (Paraquat, Diquat), Phenoxyacetic acid herbicides (2,4-D; 2,4,5-T; Silvex)

Cond’

- Dipyridinium compounds

- **Sources of poisoning**

- Due to ingestion of recently treated plant, or malicious poisoning

- **Mechanism of toxicity**

- **irritant agents which cause ulceration and necrosis of the skin and mucous membrane.**

- **These compounds easily accept electron become free radicals and reacted with fatty acids in the membrane. Then it induces lipid peroxidation. These reactions lead**

Cond’

- ***Clinical signs***

- **Clinical signs are seen after three days of exposure including emesis, anorexia, abdominal pain, dyspnea, jaundice, and CNS depression.**
- **If the affected animals survive for several days, the animal may exhibit dehydration, pallor or cyanotic mucous membrane and tachycardia and uraemia**

Cond

- **Post-mortem** *lesions*
- Pulmonary congestion, oedema, and haemorrhage intra-alveolar fibrosis, ulceration of buccal and pharyngeal tissue, congested liver, kidney, and spleen.
- **Diagnosis**
- History of any exposure
- Clinical symptoms
- Post mortem lesions
- *Differential diagnosis*
- Pneumonia, ANTU poisoning (more acute and fatal in nature)

Cond’

- *Treatment*
  - **There is no specific treatment but supportive therapies are helpful.**
  - **Avoid further absorption by emetics, gastric lavage, oral adsorbants (like activated charcoal)**
  - **Facilitate excretion by giving saline purgatives**
  - **anti-acids to reduce gastric irritation, fluid therapy, vitamin A, C and E are helpful.**
  - **Tranquilizers and sedatives are**

Toxic metals

- **Copper (CU) poisoning**

- **CU an essential component of the animal system**

Plays an important role in

- **Heamatopoesis**
- **Phospholipd formation**

Cond’

- Cu poisoning encounter through out the world
- Sheep are more susceptible than other species
- Monogastric are quite insensitive
- Acute toxicity have been seen after accidental administration of excessive amounts of soluble copper salts employed in agriculture and Veterinary practices .
- Chronic toxicity: have been seen after accidental administration of moderate amounts of Cu for prolonged time.

Cond’

- **Source of CU:**
- **fungicides, coins, wire , Cu + salts**

Toxicokinetics of Cu:

after oral intake Cu absorbed from the intestine

blood stream & distributed to the

Liver, kidneys brain……

Cond,

- **If Cu beyond the limit**
- **Saturated the cells (hepatocytes), inhibit metabolic function enzymes**
- **Leads to liver necrosis**
- **The necrosis liver release large amount of Cu into blood stream, enters to erytrocytes**
- **Erytrocytes canot release the cu easily**
- **by the action of Cu^{+2}, (Fe2+) Hb**

cond

Clinical symptoms of CU poisoning	
acute	chronic
nausea	< ruminal fermentation
Vomition	Ruminal stasis
salivation	Impairment of liver
Abdominal pain	thirst
dehydration	Diarrhea
Shock & collapse	Icterus
green colored	Hb-emia

Cond’

- **Lesion:**
  - **acute toxicity**

- **Sever gastroenteritis**
- **blood coagulation at the time of death**
- **icterus**

  - **chronic toxicity**

- **generalized icterus**
- **enlarged & yellow colored liver**
- **brownish bile**
- **Swollen kidneys**
- **Wine colored urine**
- **black and enlarged spleen**

Cond’

- **Diagnosis of Cu posoning**

- **blood level often rises to 5-20µg/ml as compared with normal levels of 1µg/ml of Cu con.**
- **150ppm to800 ppm in liver**
- **15ppm in kidneys indicate chronic toxicity**
- **History: access to Cu compounds**

- **Treatment:** Cond’

- **Ammonium Molybdate_ 100mg/kg pos/day**
- **Sodium thiosulphate= 300 to 1000 mg/kg pos/day**
- **D-penicillamine = 10 to 15 mg/kg pos twice daily**

- **prevention and control of cu toxicity**

- **regulate the amount of CU by molybdeum and sulfur in the diet**
- **Addition of Zn decreased Cu Absorption**

Mineral toxicities
Arsenic poisoning

- Forms of arsenic can be organic or inorganic.
- The inorganic form has the most toxicity.
- Many inorganic forms of arsenic come from industrial and agricultural waste.
- Our discussion will focus on the inorganic form of arsenic.

Cont...

- Found as As+3 or As+5
  - The most common As+3 (arsenic trioxide) inorganic forms are sodium arsenite, and arsenic trichloride.
  - The most common As+5(arsenic pentoxide) inorganic forms are lead arsenate, and calcium arsenate.
  - The lethal oral dose of arsenic trioxide (sodium arsenite) in most species is from 1-

Cond’

Toxicokinetics of As

- Exposure is through inhalation, drinking water, and soil
- Almost complete absorption from G.I. Tract
- After absorption As distributed through out the body accumulate in the liver & kidneys
- If intakes continues tend to

Cond’

- **Mechanism of action**
- **Trivalent compounds most toxic than pentavalent**
- **blocks enzymes activity(oxidative phosphorylation) slowing TCA cycle**
- **Increase permeability of vessels,**

cond’

- Clinical signs

Per-acute poisoning (last within few seconds to few minutes)

- Collapse of blood circulation
- dilatation of vessels(capillaries)= transudation of plasma & loss of blood= hypovolemic shock
- Vomiting and diarrhea

Cond’

- Acute poisoning:

- **stomach pain**
- **vomiting**
- **dryness of the throat**
- **Thirst**
- **convulsions**
- **Death due to circulatory collapse**

Cond’

- Chronic

- **profuse diarrhea**
- **In appetence**
- **dehydration**
- **change in skin color**
- **Skin cancer**
- **lung , kidneys bladder cancer**

Cond’

- Lesions:

- **Inflammation and redness of GIT**
- **Foul smelling of stomach content**
- **Rupture of blood vessels**
- **Fatty degeneration of parenchymatic organs**
- **Necrosis of skins(Skin exposure)**

Cond’

- **Diagnosis:**

- **History**
- **Clinical signs**
- **Post-mortem findings**
- **Chemical examination = toxicity begins>3ppm in liver and kidneys**

Differential Dx.

- **lead poisoning(nervous signs absent due to arsenic poisoning**

Cond’

- Treatment:

- **Emesis**
- **Activated charcoal**
- **Fluid therapy**
- **Blood transfusion**

Dimercaprol=6mg/kg IM, tid for 2-3 days

- **Na thiosulphate** at 20-30 g in 300 mL of water pos in horses and cattle, one-fourth this dose in sheep and goats.

Cont...

- **Lead poisoning(Pb)**

- **Is heavy metal**
- **mostly Pb poisoning seen in dogs and cattle**
- **Pb poisoning some times referred to as *plumbism***
- ***Source:***

- **Inorganic sources: Metalic Pb or lead salts old Pb tubes, pipes**

Cond’

- Organic sources:

- **lead base paints**
- **automobile batteries**
- **lead gasoline or oils**
- **Lead arsenate pesticides**

- **Absorption and elimination**:

- Inorganic lead: toxic after ingestion
- Organic lead: toxic after skin contact, ingestion, inhalation
- Absorption is promoted by calcium, zinc and iron deficit
- Transported bound to erythrocytes (90 %)
- High deposition in tissues – first in liver, then redistributed to bones , kidneys, muscles and hair.

Cond’

- **Mechanism of action**

- **Pb poisoning inhibits membrane associated enzymes, leads to blood cell fragility(anemia) & renal tubular injury**
- **Interfere with CNS activity**

- **Clinical signs:**

Cond’

- **Associated with GIT and Nervous system**

- Acute lead poisoning -In yonger cattle, signs that appear within 24-48 hr of exposure include ataxia, blindness, and salivation, spastic twitching of eyelids, muscle tremors, and convulsions.
- Subacute lead poisoning, usually seen in sheep or older cattle, is characterized by anorexia, rumen stasis, colic, dullness, and transient constipation.
- Chronic lead poisoning, which is occasionally seen in cattle, may produce a syndrome that has many features in common with acute or subacute lead poisoning

GI abnormalities, including anorexia, colic, emesis, and diarrhea or constipation, may be seen in dogs.

Cond.

- **Lesion:**

- **oil or flakes of paint or battery may found in the stomach**
- **Gastroenterities**
- **Congestion of cerbral cortex**
- **Tubular necrosis**

• Diagnosis Cond’

- History
- clinical symptoms
- postmortem lesion
- laboratory analysis: if blood con. of Pb ranges from 0.25 ppm to 0.35 ppm= Pb poisoning is indicative
- haematological examination

Cond,

- Treatment:

- **Stabilization of sever clinical symptoms**
- **Elimination of lead from The GIT**
- **Calcium disodium edetate** (Ca-EDTA) is given IV or SC (110 mg/kg/day)
- **Thiamine (2-4 mg/kg/day SC)** alleviates clinical manifestations and reduces tissue deposition of lead.
- **Barbiturates or tranquilizers** may

Acid and base poisoning

Urea and ammonia posioning

- Urea used as an fertilizer and feed additive in ruminants
- In rumen urea hydrolysis by urease into micro-flora NH_3 & H_2O
- Ammonia released in rumen by bacterial microflora.
- In small amount used by microflora. In huge amounts causes immediate and strong alkalinization of rumen content

Cond’

CAUSES OF UREA POISONING

- Excess consumption of urea.
- Sudden introduction to high quantities of urea.
- Irregular consumption of urea.
- **Mechanism of action**

- **Urea hydrolysis in the rumen**

Production of NH3 depends on

- **Amount of urea ingested with feed / water**

Cond’

- Clinical signs

- fast or delayed depends on production of ammonia in the rumen & its absorption in the blood.

- weakness, restlessness, salivation, frothing at the mouth & nose, bloat, grinding of teeth, abdominal pain, marked jugular pulse, dyspnoea and twitching of eye lids

Cond,

- **Diagnosis**
  - **History of access to urea**
  - **Clinical signs**
  - **postmortem findings**
  - **Laboratory investigation(ruminal content)**
- **Differential diagnosis**
  - **Arsenic, lead poisoning, organophasphate, nitrate poisoning, and enterotoxamia**

Cond’

- **Treatment:**
- **No specific treatment**

- **Remove source of exposure**
- **Cold water administration**
- **5% acetic acid 0.5-1 lt for sheep, 4 l for cattle to lower the pH & to slowing the rate of hydrolysis of urea.**
- **trocarization or ruminotomy to**

Mycotoxins

- mycotoxins

⎫ secondary metabolites of toxogenic fungi

⎫ produce by fungi when grow on crops

grow well

♣ relative humidity > 70%

♣ moisture15% (10-33%)

♣ between 24-25 (4-35)dc

♣ produce by different fungal spp

Cond’

- Aflatoxins: toxic metabolites of toxogenic fungi
  - *Aspergillus flavus & A. parasiticus*
  - grow on grains and nut
  - B_1, B_2, G_1 & G_2 alfatxins are known in nature
  - which fluoresce blue & green under UV light are termed as B and G, respectively
  - In their toxicity potential
  - $B_1 > G_1 > B_2 > G_2$;
  - heat resistance
  - melting points for B_1, B_2, G_1 & G_2 are

269°c, 238°c,, 245°c, & 239°c, respectively

$B_1 > 100$ µg/kg in feed consider to be toxic to cattle

fungal growth on maize

Cond,

- **Mechanisms of toxicity**

- **majority AF bound to ruminal contents**
- **2.5% reaches the intestines and absorbed**
- **metabolized by a microsomal cytochrome p–450 dependent mixed function oxidase system in liver**
- **Excess products of AF interact with N–guanyl residue of nuclear DNA of hepatocytes to Inhibit**

–synthesis of DNA

–DA–dependent RNA polymerase activity

–mRNA synthesis &

protein synthesis by interfering with

Cond’

- All animal spp are affected including man
- Susceptiplity in decreasing order is
- Duckling > rabbit > turkey > chicken>cat> dogs> guinea pig> monkey> cattle> sheep

• Clinical signs: occurs in 3 forms

Acute, sub acute, chronic

- Acute: when high amount of the toxins is consumed with short period of time
- Sub acute: consumption of moderate dose of AF for several days or weeks
- Chronic: intake of low levels of AF for

Cond’

- Acute: sudden death within 72hrs
- anorexia, depresion, ataxia, dyspnoea,
  anemia ,tremors ,convulsios and death
- Sub acute: icterus, hypoprothrombinemia, haemorrhages & heamatomas
- Chronic: commonly occurs\ decrease in weight gain & productivity, icterus,

Cond,

- Postmortem lesion

- Pale liver,, firm and fibrosed
- Yellow kidneys
- Serous exudate in the body cavities
- Oedema and ascites of mesentery
- catarrhal enteritits
- Heamorrages in thoracic & peritoneal cavities

Cond,

- Diagnosis:

- history , clinical signs, laboratory analysis

Postmortem findings

DDX.

- rodenticide poisoning(warfarin)
- Cu poisoning
- Infectious hepatitis
- coal tar poisoning

Cond’

- Prevention and treatment
- withdrawal of contaminated feed
- Providing easily digestible low fat high protein feed
- Supportive therapy with multi Vit
- Use 0.5% hydrated Na calcium aluminosilicate as feed additive
- IV 5% dextrose
- Ocytetracycline(10 mg/kg)-im at 4–5 days interval to decrease hepatic damage----
- Activated charcol 6.7 mg/kg intraruminally30% w/v

Ergotism

- **causedd by two fungal spp.**
- ***Claviceps purpuria* and *Claviceps paspalis*.**

- ***source*: *Ergot is a parasitic fungi that attack the developing ov*ary of grasses , rice, wheat and of barley.**
- **Ergot contains a number of alkaloids toxins such as**

Ergotamine, ergometrine,&ergotoxin(ergocornine, ergocristine & ergocryptine)

.

- Occurs in two forms

1. gangrenous ergotism or chronic ergotism

2. nervous or convulsive ergotism (acute)

Chronic ergotisms: caused by *C. purpurea*

- **Disturbances in the vasomotor system**
- **Potent smooth muscle stimulants,**
- **Cause intense vasoconstriction,**

Cond’

- Clinical signs:

- **Initially reddening, swelling, coldness, loss of hair or wool and lack of sensation of the affected parts**
- **irregular gait , pain in the feet, slough off if animals consume a ration containing 0.3–0.5% ergot sclerotia for several weeks**

acute forms: caused by C.paspalis

- **Rare in animals, depends on injection and climate**

Cond’

- **Diagnosis:**
  - **history, clinical signs , laboratory investigation**
  - **Of grains and feed**
  - **Observation of sclerotia on grasses head grains or hay**
  - **Sloughing off of the hooves, feet or tail in in severe cases**

cond’

- **Postmortem lesions:**
  - **necrotic lesion: gangrene of the extremities’**
- **DDX**
  - **Rule out the infectious diseases, trauma, abscess, neoplasms, deficiency or excess of selenium poisoning**
  - **From other mycotoxicoses(*Fusarium* & *Aspergillus* spp**

Cond’

- Treatment: no specific antidote
- Withdrawal
- provide a warm, clean and stress free environment
- Symptomatic treatment
- Magnesium sulphate
- broad spectrum anti bacterial for necrotic lesion & to prevent secondary bacterial infections.

Drug toxicity

- Possible mild symptoms of acute lithium toxicity include diarrhea, dizziness, nausea, stomach pains, vomiting, and weakness. More severe symptoms can include hand tremors, ataxia, muscle twitches, slurred speech, nystagmus, seizures, coma and, in rare cases, heart problems. Chronic lithium toxicity displays different symptoms, including slurred speech, tremors, and increased reflexes.

Diagnosis

- Acute toxicity is more easily diagnosed, as the symptoms will follow the one-time administration of a medication. Blood tests can also screen for levels of the medication

Cont...

- Chronic toxicity is harder to diagnose. Stopping the medication and then "re-challenging" it, later on, is one method of testing whether the symptoms are caused by the medication. This method can be problematic, however, if the medication is essential and doesn't have an equivalent substitute.

Treatment

- There are several ways in which drug toxicity may be treated. If the toxicity is the result of an acute overdose, then a person may undergo stomach pumping to remove drugs that have not yet been absorbed. Activated charcoal may be given to bind the drugs and prevent them from being absorbed into the blood (instead, it is eliminated from the body through stool). Other medication may also be given as an antidote.

zootoxins

- **Produce by lower animals**
- **Snakes**
- **Fish**
- **Toads**
- **Spiders**
- **Scorpions**
- **bees**
- **Wasps**
- **ticks**

Cond,

- Venom: poisons or toxin secreted by specialized glands of an animal
- Venomous animals: animals that producing a poison(Venom)
- composition of venom:

Proteins (Polypeptides and enzymes)HMW 0r LMW. May be Amines, lipids, steroids, aminopolysaccharides, quinones, glycosides ...

Cond’

Action and toxicity of venom depends on

- Species of the snake/ venomous animals
- Route of entry into the body
- Location/site the venom injected
- Absorption from the site of enter into the body
- Distribution
- Accumulation action at the receptors site
- Biotransformation

cond’

Snakes Venoms: produce by more than 3500

- complex mixtures of toxins
- amino acids, polypeptides, glycopeptides,Biogenic amines
- Certain cattions(K^{+},Na^{+}, Ca^{2+}, Mg^{2+}, Ni^{2+})
- Most of the snake venoms produce two type of toxins

  –Neurotoxicity(enzymatic proteins)

  –Cardiotoxicity or –haemotoxicity

Cond,

- **Venoms of snakes contain different factors such as**
- **Necrotizing**
- **Anticoagulant**
- **Coagulant**
- **Neurotoxic**
- **Haematotoxic**
- **Cardiotoxic factors**

Cond’

- **Clinical signs**
  - **Salivation**
  - **Asphyxia**
  - **Gasping convulsion**
  - **Regurgitation paralysis of tongue**
  - **death with in 2-4hrs**

cond’

- **Diagnosis**
  - Based on history of sudden death
  - Observation of the fang marks
  - Local swelling
  - Oozing of blood at the site of bite
  - cyanosis
- DDX:
  - blackleg, anthrax,botulinum, tick paralysis

cond

- Management of snake bite
  - **keep the animal undsturbed**
  - **Tight above the site of bite**
  - **Incise the local area of bite in the direction of blood vessel and infiltrate the are with 5% soap solution**
  - **Inject antivenin, antibiotics and antitoxins,Suportive treatment**

N.b. Do not use potasium permanganate

- Do not give extreme cold or hot treatment at the site of bite or incision

cobra

Koral snake

Moccasin snake

Rattle snake

Toads

- dogs and cats are exposed to toads' toxins
- toads' toxins are cardiotoxic glycosides
- Have effect on heart & smooth muscles
- they are bufogenins(bufotalin,, bufotenidin , bufotenin,bufoviridin)

clinical signs:

Salivation (foamy), vomiting, cardiac irregularities, collapse and death.

Cond’

- Diagnosis
  - history & clinical symptoms
- treatment:
  - Washing
  - Activating charcol
  - atropine sulfate iv
  - Corticosteroids
  - Propranol 0.2mg/kg to control cardiac irregularities

Bee venom

- Venom of bees is a complex mature of proteins, Non-ezymatic protein (apanin, melitin, hyaluronidase, kinins, formic acids….)
- Toxicity varies from individual to individual
- treatment

⎫ local application of weak solution of ammonia and sodium bicarbonate

⎫ Supportive therapy

Tick toxins

- ticks act as vectors of many diseases
- Cause paralysis in human animal du to neuroparalytic toxin
- sources
- ***Dermacenter andersoni (wood tick) bite***
- ***Ixodes holoycyclus bite***
- **toxins are produce by female ticks**

Cond’

- Clinical symptoms:

- Anorexia,lethargy, drooling of saliva, muscle weakness, in coordination, dehydration and complete ascending flacid paralysis (Hind limbs

Fore limbs chest muscles;

- Absence of eye and limbs touch reflexes
- Pupils dilate widely
- Death due to respiratory paralysis

Cond’

- **treatment**

- **administration of hyper immune serum**
- **Removal of ticks manualy or by using acaricides**

♣ **Control:**

- **Eradication of ticks from the animals & premises**

Fish poisoning

some of the common. fish poisonings

Name of fish	toxin	mechanism	signs
Shell fish	Saxitoxin	Inhibits inward current of Na+ across the axonal membrane	burning sensetion in lips, gums tongue pain in joints, generalized paralysis death due to respiratory failure
Puffer fish	Tetrodotoxin	alters neuronal membrane permeability to Na+ & K+	weakness, paresthesia around lips, tongue & throat salivation, hypertension, bradycardia, cyanosis flacid paralysis
Moray		Increase neural	Tingling of lips,