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Pesticides

Pesticides:- any substance or mixture of substance intended for preventing ,destroying or repelling of any pest .

Or

Pesticides:- any physical ,chemical or biological agent that may kill an undesirable plant or animal pest.

Pesticides are classified as their biological effect in to :-

1- Insecticides
2- Herbicides
3- Rodenticides
4- Fungicides and other

Mis use or extensive of pesticides are very toxic and causes many problems such as :- accumulation in the animal body occurrence of residues in food stuffs and their effect on human body. Residues in food as well as contact with it in the air ,water ,soil, plant and animal products (milk and meat).

The are two types of pesticides toxicity :-

1- Acute
2- Chronic

1- Insecticides:-

TYPES OF INSECTICIDES :-

A- Organophosphate Insecticides (anti Cholinestrase Insecticides) e.g. Dichlorvos , Diazinon , Malathion .

Organophosphorous (O.P) an organic ester of phosphoric acid ,O.P. compound have been used as pesticides and developed as warfare nerve gas agents such as (Sarin , Soman), all O.P. compound are poisonous and dangerous mis uses .

Uses of O .P :-

Used on live stock or on building as sprays , dips , fogs , or as pour on the back of animal for absorption and circulation through the body .also give orally to dogs to control (Fleas).

Mechanism of action :-

Its inhibit cholinesterase enzyme irreversibility caused build up of acetyl choline at the myoneural junction become excessive toxicity caused by excess ACH and uncontrolled parasympathetic signs .

Clinical signes of poisoning :-

1- **Muscarinic type**:- salivation , lacrimation , urination , sweating , diarrhea , vomiting , abdominal cramp, hypermotility in GIT, dyspnea, miosis and cyanosis.

2- **Nicotinic type :-** stimulation of skeletal muscles , twitching of face muscles , eyelieds and tongue.

Generalization of tetany followed by weakness , paralysis of skeletal muscles and respiratory muscles.

3- **Central nervous system type**:- vary with species

In domestic animals may exhibit excessive stimulation of C.N.S but rarely convusion seizures (but see in dogs and cats). Followed by C.N.S depression and death.

Diagnosis :-

1- Case history
2- Clinical signes
3- Aid cholinesterase activity in blood and brain (reduced)
4- Lesion :- animal with acute O.P. poisoning have non specific pulmanry odema congestion , hemorrhage , odema of bowel and other organs.

Treatment of O.P. poisoning :-

1- Atropine sulphate block central and peripheral muscarinic effect .
2- CHE reactivators (2-PAM) pralidoxime. Treatment with oxime must be instituted as soon as possible with (24-48hr.).
3- Emesis induced in oral exposure. Contraindication in depressed animal .
4- Oral administration of mineral oil (to reduced absorption) from GIT.
5- Activated charcoal (AC) 3-6mglkg in water to adsorb O.P. and elimination in feces.
6- Removal of poison : dermal exposure ;wash with detergent and water (at room temp.) without irritant the skin .
7- Barbiturate to treat convulsion .
8- Supportive therapy :- a- artificial respiration or O2 therapy.
   a- Forced feeding and fluid is very important.

9- Diphenhydramine 4mglkg p.o. l8hr. block nicotinc overstimulation in dogs.

B- Carbamates :- e.g (CARBARYL, METHOMYL, ALDECARB)

CARBAMATE INSECTICIDES ARE REVERSIBLE CHOLINESTRASE INHIBITORS WHICH HAVE ASHORT DURATION OF ACTION AND ARE GENARALLY LESS TOXIC THAN organophosphate COMPOUND.

MECHANISM OF ACTION :- CARBAMATES IS CARBAMYLATION OF ACHE UNLIKE O.P. BINDING TO ACHE . CARMATES EASILY DISSOCIATE OR REVERSIBLE FROM THE ENZYME .

CLINCAL SIGNES OF CARBAMATE POISONING ARE SIMILAR TO THOSE OP ORGANOPHOSPHATE .

C- CHLORINATED HYDROCARBONS (ORGANOCHLORINE):-

Compound are fat-soluble , low molecular weight and stable compound , also has low water solubility persist in the environment .

It selective toxicity to insects . they can easily penetrate the exo-skeleton of insects but percutaneous absorption in mammals is relatively poor .

The organochlorine insecticides are divided to their chemical classes :-

1- Diphenyl aliphatic :- e.g. (DDT dichlorodiphenyl trichoroethan), methoxychlor .
2- Cyclodienes :- e.g. Aldrin, hepatochlor used against termites النمل الابيض.
3- Miscellaneous :- e.g. lindane used on dogs and human against fleas, ticks and sarcoptic mange.

These group low volatity- chemical stability , lipid solubility slow rate of biotrans formation and degradation causes thus causes residues in milk and fat .

Mechanism of toxic action :-

1- **DDT**:- act in the peripheral and central nervous system to slow down the turning off the Na+ influx and the turning on of the K+ out flux.

2- **Cyclodienes:-** act by competitive inhibition of GABA at its receptors.

Clinical signs :-

general stimulation of the C.N.S. by chlorinated hydrocarbon tremor, convulsion , hyper excitation , muscle twitching ,
Trembling , tonic, clonic , higher fever, behavioral changes ,head pressing , chewing movements.

- In bird decreased in egg production .

Diagnosis :-

1- Case history
2- Signs of toxicity
3- Post- mortem examination (p.m).
4- Laboratory diagnosis :-

a- biological tests

b-determination of residual amounts of organochlorines in liver, kidney . adipose tissues in dead animal.
Blood , milk in living animal by using HPLC .(high performance liquid chromatography).

Treatment of chlorinated hydrocarbon poisoning :-

1- No specific antidote
2- Detoxification :-

Oral exposure :-

a- gastric lavage
b-Activated charcoal (AC)

C- Saline purgative

d- Mineral oils.

- **Dermal exposure** :- washing with water and detergent .

3- Controlling the convulsion , siezers is very important step in the treatment by using anti convulsant (barbiturate, phenobarbiturate or diazepam)
4- Rehydration and nourishment
5- Quite place.

Pyrethrin and pyrethroids

Pyrethrins :- are natural insecticides produced by flowers (chrysanthemum).

Pyrethroids:- are synthetic insecticides which are subdivided in to :-

1- Type I:- non cyano containing pyre throids e.g. (permethrin , alphamethrin).
2- Type II :- cyano- containing pyrethroids e.g :- (cypermethrin, detamethrin).

Mechanism of toxic action :-

Pyrethrins and type I pyrethroids :- act on Na+ channals in nerve membrane they induce the influx of Na+ at the termination of depolarization is referred as Na+ tail current .may inhibit ATP ase .

Type II :- interfere with binding of GABA and glutamic acid at receptor site .

Clinical signs :-

1- Tremor , ↑ sensitivity to external stimuli .
2- ↑ Body temperature .
3- Behavioral disturbance , salivation , myosis , brady cardia , ataxia , clonic seizures, finally death duo to respiration failure .
4- Grooming behavior in dermal exposure .

Diagnosis :-

1- Case history
2- Clinical signs
3- Chemical test (brain , liver , skin)
4- Post mortem P. M.

Treatment :-

1- No specific anti dote.
2- Diazepam and phenobarbital used to control convulsion seizures .
3- Atropine sulphate used to ↓ salivation and other cholinergic signs.
4- Na bicarbonate can be given as gastric lavage (within 4 hr.).
5- In case of skin infection dermal wash with cool water and soap .
6- Emetic .
7- Activated charcoal .

2-Herbicides

Herbicides:- means those chemical that act on the undesirable weeds in almost any crop.

There are two types of herbicides:-

1- Inorganic herbicides : e.g. arsenicals
2- Organic herbicides : e.g. phenoxy herbicides .

Arsenicals (Na+ - arsenite and arsenic trioxide).

Arsenic absorbed from GIT , Respiratory system and skin .it transported to liver and excreted in bile and urine .

Used as herbicides and fungicides , defoliant on cotton , wood preservatives .

Ruminates poisoning when lick plant poisoned with arsenit .

In poultry used as feed additive .

Horses poisoned after eat grass clipping from lawns treated with arsenic .

Mechanism of toxic action :-

arsenic act to inactivated a Co- enzyme (lipoic- acid) associated by pyruvate dehydrogenase .

Uncouple of oxidative phosphorylation .

Has peripheral vasodilatory effect that lead to capillary fluid loss, odema and shock.

Signs of toxicity :-

In acute toxicity :- in oral exposure :- abdominal pain duo to necrotic of GIT, vomiting , watery diarrhea , nausea , weakness, tacky cardia , body temperature, prostration and death .

Sub acute toxicity :- intoxication in dogs renal and liver damage (icterus , bilirubin urea) GIT damage

Dermal exposure :- blistering , bleeding , secondary infection of skin , cracking .

Diagnosis :-

1- Case history
2- Clinical signs
3- Determination of arsenic level in tissues > 1ppm .
4- Arsenic can be detect in urine for 3 days.

Treatment :-

1- BAL given 3-4 mg / kg I.M. every 4-6 hr.
2- N- acetyle cysteine (140- 280 mg /kg/ day) then 70-140 mg/kg/day orally in small animals.
3- Na- thiosulphate (40-50 mg/kg) or thioctic acid 50 mg /kg twice daily I.M. in large animals .
4- Gastric lavage and mineral oil .
5- Fluid therapy
6- High quality diets (small amount).

Chlorates (Na- chlorates) salts :-

Na- chlorates used as herbicides. May mixed in feed .

Cattle attracted to foliage treated with Na- chlorate.

Mechanism of toxic action :-

Na- chlorates ingestion causes hemolysis in red blood cells and conversion of HB to methemoglobin (M Hb) .

Hb $\xrightarrow{\text{Na chlorates}}$ MHb may causes mucosal surfaces irritation .

Clinical signs of toxicity :- within 1 hr.

1- Hyper salivation
2- Diarrhea
3- Vomiting
4- Hematuria
5- Hb urea
6- Ataxia
7- Cyanosis
8- Prostration and dyspnea .

Lesion :-
1- blood stained urine .
2- erosion in stomach and duodenum.
3- Dark brown tissues.

Diagnosis :-

1- Case history
2- Laboratory analysis of plasma, urine to detect chlorate (present of MHb).

Treatment :-

1- Gastric lavage .
2- Intravenous of methylene blue (4mg/kg) for dogs , 10-15 mg/kg for cattle .
3- Blood transfusion to reduced tissue anoxia .
4- Isotonic saline to elimination of chlorate.
5- Vit . C in dogs and cats .
6- Mineral oil containing Na- thiosulphate 1% inhibit further absorption of chlorate in monogastric animals .

Organic herbicides

Organic herbicides :- are plant growth regulators , some of this group are more toxic than other.

1- Bipyridyl compounds or quaternary ammonium herbicides e.g. (diquat , paraquat).

2- Phenoxy acetic and phenoxy butyric compounds e.g. :- (2,4-D(2,4-dichlorophenoxy acetic acid) and (2,4,5, tricholophenoxy acetic acid).

1- Bipyridyl compounds or Dipyridyl compounds :-

The bipyridyl compound are non volatile desiccant herbicides, act rapidly ,are inactivated on soil contact and rapidly decompose in light . they produce toxic free radicals, tissues can be irritant after contact e.g. mouth lesion after recent spraying of pastures . skin irritation and corneal opacity occur on external exposure to these chemicals and inhalation is dangerous .

Toxicity of paraquat and diquat :-

Dogs and cattle most poisoned paraquat concentrated in lung tissues up to 10 times than other tissues .

It excreted in milk and urine 90-100% in 48 hr.

Mechanism of toxic action :-

Reduce by nicotinamide – adenine dinucleotide phosphate (NADPH)

Electron transfer occur from paraquat to $O^{-}2$.superoxides which reacts unsaturated lipids of cell membranes to form lipid hydroperoxide .

lipid hydroperoxide are unstable spontaneously decompose to lipid free radicals .

ultimately resulting in membrane destruction by lipid peroxidation .

clinical signs :- Diquat

1- Effect in the GIT anorexia , gastritis , GIT distension sever loss of water into the lumen of GIT.
2- Signs of renal impairment
3- CNS excitement convulsion occur in sever affected
4- Lung lesion are uncommon.

Paraquat :-

Immediate effects include :-

Excitement , convulsion or depression and incoordination , gastroenteritis , anorexia and possibly renal involvement and respiratory difficulty .

Diagnosis :-

1- Case history
2- Clinical signs
3- Laboratory test :- a- radiographic change in lung
b- analysis of urine
c- chemical screening spot test in urine up to 8 hr.
d-Chemical analysis of tissues by spectrophotometry (1ml urine blue –green – colure +ve)

e-Lesion :- bronchodilation , pulmonary congestion hemorrhage necrosis of alveolar epithelium , fibrosis of alveoli , emphysema, hepatic and renal tubular degeneration .

Treatment :-

1- Gastric lavage to ↑elimination and reducing pulmonary damage

2- Gastric lavage consist of 30 % suspension of fulter' s earth or 6-7.5 % suspension of bentomite or activated charcoal
Gastric lavage should be repeated every 2-4hr.

3- Cathartics such as sorbitol or sodium sulphate

4- Forced diuresis may be used for ↑elimination (mannitol or furesemide).

5- Vit. E and C .
6- O2 therapy .

Phenoxy herbicides :-

Absorbed from the GIT and bound to protein . distribution to liver , kidney and excreting by urine .

Mechanism of toxic action :-

They inhibit ribonucleous synthesis – uncouple oxidative phosphorylation ↑and number of hepatic peroxisomes.

In dog affect on mucous membrane causing change in the EMG (electrical muscles graphy) .

Clinical signs :-

Depression , anorexia , weight loss , diarrhea , rumen atony , muscles weakness , tremor , hemorrhage , edema , ascites .

In dogs :- myotonia , ataxia , weakness , vomiting , diarrhea , metabolic acidosis .

Diagnosis :-

1- Case history
2- Clinical signs
3- Lab . analysis :- a- alkaline phosphatase (AP).
   b- creatine phosphokinase level (liver , kidney , muscles damage) .
4- Chemical analysis :- renal tissues , forage , urin .

Treatment :-

No spesfic anti dote .

In oral exposure :-

1- Activated charcoal in ruminate .
2- Supportive therapy to treated diarrhea, rumen atony , high quality diet .

Dermal exposure :-

Wash skin and hair with water and soap .

Rodenticides

Rodenticides :- are substance that kill rodents , especially mice and rat .

They may classified according to their chemical structure in to :-

1- Inorganic rodenticides :- e.g. zinc phosphide ,
2- Organic rodenticides :- e.g. anticoagulant (warfarin), fluoro acetate .

Inorganic rodenticides :- e.g. 1- zinc phosphide

This agent is used in developing nations because cheap and an effective rodenticides.

Mechanism of toxic action :-

The toxicity of the chemical can be accounted for the phosphine (ph3) formed following ahydrolysis reaction with the stomach on ingestion .

Zinc phosphide + H2O ⟶ PH3

Phosphine causes cellular toxicity with necrosis of the GIT and injury to the other organ such as liver and kidney .

Clinical signs of toxicity :-

Vomiting , diarrhea , cyanosis , tacky cardia , fever and albumin urea, also pulmonary edema and convulsion .

Treatment :-

1- Decontamination
2- Supportive therapy are often successful initiated early .

Fluoroacetate :-

These compound are white in color , odorless and tasteless .

Mechanism of toxic action :-

Inhibition of citric acid cycle , which is part of tricarboxylic acid cycle.

Fluoroacetate inhibit aconitase (enzyme) and prevents the convulsion of citric to isocitrate in cycle .

Inhibition of this system results in reduced glucose metabolism and cellular respiration and affected tissue energy .

Clinical signs of toxicity :-

Nausea , vomiting , abdominal pain and tachycardia , hypotention , renal failure and muscle spasms .

C.N.S. signs:- agitation seizures and coma .

Treatment :-

1- No specific anti dotes
2- Glycerol mono acetate proved a beneficial effect in the treatment of poisoned animal .
3- Supportive therapy .

Anticoagulant rodenticides :-

Compound dangerous to all mammals and birds ,most are frequent cause poisoning in pets.

Large group of compounds available as pellets , tracking power and baits .intoxication in domestic animals have resulted from combination of feed with anticoagulant concentration and feed mixed in equipment used to prepare rodent baits .

First generation : Warfarin

Second generation : brodifacoum

There are highly toxic to non target sp. (dogs, cats and potentially live stock after single feeding .

Warfarin :-

Mechanism of action :-

inhibition synthesis of vitamin K- dependent clotting factor in plasma and liver .thus adequate amounts are available to convert prothrombin in to thrombin .

Signs of toxicity :-

1- Bleeding from the nose and gums , pain in the joint from haematoma in the long bone.
2- Pain in the abdomen and back.
3- Weakness from anemia .
4- Shock and death.

Diagnosis :-

1- Case history
2- Clinical signs
3- Lab. Test :- citrated blood :-
a- Decrease P.C.V.
b- Prolong activated clotting time (intrinsic pathway).
c- Prolong partial thromboplastin time (intrinsic pathway).
d- Prolong prothrombin time (extrinsic pathway). Clotting time 25% longer than normal suggest poisoning .
4- Normal platelets and fibrin degradation products .
5- Chemical analysis of vomitus , blood and liver.

Treatment :-

1- Induce emesis .
2- Administer activated charcoal and cathartic
3- The use of specific antidote vit. K .
4- Blood transfusion are indicated if so plasma concentrations if haemorrhage is sever .
5- Vit. C is occasionally given protect capillaries from damage .
6- O2 therapy if needed.

House – hold and industrial products :-

Products available in most homes relatively with high risk

1- Automotive radiator antifreeze e.g. Ethylene glycol , cleaners , disinfectants. Essential formation like labels (trade name ingredients to evaluated risk and institute therapy .
Manufacturer :- contacted for data proper response to exposure .
Poison control center (pcc) provide information (clinical effects and appropriate therapy) .

Ethylene glycol (Anti- freeze) :-

Its dihydric alcohol, readily soluble in water
Sources :- use in water time antifreeze and summer coolant for automobile .
Other sources include :- film processing kits , hydraulic brake fluid , paints , ink , industrial solvents and rust removers .

Toxicity :- dogs and cats are more sensitive , poultry swine also affected .
Toxicokinetic :- it absorbed from GIT and distributed to the tissues metabolized and excreted within 16-24 hr. excreted unchanged in the urine .

Mechanism of toxic action :-

The intact glycol cross blood brain barrier (BBB) causes narcotic and euphoric effects , such as those with ethanol .

Glycol metabolism to several acidic metabolile causes acidosis and kidney damage .

Glycolic acid responsible for the sever metabolic acidosis which occur within 3-4 hr. of ingestion .

Renal tubular damage with development of azotemia is observed from 1-3 days after ingestion .

Clinical signs :-

Early signs :- ataxia , incoordination , tacky cardia , polypnea , poly dipsia , dehydration , then acidosis and increase of acidic intermediates in plasma , increase respiratory rate , coma and death .

If animal survived acute acidosis with oliguria , renal failure .

Gross and microscopic lesion :-

Hemorrhage in gastric mucosa , gastritis in dogs and cats to azotemia

Pulmonary odema and hyperemia , pate and swollen kidney Ca- oxalate crystals as bright rosette shape .

Diagnosis :-

1- Clinical signs

2- Lab. Analysis :- a- blood PH less than 7,3

b- increase osmolality

c- change in renal function : - (BUN) blood urea nitrogen (hyperkalemia)

- Crystal of oxalate in urine sediment
- Hyperglycemia
- Residues of ethylene glycol , oxalate , hippuric acid in blood , urine and renal tissues .

Treatment :-

1- Detoxification
2- Activated charcoal specific antidote
3- Ethanol 20% competitive inhibit of alcohol dehydrogenase to prevent metabolic of ethylene glycol to toxic acidic intermediated ethylene glycol alcohol dehydrogenase → toxic metabolic
4- Methylene pyrazol (4-mp) in gods used to competitive inhibits of alcohol dehydrogenase .
5- Supportive therapy :-
   a- Na- bicarbonate to correct acidosis .
   b- Fluid therapy saline 50% and glucose 50%
   c- Ca- borogluconate to correct hypocalciemia
   d- Corticosteroid to treat shock and pulmonary odema
   e- Low protein diet
   f- Peritoneal dialysis .

Biotoxins :-

Biotoxins :- poisons that originate from biological process :-

1- Bactria
2- Insects
3- Reptiles
4- Amphibaians (toads)

Bacteria toxin :- botulism

-produced by clostridium botulinum ,G+ , spore - forming anaerobic bacillus .

- animal exposure to toxin by ingestion food containing performed toxin and / or grossly contaminated with bacteria or by wound contaminated with spores.

Mechanism of toxic action :-

Interferes with synthesis and / or release of acetyl choline at motor end plates leading to paralysis sensory nerve are minimally affected .

Clinical signs and lesion :-

1- Sudden death without signs
2- Early signs include excessive salivation , inability to urinate .
3- Progresses to mydriasis vision disturbances and progressive flaccid motor , GIT hypo motility (chronic bloat) and death duo to respiratory paralysis .
4- Lesion :- are rare – pulmonary odema and hydro pericardium .

Diagnosis :-

1- Case history
2- Clinical signs
3- Serum analysis , GIT contents ,ruminal fluid (toxin) ,feed stuff.

Treatment :-

1- Remove any food stuff causing the disease .
2- Antitoxin therapy
3- Antibiotic (penicillin) , Metronidazole, or Amoxicillin.
4- Symptomatic and supportive care .
5- Artificial respiration
6- Treatment of wounds
7- Vaccination against Cl. Botulinum toxins with toxoid .

Reptiles (snakes) :-

- Venomous snakes which include the cobra , mamba and coral snakes .

- snake bites occur when animals groze , play in infested areas.

- in dogs more than 90% of bits located in head and extremities .

- factors affecting the response to envenomation :-

1- toxicity of venom .

2-amount of injected venom

3-sizes of animals

4-the a viability of therapy .

Mechanism of toxic action :-

Snakes venomous very complex , not full documented. In general toxin are caused tissue destruction , loss of integrity of blood vessels , impaired coagulation and ultered cardiac function odema ,shock, and hemorrhage , C.N.S and respiratory depression . bits near the nostrils or tongue , throat area may be life threatening .

Clinical signs :- depend on :-1- dosage of venom

2-location of bite

3-age of victim

Extreme pain (area of bite) , fang marks , rapid swelling around bite , salivation , tacky cardia , hyperpnea , dilated pupils , secondary infection , ecchymotic hemorrhage in bite area .

Diagnosis :-

1- Case history and clinical signs
2- Lab. Analysis ↑ or ↓ coagulation time , analysis of toxin in tissues , platelet count prothrombin time .
3- Lesion : fang marks .

Treatment :-

1- Acute corrective therapy
2- Antivenins for dogs and humans
3- Diphenhydramine
4- Treat shock and maintenance of air ways
5- Fluid and corticosteroids (prevent vascular collapse).
6- Blood transfusion to correct anemia and hemorrhage .
7- Supportive therapy :- a- analgesic
b- ventilation
c- clean bite wound and lightly wrap.