ANTIPROTOZOAL DRUGS

Anti-coccidial drugs

Anti-piroplasmal drugs

Anti-trypanosomal drugs

Anti-giardial drugs

Anti-leishmanial drugs

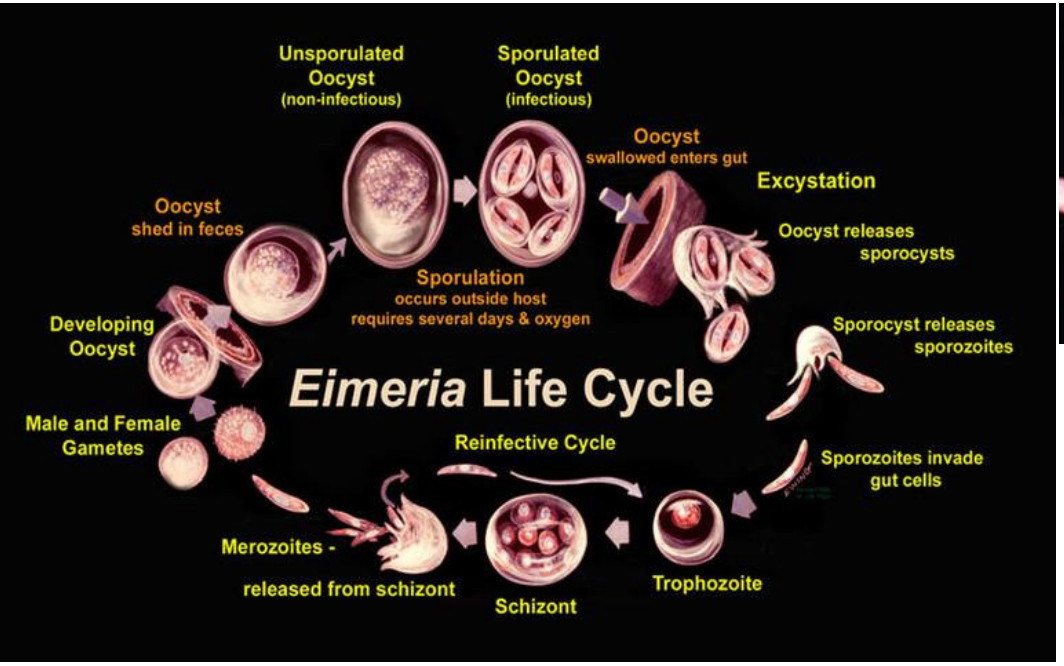
Anti-histomonad drugs

Protozoa

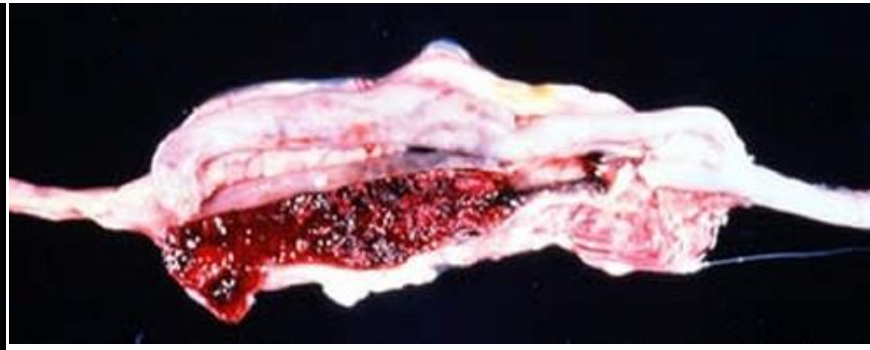
- Single-cell eukaryotic organism
- Transmitted by ticks, tsetse flies, mosquitoes and other arthropods
- Org. multiply and proliferate rapidly in both hot and tropical climate
- Zoonotic importance
- Common protozoal infections of veterinary importance are
  - Coccidiosis
  - Toxoplasmosis
  - Babesiosis
  - Theileriosis
  - Cytauxzoonosis
  - Giardiasis
  - Trypanosomiasis
  - Leishmaniasis
  - Trichomoniosis
  - Amoebiasis

Anti-Coccidial Drugs

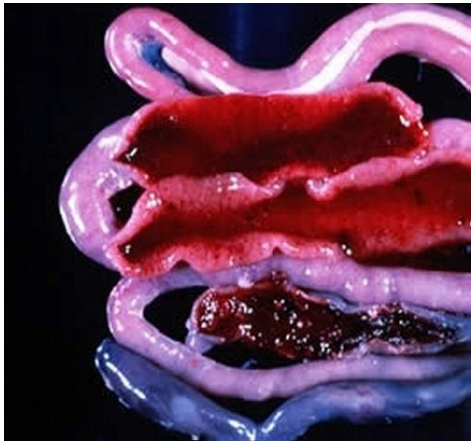
- Coccidiostat – arrest or inhibit the growth of intracellular coccidia
- Coccidiocidal – destroy coccidia during the development
- Coccidia of veterinary importance – Eimeria and Isospora
- Life cycle of coccidia – refer Parasitology course



Caecal form *E. tenella*



Intestinal form *E. necatrix*



Anti-Coccidial Drugs

- Anticoccidial Drugs
  - Effective against I and II asexual cycle, few in sexual cycle
  - Usually treatment duration is 14 to 21 days
  - In poultry, continuously administered in broiler and in layer up to initiation of egg laying
  - Low dose as prophylactic and also allow the host to develop immunity against the low population of the org.
  - Drugs used for prophylaxis and therapeutic are different, only a few drugs possess both types of activity

Anti-Coccidial Drugs - Classification

1. Thiamine Antagonists – Amprolium

2. Ionophores/Polyether antibiotics – Monensin, Lasalocid, Salinomycin, etc.

3. Folic acid antagonists
   a. Sulphonamides – Sulphaquinoxaline, Sulphaguanidine, etc.
   b. Pyrimidines – Trimethoprim, Pyrimethamine, Diaveridine, etc.
   c. Substituted benzoic acid – Ethopabate
   d. Potenatiated sulphonamides – Trimethoprim-Sulphadimethoxine, etc.

4. Quinolones – Decoquinate, Methylbenzoquate and Buquinolate

5. Pyridinoles – Clopidol

6. Guanidines – Robenidine

Anti-Coccidial Drugs - Classification

7. Nitrobenzamides – Dinitolmide and Aklomide
8. Carbanilides – Nicarbazin
9. Quninazolines – Halofuginone
10. Benzeneacetonitriles – Diclazuril and clazuril
11. Triazinones – Toltrazuril
12. Benzyl purines – Arprinocid
13. Miscellaneous drugs
    a. Nitrofurans – Furazolidone
    b. Tetracyclines – Oxy and Chlortetracyclines

Anti-Coccidial Drugs – Thiamine Antagonists

Amprolium

- Structural analogue of Thiamine or Vitamin B1
- MoA: Blocks thiamine transporter of Eimeria sps. – prevents carbohydrate synthesis
- Act on I generation schizonts – preventing differentiation of merozoites
- Active against caecal coccidia – prophylactic use
- Combined with ethopabate or sulphonamides – for both intestinal and caecal coccidiosis
- PK – confined to intestine
- Safety margin – 8x, neurological signs in dogs, encephalomalacia in sheep, inhibition of RBC production in calves in excessive dosage
- Dose:
  - Cattle: 5 mg/kg, PO – 21 days – prophylaxis, 10 mg/kg PO- 5 days – treatment
  - Dogs – 100 -200 mg, Cats – 60-100 mg (total dose) PO – 7 days
  - Swine – 25 -65 mg/kg, PO, BID – 3-4 days
  - Sheep & Goats – 55 mg/kg, PO – OD
  - Poultry – 0.012 -0.24%, PO in water for 3 days

Anti-Coccidial Drugs – Polyether Ionophores / Polyether Antibiotics

- Obtained from Streptomyces sps. Highly lipophilic
- MoA: Ion transporters,
  - form complex with monovalent (Na^+ or K^+) cations or divalent cations (Ca^{++})
  - Disrupt the membrane integrity, internal osmolality
  - Inhibit mitochondrial function, and inhibit ATP hydrolysis in coccidia
  - Affects the sporozoites and merozoites of the asexual stages of parasite
- Do not interfere with development of immunity
- Low safety margin in Equines and Turkeys
  - Cause severe CVS effects and fatalities in horses due to increase in the concentration of Ca^{++} in cardiac and skeletal muscles
- Clinical use:
  - Prophylactic use in poultry and cattle
  - Used as growth promoters in cattle

Anti-Coccidial Drugs – Polyether Ionophores / Polyether Antibiotics

Monensin

- Monovalent polyether antibiotic derived from *Streptomyces cinnamonensis*
- Prevention of coccidiosis in broilers, cattle and sheep
- Not recommended for layers over 16 weeks of age
- Horses, turkeys, guinea pigs are very sensitive
- LD_{50} in equines – 2-3 mg/kg vs 200 mg/kg in chickens
- Pre-slaughter withdrawal period – 72 h in chickens
- Dose:
  - Chickens – 100 -200 g/tonne fee
  - Cattle – 100 -360 mg/animal /day
  - Goats – 20 g/tonne feed

Anti-Coccidial Drugs – Polyether Ionophores / Polyether Antibiotics

Lasalocid

- Produced by *S. lasaliensis*
- Complexes with both monovalent and divalent cations (it is a divalent)
- Horses and dogs are very sensitive
- Pre-slaughter withdrawal period – 5 days in chickens (trans. to eggs)
- Dose:
  - Chickens – 75 -125 g/tonne fee
  - Cattle – 360 mg/animal /day, Sheep & Goats – 20 g/tonne feed

Salinomycin – Monovalent – *S. albus*

- Prevention and treatment of coccidiosis in chicken, growth promoter in pigs
- No withdrawal period is required
- Dose:
  - Broiler chicken – 60 g/tonne feed
  - Replacement layer chicken – 40 g/ tonne feed

Anti-Coccidial Drugs – Polyether Ionophores / Polyether Antibiotics

Narasin – S. aureofaciens

- Prevention of Coccidiosis (Similar to Salinomycin)
- Broilers – 70 g/tonne fee

Maduramycin – Actinomadura yumaense – More potent than other ionophores

- Adverse effects on growth and feathering at high dose
- 5days withdrawal period is required
- Dose: Broiler chicken – 5 g/tonne feed

Semduramycin

- Semisynthetic monovalent monoglycoside ionophore
- No withdrawal period
- Dose: Broiler – 25 g/tonne feed

Anti-Coccidial Drugs – Folic Acid Antagonists

Sulphonamides

- Often used in combination with Amprolium for ruminants and small animals
- MoA: inhibits the synthesis of folic acid by mimicking PABA
- Active against II generation schizonts

Sulphaquinoxaline

- Marketed in combination with Amprolium
- Withdrawal period is 5 days in chickens

Species	Prophylaxis	Treatment
Chicken & Turkey	125 PPM, PO in water or feed for 8 weeks	500 PPM, PO in water for 8 weeks
Cattle	13 mg/kg, PO	Lambs: 0.025% in drinking water for 2-5 days

Other sulphonamides used are sulphaguanidine, sulphadimidine, sulphadiazine, sulphadimethoxine, sulphamethoxypyridazine and sulphachlorpyridazine

Anti-Coccidial Drugs – Folic Acid Antagonists

Pyrimidines

- Selective inhibitors of dihydrofolate reductase – folic acid synthesis

Pyrimethamine

- Human antimalarial drug used for the treatment of toxoplasmosis in small animals and equine protozoal myelitis (EPM) in horses
- Occasionally used as anticoccidial drug
- PK: oral absorption, cross BBB, accumulates in liver, kidneys and spleen, high PPB, remains in blood for 7 days, metabolites excreted in urine and milk
- Not approved for food animals
- Combined with Sulphadoxine or Sulphadiazine
- Dose: Dogs & Cats: 1 mg/kg, PO, OD or 0.25 - 0.5 mg/kg Pyrimethamine + 30 mg/kg sulphadoxine or sulphadiazine

Anti-Coccidial Drugs – Folic Acid Antagonists

Substituted Benzoic Acid

Ethopabate

- Resembles PABA and interferes with folic acid synthesis
- Used in combination with amprolium and/or sulphaquinoxaline – synergistic effect, cover both intestinal and Caecal Eimeria
- Dose: Chicken & Turkeys:
  - Amprolium 125 ppm+ ethopabate 8 ppm in diet
  - Amprolium 100 ppm + ethopabate 5 ppm + sulphaquinoxaline 60 ppm in diet

Potentiated Sulphonamides

- Trimethoprim-Sulphamethoxazole
- Trimethoprim-Sulphadiazine
- Ormetoprim-Sulphadimethoxine

Anti-Coccidial Drugs – Quinolones

- Coccidiostatic drugs
- MoA: inhibit coccidial respiration by inhibiting CytC mediated electron transport in mitochondria, prevent their development in enterocytes
- Drug resistance – rapid and cross-resistance among members is complete

Decoquinate

- Active against invading sporozoites
- Prophylactic use, not approved for turkeys, laying and breeding birds
- Withdrawal period is 3 days when used in broilers
- Dose:
  - Calves and lambs – 0.5 to 1 mg/kg, PO – 28 days
  - Broiler chickens-20-40 g/tonne feed

Other quinolones are Methybenzoquate , Buquinolate

Anti-Coccidial Drugs – Pyridinoles

Clopidol

- Structurally similar to quinolones, acts by inhibiting electron transport system in coccidial mitochondria
- Activity against II gen schizogony, gametogony and sporulation
- Prophylaxis of coccidiosis in chicken and rabbits
- Not approved for laying birds
- Should not be mixed with other coccidiostats except methylbenzoquate
- Pre-slaughter period is 3 days in chickens
- Dose:
  - Broiler chickens & game birds: 125 g/tonne feed
  - Rabbits: 200 g/tonne feed

Anti-Coccidial Drugs – Guanidines

Robenidine

- MoA: Inhibition of oxidative phosphorylation
- Activity against late I gen and II gen schizonts
- Imparts unpleasant taste to eggs when birds are fed high dose
- Not approved for laying birds
- Should not be mixed with other coccidiostats
- Pre-slaughter period is 5 days for meat
- Dose:
  - Broiler chickens & turkeys: 30 g/tonne feed
  - Rabbits: 50-65g/tonne feed

Anti-Coccidial Drugs – Nitrobenzamides

Dinitolmide

- MoA: not clear
- Activity against I gen schizonts and arrests parasite development, effect on sporulation of oocysts
- Coccidiostat at recommended dosage, become coccidiocidal on prolonged treatment
- Not approved for laying birds
- Should be mixed with other anticoccidials
- Pre-slaughter period is 1-3 days for meat
- Dose: Broiler chickens : 125 g/tonne feed

Anti-Coccidial Drugs – Carbanilides

Nicarbazine

- Mixture of DNC and HDP
- MoA: not clear, probably inhibits energy-dependent transhydrogenase and accumulation of calcium in the presence of ATP
- Activity against II gen schizonts
- Affects egg quality and quantity, bleach brown-shelled eggs, mottled egg yolks, reduce eggshell thickness, egg weight, hatchability and production
- Medicated birds to susceptible to heat stress, growth suppressing effect
- Dose: Broiler chickens : 100-125 g/tonne feed

Anti-Coccidial Drugs – Quinazolines

Halofuginone

- Antimalarial drug -has both coccidiostatic and coccidiocidal effects
- Prevention and treatment of coccidiosis in chickens and turkeys
- Prophylactic of cryptosporidiosis in calves
- Skin ruptures in chicken – due to inhibition of collagen type I synthesis
- Not approved for laying hens and game birds
- Extremely toxic to fish and other aquatic animals
- Causes irritation to skin and eyes – extreme caution when handling drug
- Withdrawal period – 5 days before slaughter in chicken and turkeys
- Dose: Chicken and Turkeys 3 g/tonne feed- until 12 weeks of age

Anti-Coccidial Drugs – Benzeneacetonitriles

Diclazuril

- Active against both schizonts and gametocytes
- Safe compound,
- Zero day withdrawal period,
- Compatible with other anticoccidials and feed additives
- Dose: Chicken and Turkeys – 1 g/tonne feed, Lambs – 1 mg/kg, PO

Clazuril

- Drug of choice for pigeon coccidiosis
- Dose: 2.5 mg/bird, PO, once every month

Anti-Coccidial Drugs – Triazinones

Toltrazuril

- Broad spectrum anticoccidial, active against sexual and asexual stages
- Inhibits nuclear division of schizonts and microgametes
- Drug of choice for neonatal porcine coccidiosis
- Active against other protozoa such as Sarcocystis spp., Hepatozoon spp.
- Persists for longer period in tissues – withdrawal period – 21 days
- Chickens: 7 mg/kg, PO – OD in drinking water for 2 days
- Piglets: 25 mg/kg, PO at 4 days of age

Anti-Coccidial Drugs – Benzyl Purines

Arprinocid

- Active against early invasive and intracellular stages of Eimeria
- Active metabolite – Arprinocid-1-N-oxide
- Affects microsomal metabolism and inhibit DNA synthesis
- Drug resistance is common, withdrawn from the market in several countries
- Chicken : 60 g / tonne feed

Anti-Coccidial Drugs – Miscellaneous Drugs

Nitrofurans - Furazolidone

- Inhibit enzymes related to carbohydrate metabolism in coccidia
- Dogs & Cats – 8-20 mg/kg, PO – BID for 5 days

Tetracyclines – oxy and chlortetracycline

- Chickens: 0.022% oxytetracycline + 0.18 – 0.55% calcium in feed – 5 days
  0.022% chlortetracycline + 0.8 % calcium in feed - 3 weeks

Steps to Prevent Anti-Coccidial Drug Resistance

Shuttle Program:

- Different classes of drugs used in a single grow-out; different drugs are used in starter and grower rations

Rotation (Switch) Program:

- Different anticoccidial drugs are used between two or more grow-outs

Drug Mixtures

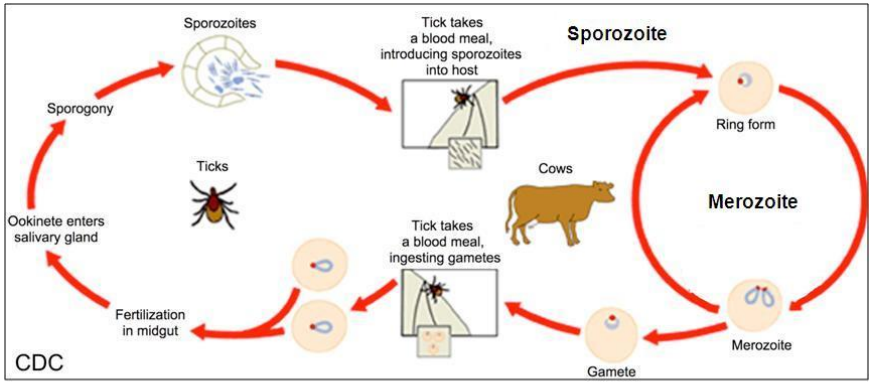
- Combination of two or more drugs – few drugs
- Many drugs are not compatible to each other

Anti-Piroplasmal Drugs

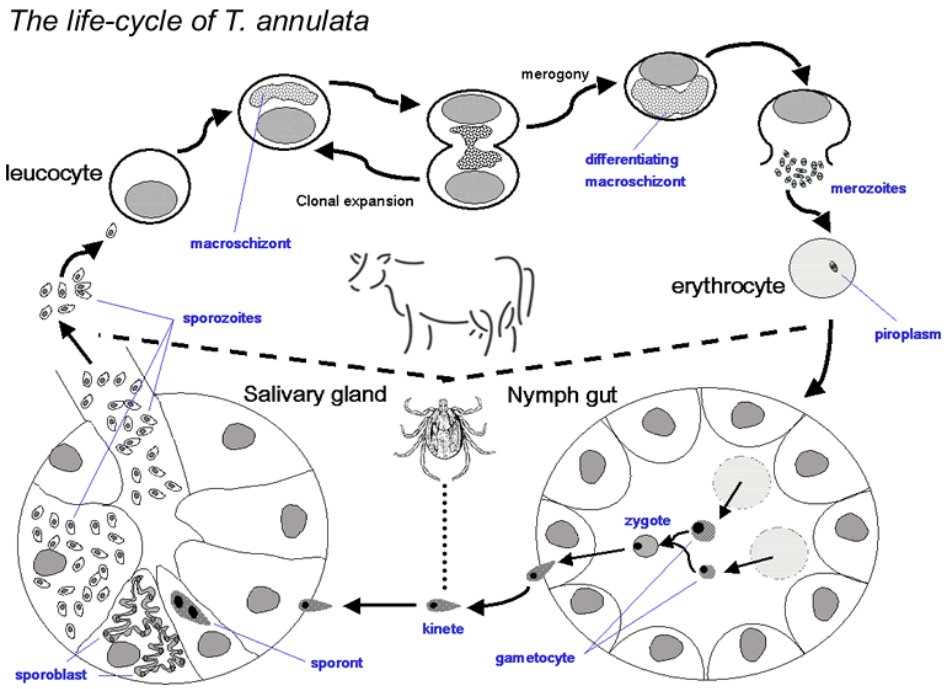
Anti-Piroplasmal Drugs

Act against three important diseases transmitted by ticks

- Babesiosis -Babesia is an intra-erythrocytic protozoan parasite and is transmitted by ticks
- Theileriosis – Theileria undergoes sequential development in leukocytes and erythrocytes of the mammalian host and causes an acute, often fatal disease
- Cytauxzoonosis - Cytauxzoon felis is a protozoal organism transmitted to domestic cats by tick bites



Life cycle of *Babesia*



Anti-Piroplasmal Drugs

Classification

1. Diamidines
    a. Carbanilide diamidines – imidocarb and amicarbalide
    b. Aromatic diamidines – diminazene, pentamidine, phenamidine
2. Quinuronium compounds – quinuronium sulphate
3. Naphthoquinones – parvaquone, buparvaquone and atovaquone
4. 8-Aminoquinolines – primaquine
5. Tetracyclines – oxy, chlor, doxycyclines
6. Quinazolines – halofuginone
7. Dyes – trypan blue

Anti-Piroplasmal Drugs - Diamidines

Carbanilide Diamidines

Imidocarb

- Used in the treatment of babesiosis, anaplasmosis and ehrlichiosis
- MoA: unwind and denature the DNA, interferes with DNA synthesis
- PK: SC/IM, accumulates in liver and brain, high PPB, excreted unchanged in urine (90%) and feces, long t1/2 – antiprotozoal activity up to 4 weeks
- Low TI, mild cholinergic signs, cattle – 10 mg/kg can cause death
  - Antidote – atropine
- Long lasting tissue residue -170 days, not recommended for food animals
- Dose
  - Dogs : 5 mg/kg, IM or SC once, may be repeated after 2 weeks
  - Cattle: 1.2 mg/kg, SC – SD (up to 3 mg/kg, SC – SD)
  - Sheep: 1.2 mg/kg, IM – SD
  - Horses: 2 -3 mg/kg, IM – SD

Amicarbalide Isethionate:

- Used for creating premunity in cattle by controlling the clinical signs, does not eradicate infection

Anti-Piroplasmal Drugs - Diamidines

Aromatic Diamidines

Diminazine

- Trypanocidal drug active against babesiosis
- Single dose can eliminate *Babesia canis* infection in dogs
- Dose
  - Dogs : 3.5 mg/kg, SC once, may be repeated after 2-4 weeks
  - Cats: 2 mg/kg, SC – SD
  - Cattle & Horses: 3 - 5 mg/kg, IM – SD, 6-12 mg/kg for *B. equi*

Pentamidine

- Antibabesial, Antitrypanosomal and Antileishmanial activities
- Effective against canine babesiosis
- Adverse effects in dogs – vomiting, hypotension, tachycardia and pain at injection site
- Dose:
  - Dogs: 16.5 mg/kg, IM, q24d
  - Cattle: 0.5 -2 mg/kg, SC

Anti-Piroplasmal Drugs – Quinuronium Compounds

Quinuronium sulphate

- Used to create premunity in endemic area, controls clinical signs without completely eradicating the infection
- Adverse reactions – muscle tremors, salivation, urination and diarrhoea
- Tachypnoea, hypotension, collapse, shock and death may occur
- Should not be repeated within 2 weeks (preferrably 3 months)
- SC – 5% solution in cattle, horses and pigs, 0.5% solution in sheep and dogs
- Dose:
  - Dogs: 0.25 mg/kg, SC
  - Cattle, sheep and pigs : 0.5 mg/kg, SC
  - Horses : 0.3 -0.5 mg/kg, SC

Anti-Piroplasmal Drugs - Naphthoquinones

- Chemically similar to ubiquinone – selectively block mitochondrial electron transport and inhibit ATP production and pyrimidine synthesis

Parvaquone

- Good activity against Theileria esp. macroschizonts and intraRBC parasites
- Single dose can eliminate *Babesia canis* infection in dogs
- Cattle: 20mg/kg, IM – SD

Buparvaquone

- Potent than parvaquone for theileriosis, long $t_{1/2}$ – 7 days in cattle
- Cattle- 2.5 mg/kg, IM

Atovaquone

- Activity against malaria and toxoplasmosis, used in conjunction with Azithromycin for treatment of babesiosis
- Dogs: 15 mg/kg, PO-BID – 3 weeks, or 13.3 mg/kg PO, TID + Azithromycin 10mg/kg, PO – OD – 10 days

Anti-Piroplasmal Drugs - Aminoquinolines

Primaquine

- Used in the treatment of *B. felis* in cat
- Exact MoA is not clear, but inhibit the functions of DNA, ubiquinone or CoQ10 – blocks cellular energy production
- Well absorbed orally, large Vd, extensive hepatic metabolism and slow excretion
- Dose: Dogs & Cats – 0.5 mg/kg, PO or IM – SD, dose > 1 mg/kg is highly toxic to cats

Anti-Piroplasmal Drugs

Tetracyclines

- Oxytetracyclines – *B. divergens* and Theileria in bovines
- Chlortetracyclines – *B. equi* in horses
- Doxytetracyclines – *B. canis* in dogs

Quinazolines – Halofuginone

- Anticoccidial, also effective against Theileria spp. In cattle
- Extremely potent drug, carefully handled due to irritation to skin and eyes
- Cattle; 1-2 mg/kg, PO –SD

Dyes – Trypan blue

- Azo dye, stains body tissues and secretes in milk
- Extravascular leakage cause irritation and sloughing of tissues
- Replaced with better drugs
- Dogs- 10 mg/kg, Slow IV as 1% solution, SD

Anti-Trypanosomal Drugs

Trypanosome lifecycle

Anti-Trypanosomal Drugs

Classification

1. Aromatic Diamidines - diminazene, pentamidine, phenamidine, stilbamidine, etc
2. Quinapyramine compounds – quinapyramine sulphate & chloride salts
3. Aminophenanthridium compounds – homidium, isometamidium, etc.
4. Carbamide derivatives –suramin
5. Antimonial compounds – antimony potassium tartrate and stibophen
6. Arsenical compounds – Melarsomine and melarsoprol
7. Dyes – trypan blue and trypan red
8. Miscellaneous compounds
    - Eflornithine and benznidazole

Aromatic Diamidines – Antitrypanosomal drug

MoA: concentrates in parasites by energy dependent, high affinity uptake system

- Binds irreversibly to DNA – interferes with DNA formation and replication
- Inhibits enzymes and proteins
- Interference with aerobic glycolysis

Diaminazene aceturate or diaceturate

- Bind to DNA @ 1 molecule for every 4-5 nucleotides
- Effective against Trypanosoma, Babesia and bacteria (cidal – Brucella and Streptococcus sps.)
- Adverse effects: CVS, CNS, hepatic and renal impairments
- Marketed in combination with phenazone, antipyretic and analgesic
- Dose:
  - Dogs: 7 mg/kg, IM, SD – repeat in 2-4 weeks
  - Cattle: 3.5 mg/kg IM / SC, resistant cases – 7 mg/kg

Quinapyramine – Antitrypanosomal drug

- Available as sulphate and chloride salts in the ratio of 3:2 and marketed as antrycide prosalt.
- Sulphate salt is rapid with short-acting and chloride salt is slow with long-acting effect – curative and prophylactic actions
- MoA: exact mechanism is not known
  - Kinetoplastic DNA condensation
  - Loss of ribosomes with aggregate formation with large no. of lysosomes
  - Trypanostatic, host defence mechanism is important to overcome infection
- Overdosage – intense trembling, salivation, sweating, tachycardia, tachypnoea, collapse and death
- Withdrawal period – 4 days in milk, 21 day for meat
- Cattle and other species – 10 % solution SC, horse -5 % solution IM
- Dose: cattle, horses and other species
  - B.wt. < 150 kg – 4.4 mg/kg
  - 150-200 kg – 1 g (total)
  - 200-350 kg – 1.5 g (total)
  - >350 g – 2 g (total)

Aminophenanthridium – Antitrypanosomal drug

Homidium/Ethidium

- MoA: binding to DNA esp. kinetoplast DNA, interference with glycosomal functions and cell division
- Not absorbed orally, but absorbed by IM route
- Single dose – curative and prophylactic for 1 month
- Dose: Ruminants & Horses – 1 mg/kg, deep IM as a single dose

Isometamidium

- Inhibits DNA functions by binding to kinetoplast DNA
- Very slowly absorbed from IM site, widely distributed , accumulated in liver
- Protection up to 2 months
- Cattle & Horses: 0.5 mg/kg, (treatment), 2 mg/kg (prevention) deep IM

Pyrithidium

- Provide protection up to 6 months
- Cattle & Horses: 2 mg/kg, IM or SC

Carbamide Derivatives – Antitrypanosomal drug

Suramin

- MoA: binds firmly to host plasma proteins – drug protein complex – endocytosis in trypanosomes– releases suramin by lysosomal proteases – inhibit serine oligopeptidase – damage intracellular membrane structure – trypanocidal
- PK: not absorbed orally, IM or SC inj. – localised reaction, IV route only
- Accumulate in phagocytes and proximal renal tubule,PPB>97%
- Low safety margin, idiosyncratic reactions
- Nausea, diarrhoea, seizures, hepatotoxicity, nephrotoxicity and spleen and adrenal damage
- Horses and donkeys – highly susceptible to toxic effects, camels –resistant
- Suramin – synergistic effect with phenanthridium compounds
- Dose:
  - Cattle: 12 mg/kg, slow IV
  - Horses: 7-10 mg/kg, slow IV
  - Camel: 8-12 mg/kg, Slow IV

Antimonial Compounds – Antitrypanosomal drug

Antimony potassium tartrate

- Expectorant, ruminotoric, anthelmintic, antiprotozoal drug
- Dose:
  - Cattle & Horses: 3-5 mg/kg, slow IV
  - Dogs & cats: 1-3 mg/kg, slow IV

Stibophen

- Antifilarial, Antischistosomal and antitrypanosomal properties
- Dogs: 30-50 mg/kg, IV or SC - SD

Other Compounds – Antitrypanosomal drug

Arsenical Compounds

Melarsomin, Melarsoprol

- Used in the treatment of human late stage African trapanosomiasis (sleeping sickness) –Ability to cross BBB.
- Binds to –SH group –Essential for metabolism and inhibit trypanothine oxidase reductase enzyme
- Narrow safety margin

Dyes – Trypan Blue and Red

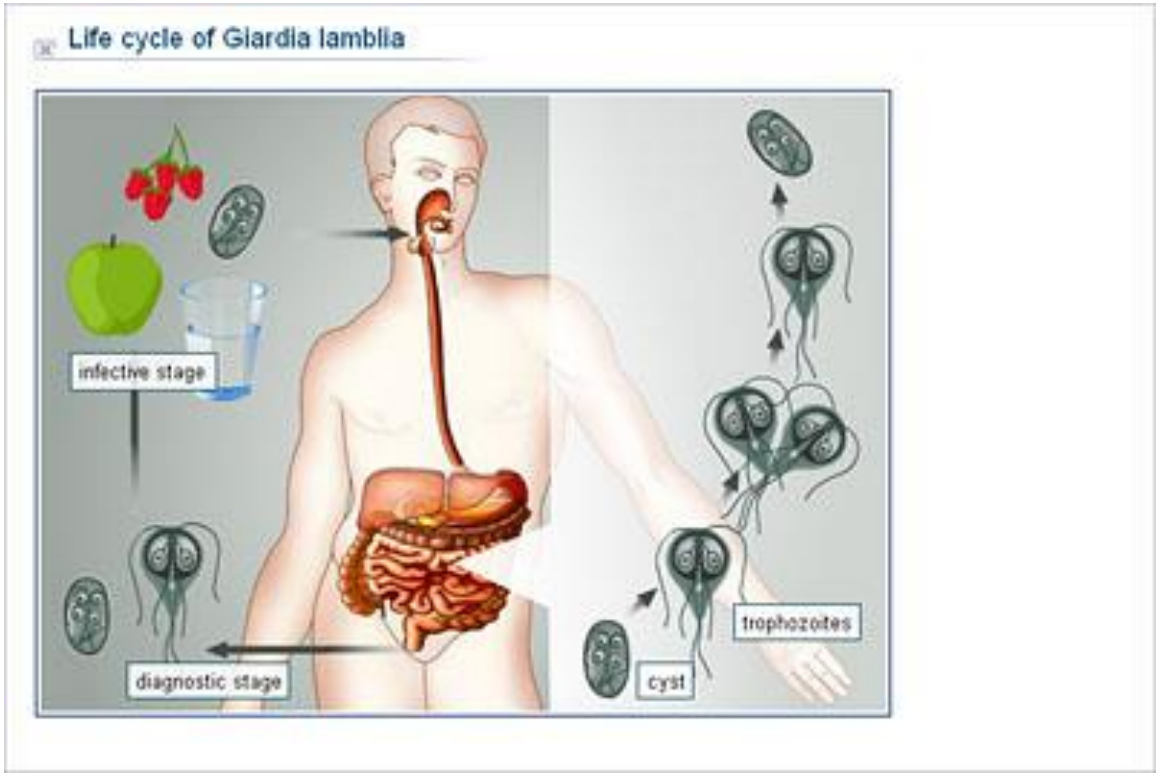
Eflorinithine

- Act on ornithine decarboxylase – regulate cell division in trypanosome
- Effective only against T brucei gambiense (west african) not against East african sleeping sickness (T brucei rhodesiense)
- Also used for facial hirsutism (excess hair growth) – topical

Benzinidazole

- Structural analogue of metronidazole
- Indicated for the treatment of Chagas disease caused T. cruzi (American tryp…)

Anti-Giardial Drugs



Anti-Giardial Drugs

Classification

1. Nitroimidazoles – Metronidazole, Dimetridazole, Tinidazole, etc.
2. Benzimidazoles – Albendazole and Fenbendazole
3. Nitrofurans – Furazolidone
4. Acridine Derivatives – Quinacrine
5. Thiazole Derivatives - Nitazoxamide

Nitroimidazoles - Anti-Giardial Drugs

Antiprotozoal (flagellates and amoebae) and antibacterial activity

Metronidazole

- MoA: unclear, metronidazole is metabolized by org. to intermediate cytotoxic metabolite – interacts with protozoal DNA – loss of helical structure – strand breakage
- PK:
  - F oral – 50-100%, absorption enhances with food in dogs, Tmax – 1h
  - Low PPB, well distributed
  - Metabolised in liver by hydroxylation and conjugation
  - Eliminated in urine and feces in 24 h, t1/2 – 4-5h in dogs, 3-4.5h in horses
  - Colour of urine may become dark due to the metabolites
- Well tolerated at recommended doses, GI disturbances.
- High doses – neutropenia, hematuria, bradycardia, etc.

Nitroimidazoles - Anti-Giardial Drugs

Metronidazole

- DI:
  - Increases bleeding time when combined with warfarin
  - Cimetidine decreases the metabolism of metronidazole
  - Microsomal enzyme inducers decreases the blood conc. of metronidazole
  - Disulfiram-like intolerance to alcohol may occur in human

- Dose:
  - For giardiosis and trichomoniasis –Dogs& Cats: 20 mg/kg, PO – OD 5-8 days
  - For amoebiasis – Dogs: 60 mg/kg, PO OD – 5 days
  - For anaerobic infections
    - Dogs: 25-50 mg/kg, PO –BID
    - Horses: 15-25 mg/kg, PO – QID
    - Birds: 50 mg/kg, PO – OD – 5days

Other drugs

- Tinidazole: Dogs- 44 mg/kg, PO, OD – 3 days, Horses – 15 mg/kg, PO-BID

Benzimidazoles - Anti-Giardial Drugs

Albendazole:

- Active metabolites albendazole sulphoxide and sulphone – antigiardial activity in dogs
- Dogs: 25 mg/kg, PO – BID for 2-3 days

Fenbendazole

- Good safety profile, antigiardial activity
- Dogs: 50 mg/kg, PO – OD for 3 days

Anti-Giardial Drugs

Nitrofurans:

- Furazolidone: antigiardial effect in cats (50 mg/kg, PO, BID for 7-10 days)

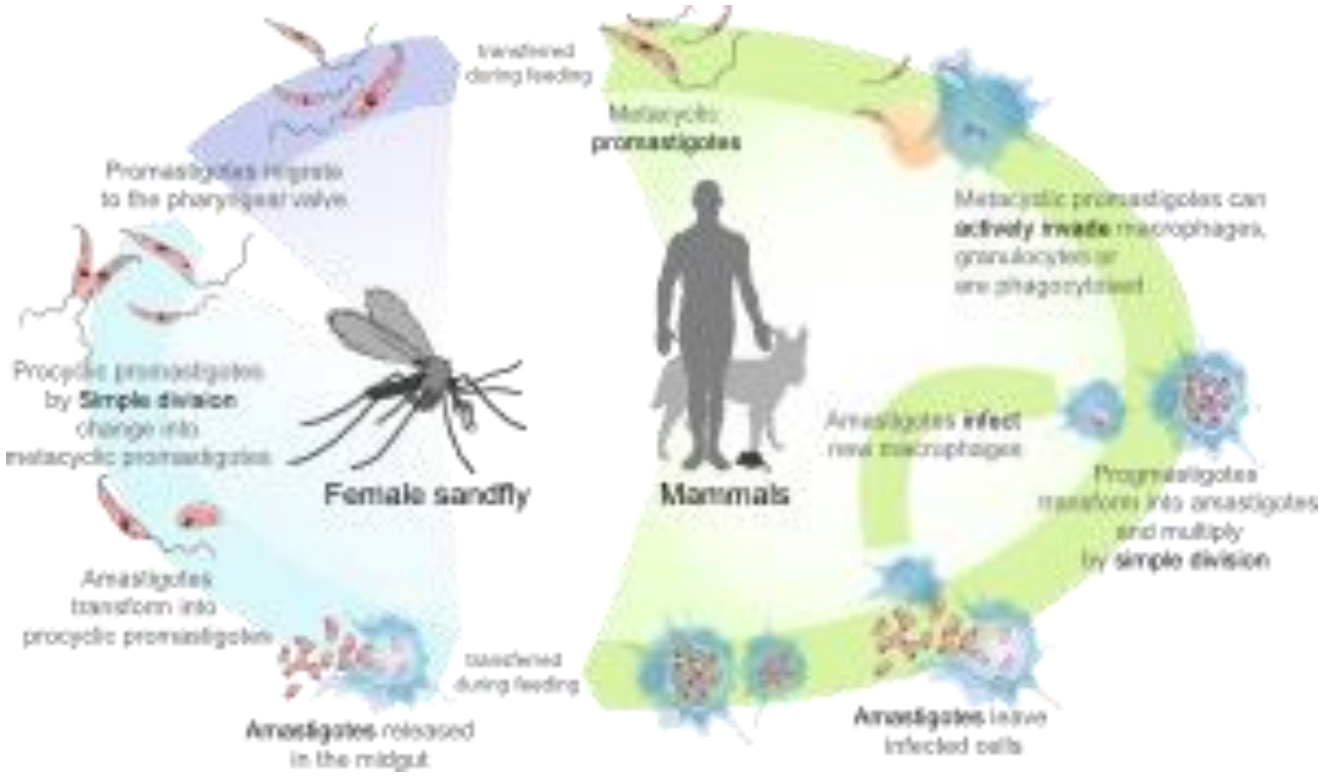
Acridine Derivatives:

- Quinacrine: used in metronidazole resistant giardiosis, intercalates DNA
  - Dogs: 50 - 200 mg, PO, TID on 1st day, followed by BID for next 6 days

Thiazole Derivatives:

- Nitazoxamide is a prodrug – active metabolite- Tetizoxanide
- Inhibits pyruvate-ferredoxin oxidoreductase(PFOR) enzyme dependent electron transfer reaction – anerobic energy metabolism
- Used in human giardial infection

Anti-Leishmanial Drugs



Anti-Leishmanial Drugs

Classification

1. Pentavalent antimonial drugs – Meglumine antimonite and Sodium stibogluconate

2. Aromatic diamidines – Pentamidine

3. Purine analogues – allopurinol

4. Polyene derivatives –Amphotericin B

5. Phospholipids - Miltefosine

Anti-Leishmanial Drugs
Pentavalent Antimonial Drugs

Meglumine Antimonite

- Used in canine leishmaniasis
- MoA: inhibit the action of phosphofructokinase – depletion of energy
- Dogs: 50-75 mg/kg, IM or SC, BID for 10 days or 100 mg/kg – alternate day for 1 month in combination with allopuriol

Sodium stibogluconate

- Phlebotoxic hence diluted in IV fluid and administered IV over 5 min
- Liposomal formulations – to target infected macrophages
- Dogs: 0.1 -0.2 mg/kg, slow IV over 5 min for 20 days

Anti-Leishmanial Drugs

Aromatic Diamidines - Pentamidine

- Used in treating both cutaneous and visceral leishmaniasis
- MoA: Interference with DNA and folate transformation, inhibition of RNA and protein synthesis, alteration in protozoal mitochondrial functions
- Accumulates in liver, kidney and spleen
- Dogs: 3-4 mg/kg, IM on alternate days for max 10 treatments

Purine Analogues - Allopurinol

- MoA: incorporation into the purine salvage pathway – inhibition of protein synthesis – death
- Xanthine urolith formation in acidic urine – adverse effect
- Dogs : 15 mg/kg, PO, BID – 3 to 6 months

Anti-Leishmanial Drugs

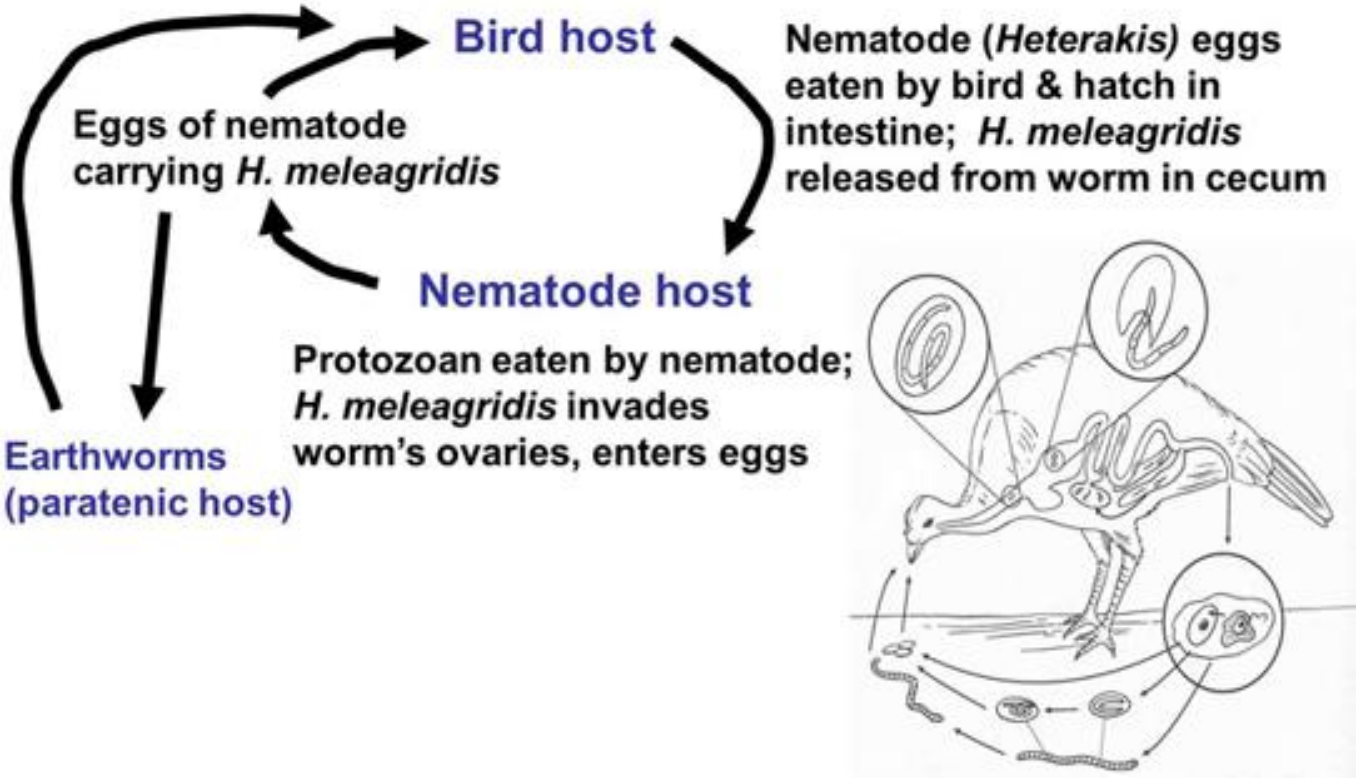
Polyene Derivatives – Amphotericin B

- Antifungal, used in the treatment of visceral leishmaniasis
- Dogs: 0.5 -1 mg/kg, IV

Phospholipids - Miltefosine

- Antineoplastic drug
- MoA: inhibit serine/threonine protein kinase – plays a key role in glucose metabolism, cell proliferation, apoptosis, transcription and cell migration
- Used for visceral and cutaneous leishmaniasis

Anti-Histomonad Drugs
or
Drugs against Blackhead disease in Turkey, Fowl, Quail and Pheasants



Anti-Histomonad Drugs

Classification

1. Nitrothiazoles – Aminonitrothiazole and Nithiazole
2. Nitroimidazoles – Dimetridazole
3. Nitrofurans - Nifursol

Anti-Histomonad Drugs

Nitrothiazoles

- Aminonitrothiazole – 0.1% in water for 14 days (treatment), 0.05% in water for 5 months (prevention) in turkeys
- Nithiazole – 0.04% in feed for 7 days (treatment), for 3 weeks (prevention)

Nitroimidazoles – Dimetridazole

- Inhibit RNA synthesis –
- Used also against Treponema hyodysenterieae (swine dysentry)
- Pre-slaughter withdrawal period – 7 days
- Turkeys, Guinea fowls, Pheasants & Partridges – 150 g/tonne feed

Nitrofurans – Nifursol

- Used as prophylactic drug for histomoniasis in turkeys
- Damage to lipids and DNA in protozoa
- Pre-slaughter withdrawal period – 5 days
- Turkeys – 50 g/tonne feed