Coccidiosis

- Parasitic disease caused by TS. protozoa (Eimeria spp.)
- cause complete destruction mucosal cs of intestine (Intestinal coccidiosis)
- Poultry (Broilers, layers, breeding hens, turkeys, pigeon & ducks)
- animals (cattle, sheep, Goats & dogs)
- Rabbits (hepatic coccidiosis - liver c.)
- Great Economic losses
Clinical Signs

typical position

ruffled feathers

difficulty staying on legs

closed eyes
1. Economic losses - decrease b. wt. immunosuppressive effect.
2. Deaths - severe bloody diarrhea (E. tenella, caecal coccidiosis)

Transmission: Infection transmitted by ingestion of sporulated oocysts with stools of diseased A.

Causes of Coccidiosis Among chickens:
- E. tenella
- E. maxima
- E. bruniti
- E. mitis
- E. necatrix
- E. acervulina
- E. mivata
Causes of Coccidiosis

Among turkeys

- E. meleagrimitis
- E. Adenooides
- E. gallepalenis

Among rabbits

- E. stadae (Hepatic cocc.)

Among cattle

- E. bovis
Coccidiosis (site parasitized by *Eimeria tenella*), poultry
Gross lesions of *E. tenella* with frank haemorrhaging into cecal pouches, broiler chicken.
COCCIDIOSIS in poultry parasitized by E.necatrix
Coccidia has 2 stages in its life cycle of Eimeria species (7 days)

Life cycle of Eimeria species

1 Asexual stage Schizogony stage

2 Sexual stage Sporogony stage
LIFE CYCLE OF EIMERIA Spp

Day 1
Oocysts  →  sporozoites

Day 2
Trophozoites  →  Schizonts  →  Merozoits

Day 3

Day 4
1st Asexual C →  Sexual C →  2nd Asexual C

Day 5
2nd SCHIZONTS  →  Merozoits

Day 6
Toltrazuril  →  Microgametes →  Macrogametes

Day 7
sporulated oocystes

Sulphonamides  →  Ethopobates  →  Dicalzuril  →  Diverdine  →  Pyrimethamine

Amprolium, Zoaline  →  Ionopores  →  Clopidol
Control of avian coccidiosis

- Destruction of oocysts in poultry houses using disinfectants
- Prevention: Coccidiostate in feed
- Vaccination layers
- Treatment of infected flocks by drugs
Action of Anticoccidial Drugs

1. *Coccidiostates*
   - *Drugs which arrest or inhibit*
   - *the growth of intracellular coccidia*

2. *Coccidiocidals*
   - *Drugs which kill or destroy intracellular coccidia during growth.*
Control of coccidiosis in poultry

**Prevention/Prophylactic**

- Used in (1) Broilers from 1 day until 45th day old
- (2) Breeders until 16th week old
- *Medicated Feed Additives*
  - Ethopobate
  - Diaveridine
  - TOLTRAZURIL (Bycox)
  - Amprolium
  - Sulphonamides

**Treatment in outbreaks**

- e.g. Sulphonamides
- Ethopobate
- Diaveridine
- TOLTRAZURIL (Bycox)
- Amprolium hydroch

**Ionophores**

- Monensin
- Narasin
- Maduramycin
- Semduramicin
- Salinomycin
- Lasalocid

**Polyether antibiotic**

**Chemical anticoccideals**

- Nicarbazine
- Amprolium
- Clopidol
- Robinidine
- Halofuginen
- Dicalzuril
- Methyl benzoquate
### Chemicals

- Nicarbazin *(NICARB)*
- Clopidol *(COYDEN)*
- Halofuginon *(STENOROL)*
- Amprolium *(AMPROL)*
- Robenidine *(CYCOSTAT)*
- Diclazuril *(CLINACOX)*

### Ionophores

- Monensin *(COBAN)*
- Narasin *(MONTEBAN)*
- Lasalocid *(AVATEC)*
- Salinomycin *(COXISTAC)*
- Maduramycin *(CYGRO)*
- Semduramycin *(AVIAX)*
1- **Ionophores (Polyether Antibiotics)**

- Antibiotics extracted from *actinomyces* spp.
- Commonly used as Preventive (prophylactic) effective coccidiostate as medicated feed (premix) in broilers and replacement layers or breeders up to 16\(^{th}\) week of age.
- **Monensin** act as growth promoters in calves
- **Salinomycin** & **Maduramycin** as growth promoters in broilers
- **Low therapeutic index** & double therapeutic dose → Toxicity
  - Should mixed well with feed to minimize side effects
Ionophores Mechanism of action

- MOA: interfering with transport of K+ & Na+ ions through E. membrane → influx of positively charged ions → upset of osmotic balance
- Causing disturbances mitochondrial function of intracellular coccidian (Selective to E. spp.)
- Ionophores activity on Asexual stage ↓ Sporozoites merozoites development in first 2 days of c. L.C.
Pharmacokinetics:

- Ionophores poorly absorbed from GIT after oral administ.
- Short withdrawal time (3-5days).

Contra-indications:

1. Should not mixed with other anticoccidials
2. Not given with “Taimulin” to prevent cardiac toxicity

Toxicity:

1. A narrow safety margin should mixed well with feed.
2. Cardiac toxicity as result of ionic disturbances.
3. Immunosuppression → failure of vaccination
## Ionophores

<table>
<thead>
<tr>
<th>Name</th>
<th>Source</th>
<th>Action</th>
<th>Resistance</th>
<th>Withdrawal Time</th>
<th>Uses and Dosage</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- Monensin (Monovalent polyether)</td>
<td>Streptomyces Cinammonensis</td>
<td>Effective against all types of Eimeria species. Growth promoters for cattle by helping the production of ruminal propionic acid.</td>
<td>Cross resistance with Lasalocid. Resistance against E. tenella occurs.</td>
<td>3 days</td>
<td>Preventive for broilers 100-120 ppm in feed (55 days). Replacement years 100-120 ppm continuously up to 16 week of age.</td>
<td>- Not to be given to laying hens produce eggs for human consumption.</td>
</tr>
<tr>
<td>2- Lasalocid (Divalent Pothyether).</td>
<td>Streptomyces Lasaliensi</td>
<td>Effective against Eimeria species</td>
<td>Resistance of some strains has been recorded.</td>
<td>5 days</td>
<td>As Monensin Dose : 75-90 ppm.</td>
<td>- Not to be given to other breeds of poultry or animals.</td>
</tr>
<tr>
<td>3- Salinomycin</td>
<td>Streptomyces albus</td>
<td>Act as preventive against coccidiosis in broilers Effective against all Eimeria species Growth promoter in broilers.</td>
<td></td>
<td>5 days</td>
<td>in Broiler 60 ppm in feed continuously as directive or rotation or shuttle program.</td>
<td>- Not used in layers or breeder or animals species. - Not used with other anticoccidials.</td>
</tr>
<tr>
<td>Name</td>
<td>Source</td>
<td>Action</td>
<td>Resistance</td>
<td>Withdrawal Time</td>
<td>Uses and Dosage</td>
<td>Contraindications</td>
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<tr>
<td>4- Narasin</td>
<td>Streptomyces</td>
<td>Effective against intestinal and caecal coccidiosis only in broilers.</td>
<td>-</td>
<td>5 days</td>
<td>Broilers 70 ppm in feed continuously till the 55th of age.</td>
<td>Not used in laying hens</td>
</tr>
<tr>
<td></td>
<td>aureofaciens</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5- Maduramicin</td>
<td>Actionmadura</td>
<td>Effective against all species of Eimeria. More potent than other types.</td>
<td>-</td>
<td>5 days</td>
<td>Broilers 5 ppm feed continuously</td>
<td>Not given to laying hens</td>
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<tr>
<td>6- Semduramicin</td>
<td>Actinomadura</td>
<td>Highly effective against all Eimeria species infecting poultry. Growth promoter</td>
<td>No resistance occurs</td>
<td>5 days</td>
<td>Broiler: As preventive against coccidiosis. Dose: 25 ppm in poultry feed Layers and Breeder 25 ppm in feed.</td>
<td>Can be used without side effects in layers and breeders.</td>
</tr>
</tbody>
</table>
Folic acid antagonists
**Sulphonamides & ethopabate**

- **sulphadimethoxine**, **sulphaquinoxaline**, **sulphachloropyrazine**, **Sulphadimidine**,

- **Action**: *antibacterial* & *anticoccidial* actions.

- First synthetic anticoccidials used successfully for **treatment of coccidiosis** in all animals & poultry.

- More effective against intestinal than caecal coccidia in chickens – large dose treat both caecal & intestinal coccid.

- Systemic sulphonamides for **ttt hepatic coccidiosis in rabbits**

Prof.Dr/ Nehal  4/29/2014
- **MOA:** Sulphonamide interfere with utilization PABA $\rightarrow$ essential for formation of folic acid $\rightarrow$ formation of RNA of E.spp. (coccidiostate)

- Sulpha drugs produce action by destroying schizonts containing merozoites (3rd day of L.C.)

- Vitamin antagonists (Amprolium & Diaveridine) potentiate sulph. action (synergistic effect, coccidocidal) for treating caecal coccidiosis (E. tenella).

- Sulpha drugs not used for treatment of coccidia in laying hens producing egg for human consumption.

- Sulpha drugs adminst. as WSP in drinking water for poultry
Diaveridine - Ormethoprim & Pyrimethamine

- Active against the protozoan enz dihydrofolate reductase.
- Have synergistic activity with sulfonamides.
- Used as coccidiostates alone or in combination with sulpha drugs (sulphadimidide, sulphaquinoxaline).
- D. interferes with transformation of dihydrofaltalate into tetrahydrofaltalate (Folinic acid) by antagonizing dihydrofaltalate reductase enz. → subsequently reduce RNA.
Vitamin Antagonists

Amprolium hydrochloride

- Amprolium has a safety margin ~8:1 when used at the highest level in feed (125–250 ppm).
- **Amprolium** is a **Coccidiostate** used for prevention & treatment of broiler chickens, laying hens, turkeys, sheep, goats, calf.
- Because amprolium has poor activity against some Eimeria spp, its spectrum extended by using it with folic acid antagonists, ethopabate & sulfaquinoxaline.
- The primary use of amprolium (in water) for treatment during outbreak.
- **MOA:** Amprolium a thiamine (vit B1) analogue → competitively inhibit thiamine utilization by coccidia.
Amprolium hydrochloride (Amprol)

- Chemical anticoccidial mixed with poultry feed or administered in drinking water.
- Amprol act on 1st generation schizont to prevent merozoite formation + activity against sexual Stage & sporulated oocyst.
- Used as mixture with Ethopabate as preventive
- For treatment of outbreaks mixed with sulpha
- Amprolium used safely in laying hens in feed (prevention) or in drinking water for treatment
- Amprolium has no withdrawal time.
Clopidol & quinolines (eg, Decoquinate, Methylbenzoquate)

- Coccidiostatic against early development of Eimeria spp by inhibiting mitochondrial energy production.
- Inhibit the mitochondrial respiration of E. by antagonizing the invasion of sporozoites in the first day of life cycle.
- **Clopidol & quinolines** have a broad species spectrum & mixed together for synergism as preventive medicated feed→ resistance develop rapidly

**Clopidol**
- Coccidiostate against sporozoites in 1st day of L. C. E. Spp.
- Cross resistance with other chemical anticoccidials
- used in combination with methyl benzoquate as feed premix in broilers & replacement flock up to 16 wk.
Halofuginone hydrobromide

- **Halofuginone** related to the antimalarial drug febrifuginone
- Effective against asexual stages of most species of Eimeria.
- has both coccidiostatic & coccidiocidal effects
- coccidia become resistant after extended exposure
Robindine

- A guanidine comp, allows initial intracellular development of coccidia but prevent formation of mature schizonts.
- Both coccidiostatic if given short term & coccidiocidal long term.
- Effective against intestinal & caecal coccidia in poultry, & rabbits.
- A primary coccidiostatic, acting on 1st generation schizonts & coccidiocidal against 2nd generation schizonts.
- MOA: inhibits the oxidative phosphorylation of Emeria sp.
- A 5-day withdrawal period to eliminate untoward flavor caused by residues in poultry meat.
- Drug resistance develop during use.
Nicarbazin

The first product to have truly broad-spectrum activity

- **Coccidioidal** against E. spp. used as preventive premix in broiler
- **MOA:** acts by suppression development of 2nd generation-schizonts. via inhibition of succinate-linked nicotinamide adenine dinucleotide reduction & the energy-dependent transhydrogenase, and the accumulation of calcium in the presence of ATP.

- Nicarbazin toxic for layers, causing mottling of egg yolks, decrease egg production and hatchability & blanching of brown egg shells.

- A 4-day withdrawal period is required in broilers.

- Medicated birds at increased risk of heat stress in hot weather.

- Cause stress when mixed with feed in summer.
Diclazuril (Benzen acetonitrile)

- **Preventive** against coccidiosis
- **Action:**
  - **Diclazuril** is very active against all species of Emeria infecting chickens, turkeys and rabbits.
- **MOA:** **Diclazuril** act against zygots (gametocytes)
- **Doses:** 1 ppm in feed for Broilers, Turkeys and Rabbits
• Toltrazuril Act as coccidicidal for treatment of coccidiosis particularly due to E. tenella.

• Toltrazuril Used in drinking water for treatment in chicken, rabbits and turkeys.

• Doses: 25 ppm in water for 1 - 2 days.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Use Level (% in feed)</th>
<th>Withdrawal Time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amprolium</strong></td>
<td>0.0125–0.025</td>
<td>0</td>
</tr>
<tr>
<td><strong>Amprolium + ethopabate</strong></td>
<td>0.0125–0.025 + 0.0004</td>
<td>0</td>
</tr>
<tr>
<td><strong>Clopidol or meticlorprindol</strong></td>
<td>0.0125–0.025</td>
<td>0</td>
</tr>
<tr>
<td><strong>Decoquinate</strong></td>
<td>0.003</td>
<td>0</td>
</tr>
<tr>
<td><strong>Diclazuril</strong></td>
<td>0.0001</td>
<td>0</td>
</tr>
<tr>
<td><strong>Dinitolmide (zoalene)</strong></td>
<td>0.004–0.0125</td>
<td>0</td>
</tr>
<tr>
<td><strong>Halofuginone hydrobromid</strong></td>
<td>0.0003</td>
<td>4–7</td>
</tr>
<tr>
<td><strong>Lasalocid sodium</strong></td>
<td>0.0075–0.0125</td>
<td>3</td>
</tr>
<tr>
<td><strong>Maduramicin ammonium</strong></td>
<td>0.0005–0.0006</td>
<td>5</td>
</tr>
<tr>
<td><strong>Monensin sodium</strong></td>
<td>0.01–0.0121</td>
<td>0</td>
</tr>
<tr>
<td><strong>Narasin</strong></td>
<td>0.006–0.008</td>
<td>0</td>
</tr>
<tr>
<td><strong>Narasin + nicarbazin</strong></td>
<td>0.003–0.005</td>
<td>5</td>
</tr>
<tr>
<td>Drugs</td>
<td>Feed or Water</td>
<td>Active Ingredient: Treatment, Duration</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Amprolium</td>
<td>Water</td>
<td>0.012–0.024%, 3–5 days; 0.006%, 1–2 wk</td>
</tr>
<tr>
<td>sulfachloropyrazine monohydrate</td>
<td>Water</td>
<td>0.03%, 3 days</td>
</tr>
<tr>
<td>Sulfadimethoxine</td>
<td>Water</td>
<td>0.05%, 6 days</td>
</tr>
<tr>
<td>Sulfamethazine (sulfadimidine)</td>
<td>Water</td>
<td>0.1%, 2 days; 0.05%, 4 days</td>
</tr>
<tr>
<td>Toltrazuril</td>
<td>Water</td>
<td>25 ppm, 2 days</td>
</tr>
</tbody>
</table>
Anticoccidial drugs-resistant

- Continuous use of anticoccidial drugs promotes drug-resistant to coccidial strains.
- Various programs used to slow or stop resistance.
  1. The use one anticoccidial continuously through succeeding flocks, change to alternate anticoccidials every 4–6 mo.
  2. Change anticoccidials during a single growout (shuttle prog).
- Little cross-resistance to anticoccidials with different modes of action, but a widespread resistance to most drugs.
- Coccidian tested in lab. to determine the most effective prods.
- **Shuttle programs** is common practice & offer benefit in slowing the resistance. in which 1 group of chickens is treated sequentially with different drugs (usually a change between starter & grower rations),