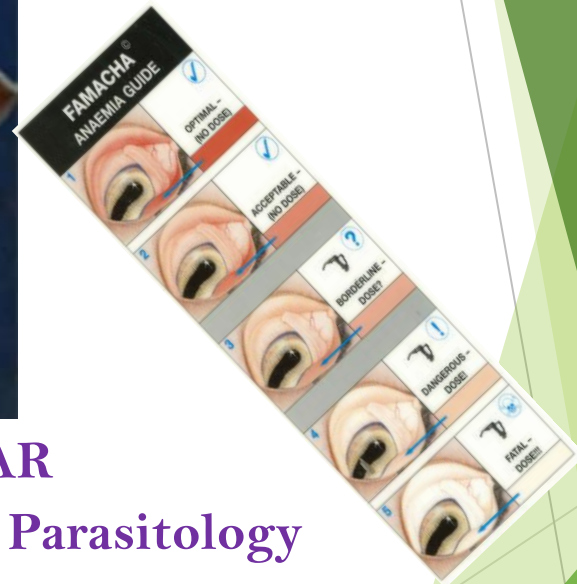




Anthelmintic Resistance



Fenbendazole

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Anthelmintics

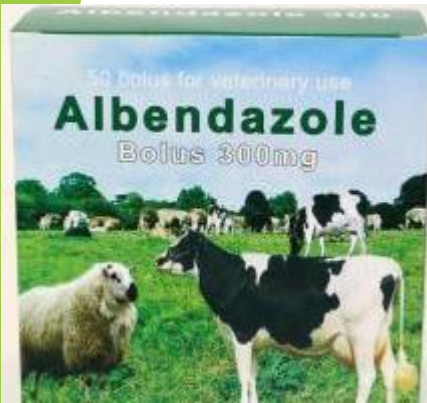
- Drugs use to expel the helminth parasites from the body of the host by either stunning or killing are called Anthelmintics
 - e.g. Albendazole, Levamisole, Piperazine salts etc.
- They may also termed vermifuge (those that stun) or vermicide (those that kill).
- First chemical class of modern anthelmintics developed was the benzimidazoles.
- Thiabendazole was first drug introduced in this class (benzimidazoles) in 1961.



Anthelmintics

Chemical groups	Examples	Mechanism of action
Benzimidazoles	Thiabendazole, Mebendazole Fenbendazole, Albendazole, Triclabendazole, Oxfendazole & Oxibendazole	Interfere with energy metabolism by inhibition of polymerization of microtubules leads to starvation of parasite. Wide margin of safety and frequently develop resistance against nematodes of sheep and horses.
Imidazothiazoles	Tetramisole and Levamisole	Cholinergic agonists result in spastic paralysis
Tetrahydropyrimidines	Morantel and Pyrantel	Acetylcholine agonist and depolarizing neuromuscular blocking which result in spastic paralysis.
Organophosphates	Dichlorvos, Haloxon and Trichlorphon	Cholinesterase Inhibitor and causes spastic paralysis
Piperazines	Piperazine salts	Anticholinergic action – block neuromuscular transmission leads to flaccid paralysis.
Macrocyclic Lactones (Macrolides)	Ivermectin, Doramectin, Moxidectin and Selamectin	Potentiate GABA or bind to glutamate chloride channels causing flaccid paralysis
Salicylanilides or substituted phenols	Niclosamide, Oxyclozanide, Closantel and Rafoxanide	Interfering ATP production in parasites by uncoupling oxidative phosphorylation.
Isoquinolones	Praziquantel and Epsiprantel	Paralysis and tegumental destruction of parasite

Anthelmintic



- **Anthelmintics are still considered as the most important control measures against parasitic infections.**



Anthelmintic Resistance

- ⌚ Anthelmintic resistance is a heritable change in the ability of individual parasites to survive the recommended therapeutic dose of an anthelmintic drug.
- ⌚ First report of anthelmintic resistance in India was in *Haemonchus contortus* by Varshney and Singh against phenothiazine and thiabendazole in sheep in 1976.

Anthelmintic Resistance

- ⌚ Resistant worms pass their resistant genes onto offsprings (resistance is permanent)
- ⌚ Resistance cannot be prevented but can be slowed down

Anthelmintic Resistance

Types of Anthelmintic Resistance:

- ⌚ **Side resistance:** When parasite strain is resistance to chemically related drugs having similar mode of action. e.g. A parasite strain resistant to Fenbendazole shows resistance to Thiabendazole.
- ⌚ **Cross Resistance:** When a parasite strain is resistant to chemically unrelated drug with different mode of action. e.g. parasite strain resistant to Fenbendazole shows resistance to Tetramisole.
- ⌚ **Multiple resistance:** When a parasite strain is resistant to two or more chemically unrelated anthelmintic groups with different mode of action. e.g. A parasite strain resistant to Fenbendazole shows resistance to Levamisole and Ivermectin also.

Anthelmintic Resistance

Reasons of Anthelmintic resistance:

- ⌚ Repeated use of the same class of anthelmintic
 - ⌚ Under dosing of anthelmintic
 - ⌚ Drenching of goats with anthelmintics at doses recommended for sheep and cattle
 - ⌚ anthelmintic drenches after feeding and poor administration of oral drenches
- are the factors responsible for development of anthelmintic resistance.

Anthelmintic Resistance

Four mechanisms by which the parasite exhibit resistance to anthelmintics:-

- Drug inactivation or modification,
- Alteration of target site
- Alteration in metabolic pathways
- Reduced drug accumulation by decreasing drug permeability or increasing the active efflux of the drug across the surface.

Anthelmintic Resistance

- ⌚ Based on published data, *Haemonchus contortus* seems to be the species most involved in case of anthelmintic resistance.
- ⌚ Indigenous breed of East Africa, Red Masai is the most resistant and the Hampshire Down being least resistant breed of sheep to *Haemonchus contortus* infection.
- ⌚ **Refugia** term used to describe the proportion of a parasite population that is not exposed to a particular drug, thereby escaping selection for resistance.
- ⌚ **Role of Refugia** is in preventing anthelmintic resistance.

Anthelmintic Resistance

Techniques for Detection of Anthelmintic Resistance

Method	Technique	Anthelmintic
<i>In vivo</i> tests	Faecal egg count Reduction test (FECRT-most common), Critical Anthelmintic Test & Controlled Anthelmintic Efficacy Test	All groups of anthelmintic
<i>In vitro</i> tests	Egg Hatch Assay (EHA)	Benzimidazole Levamisole
	Tubulin Binding Assay	Benzimidazole
	Larval Paralysis Test	Levamisole
	Larval Migration Inhibition Assay (LMIA)	Ivermectin/Levamisole
	Larval Feeding Inhibition Assay (LFIA) Larval Development Assay (LDA, DrenchRite Assay)	All groups of anthelmintic

Anthelmintic Resistance

⌚ According to WAAVP, $FECRT \% = 1 - (X_t/X_c) \times 100$,
where,

X is the anthelmintic mean EPG 10-14 days post-treatment,

t is the treated and c is the control group.

For the application of this test, the mean faecal egg counts (FEC) should be at least 150 eggs per gram.

Anthelmintic Resistance

Quantitative Examination of Faeces

Egg Counting Methods:

Mc Master Method:-

Procedure -

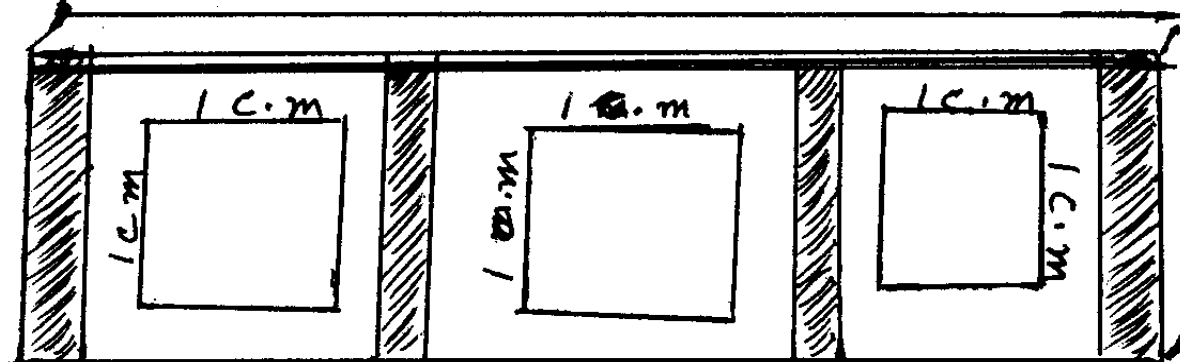
- In this method a special counting is used for the estimation of no. of egg or larvae per gram of faeces.
- Counting slide having two counting chamber is made of two glass slides separated by three or four narrow transversely placed strips of glass 1.5 mm thick, so that two or three spaces of 1.5 mm depth are obtained between the two slides. On the under surface of the upper slide an area of 1 cm² is ruled over each space.
- The volume underneath this ruled area will therefore be 0.15 ml.

Anthelmintic Resistance

Quantitative Examination of Faeces

Egg Counting Methods:

Mc Master Method:-



Mc Master Slide

Anthelmintic Resistance

Quantitative Examination of Faeces

Egg Counting Methods:

Mc Master Method:-

Procedure -

- Weigh 3 g of faeces and add 42 ml water in a container.
- Homogenize and pour the suspension through a tea strainer.
- Take 15 ml of the filtrate in to a centrifuge tube and centrifuge at 2000 rpm for 2 minutes.

Anthelmintic Resistance

Quantitative Examination of Faeces

Egg Counting Methods:

Mc Master Method:-

Procedure -

- Pour off the supernatant, agitate sediment and add saturated sodium chloride solution to 15 ml mark of centrifuge tube.
- Mix the solution thoroughly and fill the chambers of Mc Master slide.
- Examine one chamber under microscope and multiply number of eggs or larvae under one etched area by 100 or two chambers and multiply by 50 to arrive at the number of eggs per gram (EPG) of faeces.

Anthelmintic Resistance

Eggs per gram (EPG) counts in different animals Vs levels of infection: -

Parasite	Animal	level of infection		
		Mild	Moderate	Severe
Nematodes	Cattle	50-300	300-600	>600
	Sheep	100-500	500-2000	2000-6000
	Horse	500	800-1000	1500-2000
<i>Fasciola</i> spp.	cattle	10-100	100-200	>200
	Sheep	50-300	300-600	>600

Anthelmintic Resistance

Management of Anthelmintic Resistance :

- ✓ Strategic drenching based on epidemiological studies,
- ✓ Annual rotation of anthelmintic class,
- ✓ Never underdose instead of give full therapeutic dose of an anthelmintic recommended by the manufacturer,
- ✓ Simultaneous use of combinations of two anthelmintics which have different mode of action.

Anthelmintic Resistance

Practices that help slow development of drug Resistance :

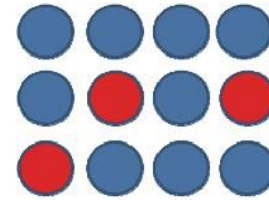
- Targeted, selective treatment
- Leaving some animals untreated
- Dosing based on accurate weight
- Depositing drug over tongue
- Leaving treated animals in dry lot or barn for 48 hours
- Fasting animals when using benzimidazoles or avermectins

Anthelmintic Resistance

Targeted Selective Treatment (TST)

- ✓ Treating only animals that require or will benefit from the treatment.
- ✓ This reduces the use of anthelmintics and maintains some animals in-refugia (animals with worms unexposed to drug).
- ✓ This approach slows development of anthelmintic resistance.

Parasite population within the herd:

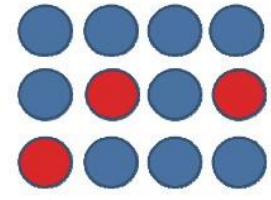


Treat entire herd, so no refugia is preserved.

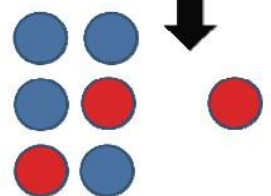


All susceptible parasites die. Only resistant parasites remain to breed and pass on resistance genes to their offspring.

Parasite population within the herd:



Treat only 50% of herd, so some refugia is preserved.



Some susceptible parasites remain to dilute the resistant parasites, slowing the development of a fully resistant parasite population.

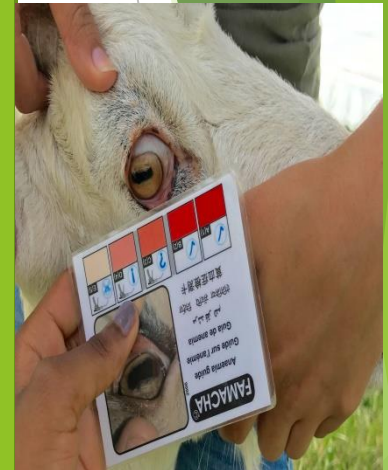
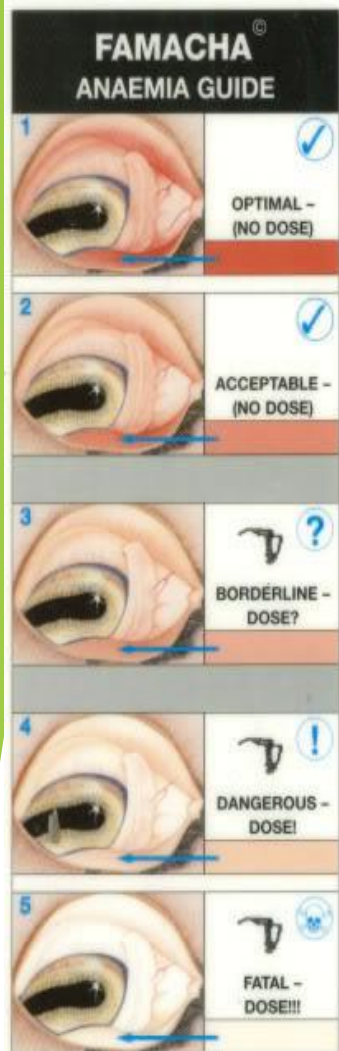
Key:

● Susceptible parasite ● Resistant parasite

Anthelmintic Resistance

FAMACHA (Faffa Malan CHArt)

- It is an acronym derived from the name of the originator of the idea, Dr Faffa Malan (Faffa Malan CHArt).
- It helps in to select blood sucking nematodes (*Haemonchus* sp. only) infected animals for anthelmintic intervention.
- It is a system whereby you examine the lower eyelid of the sheep /goat and administer treatment only if signs of anaemia are present.
- Animals with red color can be left untreated, whereas paler scores indicate that an animal should be treated.
- Only animals whose PCV are 15% or below are drenched.
- Reduces the number of treatments and saves anthelmintic usages.
- FAMACHA system was developed for sheep but do work with goat with slight modifications.





**THANK
YOU**