ANTIPARASITIC RESISTANCE

RECENT HISTORY AND RESPONSIBLE USE

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Overview

Antiparasitic resistance is a global issue for grazing livestock

- Defining antiparasitic resistance
- Brief history of antiparasitic resistance in North America and globally
- Methods for slowing the development of antiparasitic resistance on a farm

Background

- **Common gastrointestinal nematodes (roundworms) of grazing livestock**
  - Haemonchus*
  - Trichostronglyus*
  - Ostertagia*
  - Cooperia
  - Strongylus vulgaris*
  - Cyathostomes
  - Parascaris equorum

*most pathogenic

Background

- Internal parasitism has a large impact on livestock owners

- Results in:
  - Weight loss
  - Decreased milk production
  - Decreased fertility
  - Increased susceptibility to other diseases
  - Death

Background

- **Major antiparasitic drug classes**

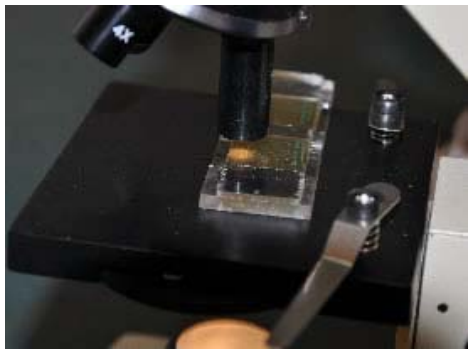
Antiparasitic Drug Class	Examples
Benzimidazoles	Thiabendazole, albendazole, fenbendazole, oxfendazole, oxibendazole
Imidazothiazoles	Levamisole
Tetrahydropyrimidines	Morantel tartate, pyrantel
Macrocyclic lactones	Ivermectin, doramectin, eprinomectin, moxidectin
Piperazines	Piperazine
Isoquinolones	Praziquantel*

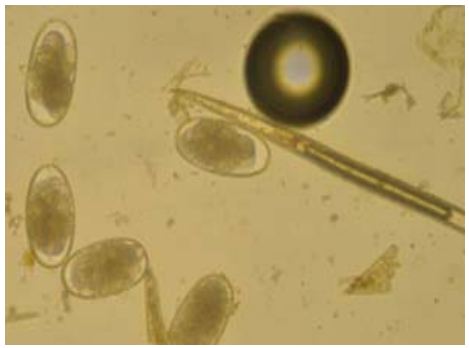
Defining antiparasitic resistance

- **Definition:**
  - Ability of a parasite to survive treatment with an antiparasitic drug that is generally effective against the same parasite species at the same dose and against the same stage of infection.
    - **Due mostly to gene mutations in the parasite which are passed to subsequent generations of parasites**

Measuring antiparasitic resistance

Fecal egg count reduction test:
Egg reduction < 90% post-treatment indicates antiparasitic resistance





First global reports of antiparasitic resistance (Kaplan 2004)

Drug	Host	Year of initial drug approval *not necessarily in US	First published report of resistance
Benzimidazoles			
Thiabendazole	Sheep	1961	1964
	Horse	1962	1965
Imidothiazoles-tetrahydropyrimidines			
Levamisole	Sheep	1970	1979
Pyrantel	Horse	1974	1996
Macrocyclic lactones			
Ivermectin	Sheep	1981	1988
	Horse	1983	2002
Moxidectin	Sheep	1991	1995
	Horse	1995	2003

Antiparasitic resistance: North America

Small ruminants:

- The HOT (Haemonchus, Ostertagia [Teladorsagia], Trichostrongylus) complex is the primary concern
- Since 2003, resistance well-documented and widespread, mostly in Southeast U.S.

First case of TOTAL antiparasitic failure in U.S. in goats: 2004

Antiparasitic resistance: North America

Cattle:

- 2009 data confirmed resistance to macrocyclic lactones across 9 states
- *Cooperia* spp. resistance becoming a problem

Antiparasitic resistance: North America

Horses:

- Resistance in small strongyles to benzimidazoles is high throughout the country
- Overall equine nematode resistance to antiparasitics in U.S. uncertain

Antiparasitic resistance: South America

Cattle:

Country	Antiparasitic class	Route of administration	# of farms with antiparasitic resistance	Nematode species/genera
Argentina	ML, BZ	Injectable, oral	16	*Cooperia* spp., *Ostertagia ostertagi*
Brazil	ML	Injectable	23	*Cooperia* spp., *Haemonchus* spp., *Oesophagostomum* spp.

Antiparasitic resistance: South America

Sheep in Argentina:

	Farms with resistance detected
Buenos Aires	7/32
Corrientes	19/20
Entre Rios	5/10
Flock size	
< 100	3/7
100 – 500	6/29
500 – 1000	2/6
> 1000	16/19
# treatments per year	
< 4	14/41
> 4	21/25

Antiparasitic resistance: Europe/Asia

- In general, antiparasitic resistance in Europe is relatively low, however:
  - 2007 report of resistance to all 3 major anthelmintic classes in Scotland (Sargison, et al 2007); other sporadic reports elsewhere
- Reports of antiparasitic resistance in India, Middle East
  - 2015 report from India demonstrating resistance in sheep to levamisole and albendazole (Manikkavasagan, 2015)

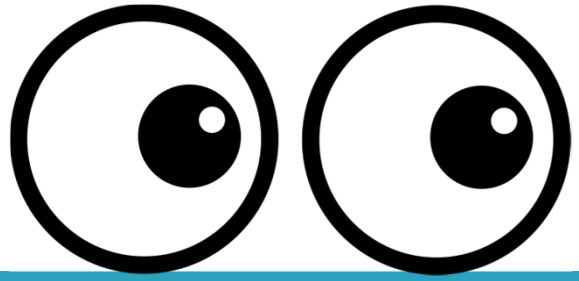
Antiparasitic resistance: Australia/New Zealand

- Cattle: in the North Island of NZ, a reduction in FEC of > 95% was demonstrated in only 7% of beef cattle farms (4/61) for albendazole, levamisole, ivermectin.
- Sheep: very serious growing problem:
  - 2000, 40% sheep farms in Western Australia had avermectin-resistant *T. circumcincta*
  - 2005, 60%
  - 2012, estimated 80% of farms

Antiparasitic resistance: Africa

- First case of ivermectin resistance in sheep reported by Van Wyk in South Africa in 1987
- Reports of antiparasitic resistance from other African countries
  - Primarily from Kenya and South Africa
  - Mainly in sheep
  - *Haemonchus contortus*

Uncertainty!



Parasitologists are uncertain of the current prevalence and distribution of antiparasitic resistant parasites in the U.S. in livestock species, particularly beef cattle and horses

KEY: you only find antiparasitic resistance when you look. Many countries don't have the personnel, infrastructure, or tools to look for resistance

History of U.S. antiparasitic use

- **Recent history:**
  - Ivermectin and other macrocyclic lactones (MLs) were highly effective when first approved in 1980s/1990s
  - Producers became heavily dependent on drugs for control of parasites, resistance has spread

Factors contributing to antiparasitic resistance

- **Parasite factors**
  - Genetics, biology
- **Management factors**
  - Treating too frequently
  - Under-dosing
- **Drug factors**
  - Sub-therapeutic drug levels after initial therapeutic level

Responsible use

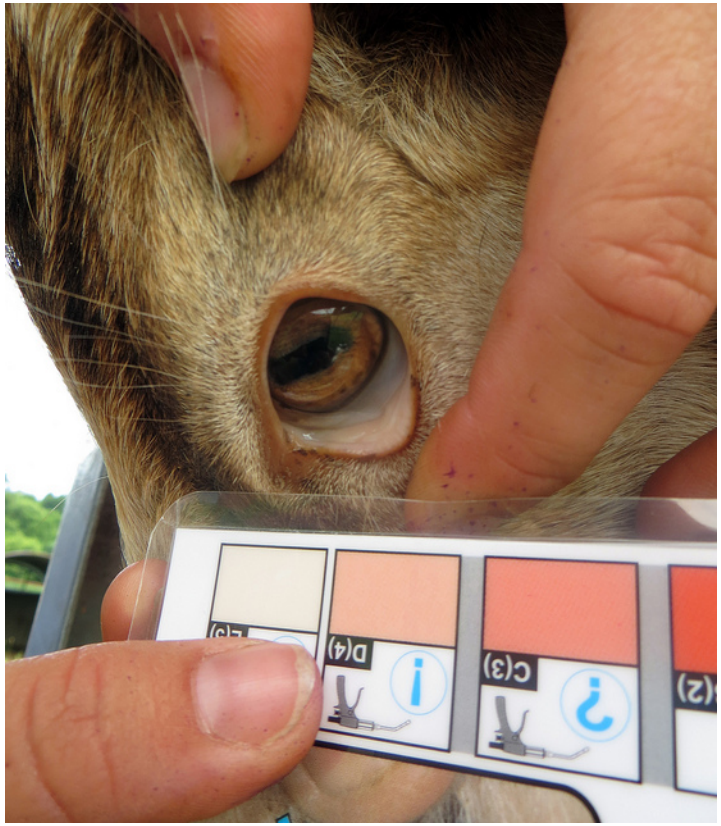
Need for a change in the way veterinarians and producers view parasites:

From parasite elimination to parasite control

Evaluating parasitism

- Weight loss/body condition score
- Diarrhea scores
- Poor coat
- Bottle jaw
- Fecal egg counts
- Age of animal/susceptibility risks

Evaluating parasitism: FAMACHA



Responsible management

- Weigh/weight tape animals to ensure proper dosing
- Follow label directions for adequate administration
- Quarantine new livestock, if possible
- Reduce grazing density on pastures, if possible
- Cull chronic poor-doers, if possible
- Avoid deworming the entire herd: Use Targeted Selective Treatment (TST)

Refugia

The proportion of the total parasite population that is not selected for anthelmintic treatment

- Those parasites that are in "refuge" from the drug
- Therefore have no selection pressure to develop resistance
- A benefit of refugia is to maintain a proportion of susceptible parasites on the farm

Targeted Selective Treatment – a success story

- Recent paper from Botswana (Walker, et al, 2015) demonstrated viability of TST of individual animals in small farms in low-income economies
  - Farmers taught to evaluate health of goats and only treat when needed based on:
    - FAMACHA, bottle jaw, body weight, diarrhea scores
  - Results showed that farms that used TST did not suffer losses at a higher rate than farms treating all animals
    - TST is feasible and effective for resource-poor farmers
    - TST helps reduce use of antiparasitics

Role of education

- In the U.S., many veterinary schools are starting to emphasize parasite management and vets are becoming more aware of the emergence of resistance in the U.S.
- This is where collaboration and communication play a vital role
  - Both locally and globally!

Final Thoughts

- Global antiparasitic resistance has a large impact on animal welfare and economies, both locally and nationally.
- Education is key in spreading the word about responsible use of antiparasitic drugs.

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