Antiprotozoal

Parasitic protozoa are responsible for several diseases in man and animals

a-Tissue parasites (coccidiosis and Entamaebia)

b-blood parasite (Babesia, Thieleria, Anaplasma and Trypanosoma).

I-Anticoccidial drugs

These are drugs used for treatment of coccidiosis in animals or poultry.

They may be coccidiostatics or coccidiocidal.

Anticoccidials may act on

1-extracellular stages (sporozoites merozoites) to prevent pentration of cells

2-or on intracellular stages to inhibit development,

3-few act on sporulation of the oocyst.

- The major problem is the development of drug resistance against anticoccidials.
- The speed of development of this resistance depend on
- 1- mechanism of action of the drug

- 2- also cross resistance occur to drugs with same mode of action.

- Resistance is slowly appear with ionophores and rapid with quinolones.
- Drugs combinations decrease resistance.

- Ideal anticoccidical drug must be
- cheep,
- broad spectrum
- leaving no residues .

Types of coccidiosis :-

a-hepatic coccidiosis

b-intestinal coccidiosis

c-cecal coccidiosis(E.tenella)

prevention&control of coccidiosis:-

1-hygienic control:-

that's by a- dry litter

b- good ventilation

c- avoid the dropping to reach the cages

2- Immunization:-

3-Treatment with Anticoccidials:-

1-Sulphonamides

Were the first effective anticoccidals used .

But because of drug resistances and development of new broad spectrum anticoccidials sulphonamides are **infrequently used** in modern poultry production,

However still of value in upper intestinal tract chicken infection.

They still widely used in treatment of coccidiosis of ruminants and small animals.



- **Mode of action:**
- Compete with PABA essential for folic acid synthesis resulting in destruction of schizonts containg merozoites.

- Coccidiosis may be intestinal or hepatic.

- **a-Intestinal coccidiosis:**
- treated with Sulphaguanidine, sulphaquinoxaline, Sulphamethizine, sulphadimidine and sulphamerazine.

- **b-Hepatic coccidiosis :** treated with systemic sulphonamides either by IM injection or in food and drinking water.

- **b-Sulphadimethoxine & sulphachloropydiazine**
- are more effective than other sulphonamids used 0.5- 1.5 % in food.
- **c-Sulphamethezine**

  used 5 mg/kg ration
- **Sulphadimidine**

  used as 16 % solution added as 0.2 % in the drinking water or as 33 % solution to be injected in hepatic coccidiosis.
- **d-Sulphaguandine** used 0.5-1.5 % in food.

e-Sulphonamide combination decrease the occurrence of resistance and increase efficacy:

i-ormetoprim and sulphadimethoxine (68.1 gm and 11.35 g/ton ration)

ii-pyrimethamine with sulphaquinoxalione

iii-pyrimethamine with sulphadoxine (25mg and 500mg

IV-sulphaquinoxaline and amprolium

- **2-Nitrofurans**

Including nitrofurazone, furazolidone, furaltadone were used for treatment and prevention of coccidiosis

- but become of limited value because of potential carcingenic activity.

3-Dinitro Compounds:

a-Nicarbazin (Nicarb):

It is used as prophylactic only for coccidiosis in broilers at dose of 125 ppm in food especially in starting period because of potential growth suppression. It is not used in layers as it may reduce egg production, decrease hatchability, thin egg shell and mottled egg yolk.

b-Dinitrolomide:

Used as prophylactic at dose of 0.0125 % in food by inhibiting sporulation of the oocyst.

4-Vitamin antagonists

a-Amprolium hydrochloride:

It is safe coccidaostatic agent, competitively inhibits the active transport of thiamine.

Affects first generation shizont to prevent production of merozoites, some activity on sexual stage and sporulating oocyst.

It is given in food 36.3 - 113.5 g/ton or 0.012 % in drinking water and may be combined with sulphonamides as sulphaquinoxaline or sulphadimidine it can be used safely in laying hens.

b-Diaverdine:

It is coccidiostatic drug, antagonizing folic acid essential for Eimeria.

given combined sulphquinoxaline.

It has low toxicity.

c-Ethopabate:

It antagonizes PABA needed for folic acid synthesis.

It can be used with diaverdine or pyrimethamine.

d-pyremethamine:

It is folic. folinic acid antagonist given with diaverdine or sulphaquinoxaline to potentiate anticoccidial activity.

5-Hydroxy and naphthaquinines

a-Buquinolate:

It is coccidiostatic allow penetration of sporozoties but not development, active against all species of coccidia in chicken

b-Clopidol:

It resembles buquinolate used as 0.01 % in food, However there is cross resistance to bequinolate. It needs 5 days withdrawal period.

c-Decoquinate:

It is the most active and more safe one .

it is not used in laying or breeding birds and needs 5 days withdrawal period from meat.

6-Robenidine (Cycostat)

It acts on first generation schizont preventing formation of merozoites.

It causes unpleasant taste of meat and egg and needs 5 days withdrawal period.

It is used against ionophores resistant strains in feed at rate of 33 ppm.

7-Ionophores

A group of broad spectrum coccidiostatic antibiotics.

They act by interfering with cellular ion transport accumulating Na and Cl intracellular.

They act on extraceullar sporozoites

a-Monensin (Coban):

Produced from Streptomyces cinnamonensis. It is effective for prophylaxis of coccidiosis in broilers fed at 99-121 ppm.

It may cause weight gain supperession.

b-Lasalocial (Avatec): It is related to monensin but of greater activity and toxicity lasalocid is transmitted to egg and also may cause wet litter. Given at rate of 75.125 ppm in feed

c-Salinomycin (cox): It is used for prevention of coccidiosis in broilers feed at 6 ppm, affecting sporozoites, early and late asexual stage and must not used in layers.

d-Naracin sodium (Monteban): It is used for prevention of coccidiosis in broilers given in feed 70 ppm.

8-A prinocid (Arpocox)

It acts by inhibiting nucleic acid synthesis.

It is rapidly metabolized

used 60 ppm for prophylaxis

with no adverse effect.

9-Toltrazuril (Baycox)

It is a broad spectrum anticoccidial, affects all stages of Eimeria.

Given in drinking water 25 ppm.

it needs 19 days withdrawal period as it is slowly removed from meat.

II-Antimaebic drugs

These are used for treatment of amaebic dysentery and they include:

1-Emetine

It is alkaloid obtained from ipecac root or prepared synthetically.

Emetine is **direct acting systemic amacebicide**, administrated parentally because when given orally erratically absorbed.

It acts mainly on the trophozoites.

Slowly eliminated from body via kidney with trace amounts detected in urine 1-2 months after the end of the therapy.

It is especially of value in sever invasive intestinal amaebias, amebic hepatitis and amebic abscess.

Dose:

mg/kg B.wt with 60 mg/day maximum dose. For a period not more than 10 days.

It is contraindicated in cardiac, renal disease hypotension & pregnancy.

Side effects:

Nausea, vomiting, diarrhea, tenderness and stiffness of muscles, cardiac depression

Derivatives of emetin:

a-Dehydro emetine:

less toxic and cummlative than emetine (1.5 mg/kg not exceed 90 mg/day) IM

b-Emetine bismuth iodode:

it is given orally 200 mg/day for 12 day.

2-Hydroxyquinolines

These are iodinated compounds include: Chinioform (yatran), iodocholorohydroxyquin (viofofm), Diiodohydroxyquin (Diodoquen).

It is **only effective for intestinal amaebiasis** acting on the trophozoites.

Side effects:

Neurotoxicity, optic atrophy and visual loss may improve after discontinuation.

Dose: Chinioform (0.75-1 gm/day for two days), vioform (0.75-1 gm/day for to days), Diodoquin (1.5-2 gm/day for 3 weeks)

3-Metronidazole (Flagyl)

It is very effectively eradicates amebic tissue infections (liver abscess, intestinal wall and extraintestinal infection) .

It has Short half life must repeated every 8 hours.

Mode of action:

occur in 4 steps:

1-entry to protozoal cell.

2-Reductive activation

3-Toxic effects of reduced products

4-Release of inactive end products.

Side effects:

Glossitis, stomatits, nausea, emesis and in high dose nervous signs and suspected as mutogene and carcinogens

Use and dose:

E. histyhtica in dog orally 15-30 mg/kg. b.wt and it is used for treatment of in cat 10.25 mg/kg twice for daily 5-7 days.

4-Chloroquine phosphate

It is antimalarial with special therapeutic value in **amaebic heapatitis** as **it localized in liver in concentration several hundred times greater than that of plasma.**

It is given orally at a dose of 1 g daily for two days then 500 mg/day for 2 or 3 weeks.

It is of low toxicity and the dose may increased and duration prolonged if needed.

5-Pentavalent organic arsenicals

Carbarsone and Glycobiarsol effective against **amaebic hepatitis** by interfering with SH group containing enzyme in the parasite.

Carbarsone readily absorped from GIT and slowly excreted by kidney while Glycobiarsol is poorly absorbed and exerts its effect on intestine

Dose: of Carbarsone 250 mg tid for 10 days and for Glycobiarsol 500 mg tid for 10 days.

It is contraindicated in renal and hepatic diseases

6-Antibiotics

a-Paromomycin

Aminoglycoside antibiotic

it has direct amaebicidal activity in mild and moderate amaebic infection.

Dose 25 mg/kg b.wt orally for 5 days.

Side effects

mild GIT upsets, mal-absorption diarrhea .

b-Fumagillin

as paromomycin given at a dose of 10-20 mg Tid for 10 days

c-Tetracycline:

has **very week direct amaebicidal** action may eradicate intestinal amaebiasis but not used in pregnant or young animals .

III-Antipiroplasmal drugs (Babesiocidal)

These are drugs used for treatment of babesia infection in animals.

1-Trypan blue

Is one of **Azo dyes** and considered as treatment for babesiasis

it is safe nontoxic but stains tissues, secretions and milk with blue green color persist for several weeks .

2-Quinuronium suphate (Acaprine)

It is a complex urea compound affecting most species of babesia in different animals e.g horse (B. Caballi), cattle (B. bovis & B.Bigemina) , sheep & goat (B.motasi & B.ovis) , pig (B.suis) and dog (B.canis).

N.B must give **with atropine sulphate** to avoid its side effects as it is parasympathomimitc

dose:

horse 0.3 0.5 mg/kg B wt., Cattle , sheep & pig 0.5 mg/kg B.wt.

It must be give s/c at conc. 5 % in all animals except sheep and dog 0.5 %.

Side effects:

It possesses anticholinestrase activity overcomed by pre-administration of atropine.

It stimulate release of histamine.

Toxicity:

Sever shock may occur with rapid fall in blood pressure resulting in sudden death.

In other cases muscle tremors, salivation, urination and defecation these symptoms may persist for 6-10 hours.

3-Amicarbalide isethionate

It is chemically related to quinuronium sulphate and replaced it because of low toxicity .

Dose & route:

can be used 5-10 mg/kg .B. wt I/M, S/C or by slow I/V .

Haemoglobin level in urine fall considerably within 48 hours but may need second dose after 24 hour from the first .

4-Imidocarb (Imizol)

It is recommended for prophylaxis and treatment of babesiasis and anaplasmosis .

Dose & route:

Can be given by I/M and S/C

Babasiasis therapy

Cattle 1.2 mg/kg B.wt.

Horse 2.4 mg/kg B.wt.

Dog 6 mg/kg B.wt

Anaplasmosis therapy

Cattle 3 mg/kg B.wt

**needs withdrawal period 23 days before slaughter .

4-Diminazene aceturate (Berenil)

It is mainly a trypanocidal drug and also active as babesiocidal in cattle, sheep horse and dog

given at dose of 3.5 mg/kg I/M or S/C.

IV-Drugs for Anaplasmasis and Thileriasis

These are drugs used for treatment of anaplasma or thileria infection in animals .

1-Tetracylines

Can be useful to treat thileria & anaplasma

must be given early and in large dose for long period

2- Dithiosemicarbazone

Given I/V daily for 10 days completely eradicate anaphasma marginalae.

It is synergistic to tetracycline with less toxic effects.

3-Imidocarb

babesiocidal drug and of value in treatment of anaplasma and thileria.

4-parvaquone (clexon)

Given as single curative treatment for thieleria in cattle at a dose of 20 mg/kg B.wt I/M.

5-Buparvaquone (Butalex)

As parvaquone but at a dose of 2.5mg/kg.B. wt

Tryopanocidal drugs

These are drugs used for treatment of trypanosoma infection

1-Quinapyramine chloride and sulphate (Antrycid)

Its salts are sulphate&chloride.

(Mix. of 2 parts of chloride to 3 parts of sulphate) then take 0.25 mg/kg/s.c that dose give good protection till 230 day in cattle against T. congelense

Sulphate salt is water soluble so it rapidly and short acting while chloride is slightly soluble, slowly absorbed and long acting used as prophylactic.

Action and uses:

It is active against T. congolense, T. evansi, T. vivax, T. equiperdum, T. equinum and less active on T. brucei.

The drug act by inhibition of growth and cell division

Dosage:

given s/c at concentration 10 %

Weight of animal	dose
Less than 150 kg	4.4 mg/kg B. wt.
150-200 kg	1 g
200-350 kg	1.5 g
over 350 kg	2 g

Side effects:

It is histamine releaser

Anticholinestrase activity

and cause local reaction at the site of injection may cause sloughing.

These side effects can be overcomed by pre-administration of antihistaminic and atropine.

2-Phenanthridinium compounds

They act by inhibiting trypanosomal cytoplasm division

cross resistance frequently occur between them.

Includes dimidium bromide, Homidium bromide, pyrithidium and metamidium.

a-Homidium bromide (ethidium)

It is active against T. congolense and T. vivax, some activity on T. brucei with some prophylactic action but inactive on T. evansi.

dosage:

Administered by deep I/M to avoid sever local irritation from s/c injection.

It serves both curative and prophylactic.

b-Pyrithidium (prothidium)

It is prophylactic against T. conglense, T. Vivax and T. brucei, giving protection for 6-8 months and two months in areas of great risk.

it can be administered by s/c or deep I/M but local swelling at the site of injection can be expected. dose 2 mg/kg. B.wt.

3-Dimenazene aceturate (Berenil)

It is effective against T. Viva x and T. congolense less on T. brucei.

Dose:

for bebasia, T. vivax and T. congolense 3.5 mg/kg b.wt by I/M or s/c injection.

4-Suramin (Naganol)

Used for the treatment not a prophylactic

It has marked curative and less useful prophylactic properities against T. evansi, T. brucei, T. equinum and T. equiperdum but inactive on T. vivax and T. simisimiae.

Dosage:

Horse 7-10 mg/kg .B.wt. repeated weekly for 3 weeks. Camel 8-12 mg/kg .B.wt. Cattle 12 mg/kg B.wt.

Suramin is potential toxic for its very narrow therapeutic index, horses and donkeys are very susceptible but **camels are resistant.**

Toxicity:

Symptoms of liver, kidney spleen and adrenal gland damage

N.B suramin seems to be synergistic potentiator of phenanthridium and quinapyramine derivatives.

Prophylactic complex:

These being slowly absorbed and valuable as prophylactic. e.g suramin prothidium and suramine Homidium give protection for 8 months.

5-Samorin

This drug is used as prophylactic for a period of 6 monthes