#### NEW DEVELOPMENTS IN PARASITE MANAGEMENT AND SHEEP HEALTH

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- Validation of parasite species identification using PCR (collaborative work with Dr. John Gilleard at University of Calgary)
- Using CarLA salivary antibody to detect immunity to GIN parasites
- Update on the Ontario maedi visna program
- Draxxin and foot rot of sheep

#### WHAT IS NEW IN ANTHELMINTICS?

#### Broad Spectrum Anthelmintics - Canada

#### Benzimidazoles (BZ)

- Fenbendazole drench (Safeguard, Merck)
- Albendazole drench (Valbazen, Zoetis)
- Imidazolthiazoles (LV)
- Levamisole only as a compounded drug should we be using it?
   Macrocyclic lactones (ML)
- \*Ivermectin drench /injectable (several) licensed for sheep
  - Moxidectin (Cydectin, Boehringer) only pour-on in Canada
- Amino-acetonitrile derivatives (AAD)
- Monepantel (Zolvix, Novartis) not in Canada
- Combination
  - \*Derquantel (spiroindoles) + abamectin (Startect, Zoetis)
- \* Licensed for sheep in Canada

#### Combination Drenches?

- Combination dewormers are used commonly outside North America
- Startect is the first combination drench licensed for livestock in Canada
- Evidence that dewormer resistance will develop more slowly if a new drug is used in combination





- Dose is 2 mg derquantel and 0.2 mg abamectin / kg bw
- = 1 mL of Startect per 5 kg bw (0.2 mL/kg bw)
- Available in 1 L and 5 L sizes

#### Startect<sup>™</sup> Label

#### Indications:

- Treatment and control of gastrointestinal nematode and lungworm infections and their associated diseases
- Efficacy against
  - H. contortus and inhibited larval stages
     Teladorsagia circumcincta and inhibited larval stages
- Trichostrongylus colubriformis
- As well as many other GIN and Dictyocaulus filaria (lungworm) adults
- Efficacy as reported but higher based on field trials
- > 95% against adults and L4 of Trichostrongylus and Nematodirus and adult Haemonchus
- < 95% against adult and L4 Teladorsagia and L4 Haemonchus</p>
- > 95% efficacy against GIN known to be resistant to other dewormers including abamectin and derquantel when given independently

#### Startect<sup>™</sup> Label

- Contraindications
- Extremely toxic to horses
- Do not use in other species as severe reactions, including deaths, will occur
- Do not use in GOATS
- Cautions
- Do not treat lambs < 6 weeks of age or < 10 kg bw</li>
- Care not to damage mouth or pharynx when treating
- Do not retreat for 28 days after last treatment
- Warnings
  - 14 day meat withdrawal
- Do not use in lactating ewes producing milk for human consumption

#### Startect<sup>™</sup> Label

- Adverse reactions
- Mild transient coughing occurs commonly after drenching
- Overdose:
- Adverse events at dosing 4.5 X dose on label (0.9 mL/kg bw)
- Up to 3X the dose is not considered toxic
- Toxicity includes dullness, depression, incoordination, weakness, decreased GI motility, abnormal breathing, recumbency and death
- Non-fatal resolve spontaneously

#### When should we use Startect?

- When anthelmintic resistance is known or strongly suspected in a group of sheep
- E.g. as a quarantine drench
- Buy in sheep that may have resistant parasites
- Isolate and treat with Startect and let them "poop out" the resistant eggs
- Then put on contaminated pasture so they get infected with the "farm" parasites that aren't resistant
- If AR present on the farm, can be used to selectively treat infected sheep
  - Don't treat everybody unless good refugia or eventually resistance will develop



#### Flukiver - Label

- Indication
  - For the treatment of *Haemonchus contortus* (Barberpole worm) in sheep and lambs
  - It is <u>not effective</u> against other GIN parasites
- Dosage
  - $\circ$  10 mg per kg body weight / 1 mL per 5 kg body weight
- How does it work?
  - After drenching, it is absorbed into the blood stream with peak levels 24-48 h later.
- $\ensuremath{\,^\circ}$  It is bound to albumin the major protein in blood
- Not much closantel in the tissues
- Blood sucking parasites ingest the closantel when drinking blood – the drug then kills the parasite

#### Flukiver - Label

- Flukiver only kills stages of Haemonchus that are feeding
- Not effective against hypobiotic L4 stage that occurs in the winter
- But Flukiver is very slowly excreted from the animal • Half-life of the drug is 2 to 4 weeks
- So it is persistent
- Do not treat more frequently than every 49 days
- Withdrawal for meat is 49 days
- Never use in lactating dairy sheep
- Overdosing can cause signs of toxicity blindness, incoordination, weakness
- In our study, we saw no adverse signs

#### When should we use Flukiver?

- When Haemonchus is the primary parasite in the flock
- Use when active infections, i.e. not the middle of winter
- As with all anthelmintics
- Don't deworm everybody unless a good level of refugia use selectively Monitor treated animals using FAMACHA as well as fecal egg counts



	Benzimidazole	Ivermectin	Startect	Closantel
Hypobiotic Larvae	+	++	++	_**
Persistent Activity	-	+/-	+	+
Tapeworms	+/-	-	-	-
External Parasites	-	+	+	+/-
Liver Flukes	+/- *	-	-	+
+ = good activity;	elmintics against th ++ = much activity; - =		slight or variable	

#### Suggested dosages of anthelmintics

(bw = body weight; 1 kg = 2.2 lb)

	Benzimida- zoles	Ivermectin	Startect	Closantel
Sheep mg/kg bw	5	0.2	0.2 mL <sup>t</sup>	10
Goat mg/kg bw	10	0.3	NO	10**
	0.2 mg abameo Startect is not r			

- In Canada, Startect is not recommended for lambs < 6 weeks of age and < 10 kg  $\,$ bw; nor in dairy ewes

\*\* Although 10 mg/kg is effective in goats, there is less persistency of action

#### Why Don't Anthelmintic Treatments Work?

- Drench failure
- Re-exposing to very high load of parasites Drench and turn to heavily contaminated pasture
- Chronic damage to abomasum
- Anthelmintic resistance

#### **Drench Failure**

- Using a drug against a parasite where it has no efficacy
- E.g. ivermectin doesn't work against tapeworms



#### Drench Failure:

#### Did Not Give an Effective Dose

- Underestimated weight
- "eye ball"
- Dosed to average rather than heaviest
- Incorrect drench technique
- Drug from a suspect source or expired



#### Anthelmintic Resistance

- If can rule out reasons for drench failure, it may be that parasites are resistant to the drench
- All populations of parasites have some naturally genetically resistant parasites
- Difference is proportion
- Our job is to make sure the proportion of resistant parasites on a farm remains small
  - Keep an effective refugia when deworming
  - Only deworm when it is needed and ideally only those animals that need it







## Haemonchosis is the most important parasitic disease in Ontario flocks

- Lambs in summer during grazing
- Type 1
- Ewes and then lambs contaminate
   pasture
- Ewes in spring during lambing
- Type 2

a year???

- L4 stage overwinters in ewes
- Anthelmintic resistance is widespread
- Why when we only deworm a few time





If deworming all ewes at lambing is a risk for anthelmintic resistance... How can we prevent clinical disease due to *Haemonchus contortus* but still maintain refugia in the flock?



#### Objectives

- 1. Can we accurately identify those individuals that require treatment?
- 2. Does selective treatment of ewes with closantel at lambing control *Haemonchus* on farms as effectively as whole flock treatment?



#### Study Design

- Longitudinal study 2013 & 2014
- Six sheep farms
  - Documented anthelmintic resistance in Haemonchus contortus
    - Not to closantel as novel anthelmintic in Canada
  - Pasture ewes with nursing lambs

#### Treatment of Ewes at Lambing

- 3 farms all ewes treated
- 3 farms targeted selective treatment of ewes
- Closantel given orally based on individual body weight (10mg/kg)
- Fecal egg counts, clinical parameters and pasture larval contamination levels





## Treatment Criteria for TST Ewes One or more of: Raising three or more lambs Previous grazing season was first grazing season Body condition score <= 2.0</li> FAMACHA score 4 or 5 (pale)

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Multivariable analysis associated with *Haemonchus* fecal egg counts in 239 periparturient ewes

- FAMACHA© score is the most predictive of Haemonchus-specific fecal egg counts (p=0.002)
- 4 & 5 compared to 1 & 2 232% higher FEC
- $\circ$  Deterministic modeling suggests treating ewes 3, 4 & 5 for optimal detection
- Body condition score not significant (p=0.132)
- Significant in univariable; likely may be important

# **Objectives** Can we accurately identify those individuals that require treatment? Does selective treatment of ewes with closantel at lambing control *Haemonchus* on farms as effectively as whole flock treatment?



Targeted Selective Treatment (TST) versus Whole Flock Treatment (WT)

- Mean number of additional treatments of ewes and lambs
  - Whole flock 1.1 (2013) and 1 (2014)
  - Targeted selective treatment 1 (2013) and 1 (2014)
- Number of deaths attributed to parasitism
- 2013 WF 5 & TST 6
- 2014 WF 0 & TST 0











EVALUATING THE ACCURACY AND RELIABILITY OF THE FAMACHA® EYE COLOUR CHART USING DIFFERENT LIGHT SOURCES ON SHEEP FARMS IN SOUTHERN ONTARIO



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So, what's the problem?







#### Objectives

- Determine if the accuracy of scoring using the FAMACHA<sup>®</sup> chart changes when different light sources are used.
- 2. Evaluate the reliability of  $\mathsf{FAMACHA}^{\textcircled{0}}$  scoring by different readers.

#### Goal

Make *practical* recommendations to sheep producers regarding the ideal use and reliability of the FAMACHA<sup> $\odot$ </sup> chart as a health management tool.





	ults		
	for the logistic regression analyses evaluate the readers (independently) for each light so		The odds of correctly differentiating anemic vs. non-
Light Source	Odds Ratio (95% CI)	p-value	anemic animals were significantly
Barn	Reference category		lower for both readers when using
LED			LED light, as compared to using
Reader 1	0.24 (0.08-0.72)	0.011	ambient barn light.
Reader 2	0.44 (0.19-0.98)	0.046	and bene barning.ref
Natural			
Reader 1	0.97 (0.17-5.43)	0.972	Neither natural light nor the
Reader 2	0.70 (0.23-2.09)	0.522	flashlight had a significant effect
Flashlight			on the ability of the readers to
Reader 1	0.70 (0.20-2.45)	0.574	,
Reader 2	0.83 (0.34-1.97)	0.666	correctly differentiate anemic vs.
			non-anemic animals.







#### COMPARISON OF DIFFERENT METHODS FOR DETERMINING THE PARASITE SPECIES COMPOSITION OF GASTROINTESTINAL NEMATODE TYPE EGGS IN THE FECES OF SMALL RUMINANT FECES

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## How can we tell which parasites are infecting our sheep?

- The eggs of *Haemonchus, Teladorsagia* and *Trichostrongylus* appear th
- Trichostrongylus appear the same under a microscope
- Strongyle-type eggs
- To differentiate, we need to hatch the eggs and allow development to third stage (L3)
- Difficult, labour and time intensive







 Compare species identification using cultured L3 and visual identification to cultured L1 and PCR

Traditional L3 larvae method	New L1 larvae method
1 week to culture	48 hours to culture
Culture feces with eggs in ramekin	Fecal float in petri dish
Incubate feces/eggs, stir and mist daily	Recover eggs in sieve and centrifuge
Baermannize feces, collect L3 Iarvae 24hrs later	Culture eggs in petri dish at room temperature.
ID first 100 under microscope	Count hatched larvae, preserve in ethanol, send for PCR

















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	CarLA® 2016 Oct	CarLA® 2017 Mar	CarLA® 2017 May	CarLA® 2017 Aug	CarLA® 2017 Oct
CarLA® 2016 Aug		0.12 p = 0.23	0.10 p = 0.31	0.09 p = 0.37	0.12 p = 0.24
CarLA® 2016 Oct		0.23 p = 0.02	0.27 p = 5.2 e <sup>-3</sup>	0.19 p = 0.05	0.45 p = 1.2 e <sup>-6</sup>
CarLA® 2017 Mar			0.15 p = 0.12	0.25 p = 9.4 e <sup>.3</sup>	0.15 p = 0.14
CarLA® 2017 May				0.071 p = 0.47	0.38 p = 7.5 e <sup>.5</sup>
CarLA® 2017 Aug					0.46 p = 6.5 e <sup>.7</sup>

0.06 p = 0.54	0.03 p = 0.74	0.09 p = 0.35	0.14	-0.03	0.16
		p = 0.35	p = 0.14	p=0.79	p = 0.10
-0.13 p = 0.20	-0.07 p = 0.46	-0.04 p = 0.72	-0.13 p = 0.21	-0.07 p = 0.49	-0.09 p = 0.34
-0.28 p = 4.0 e <sup>-3</sup>	-0.07 p = 0.46	9.8 e <sup>-4</sup> p = 0.99	-0.04 p = 0.70	-0.15 p = 0.14	-0.13 p=0.18
	-0.49 p = 8.9 e <sup>-8</sup>	-0.24 p = 0.01	0.11 p = 0.27	-0.23 p = 0.017	-0.11 p=0.27
			0.15 p = 0.12	0.07 p = 0.46	-0.05 p = 0.60
				-0.06 p = 0.57	-0.10 p = 0.32
	p = 4.0 e <sup>-3</sup>	p=4.0 e <sup>-3</sup> p=0.46 -0.49 p=8.9 e <sup>6</sup>	p=4.0e <sup>3</sup> p=0.46 p=0.90 0.49 p=8.9e <sup>4</sup> p=0.01	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

#### Conclusions

- Sheep grazing under Ontario climate conditions developed detectable salivary CarLA® by the end of their first grazing season
- This response waned over winter (in the absence of L<sub>3</sub> exposure) but was greater and more rapid in the second grazing season



- High periparturient CarLA® titre was correlated with reduced FECs in the periparturient period and early summer
  - Selection of replacement ewes with elevated CarLA<sup>®</sup> may reduce pasture contamination





#### What about vaccination?

- Immunity to GIN parasites is short-lived; parasites are very completed creatures
- Barbervax (Moredun) is effective against Haemonchus contortus
   Made from whole Haemonchus parasites obtained from specially infected lambs at slaughter
- Vaccinate lambs every 6 weeks for grazing season
   Replaces drenching if Haemonchus is the parasite of concern
- Useful for Canada?



## FR

#### Ontario Maedi Visna Flock Status Program

- In existence for over 15 years
- This year we did some modifying of the protocols based on research and experience with the program
- Run by Ontario Sheep Farmers (not me!)
- It is open to any producer in Canada
- Only caveat is that the serological test must be acceptable to the program
- At this point it doesn't accept results from the AGID or VMRD test because of sensitivity and specificity issues, i.e. false positives and false negatives.
- My understanding is that the BC Abbotsford lab and Prairie Diagnostics use the VMRD kit

#### Is Maedi Visna Important?

- Lots of very good research to show that seropositive sheep are less productive than seronegative sheep
- Don't need to see lots of clinical disease to have economic losses





#### Economic Costs?

- Work done in the early 2000s (Jim Fisher and Paula Menzies), showed that
- Purebred producers would make back cost of program within 2 years of reaching B status
  - Mostly through increased sales of breeding stock
- Commercial producers with 10% seroprevalence (low) would make back the cost of the program within 5 years of reaching B status
  - Much faster if seroprevalence is higher
  - Because of improved productivity
- · Need to repeat this study using more scenarios
- Is it worth a large commercial flock to eradicate MV?

#### Draxxin, Zoetis

- Tulathromycin is a macrolide antibiotic
- It is traditionally used to treat respiratory disease in beef cattle
- It has recently been licensed for sheep
- Treatment of ovine foot rot associated with *Dichelobacter nodosus* when systemic treatment is required due to presence of active lesions
   Not assessed for treatment of other diseases such as pneumonia
- Single dose subcutaneous injection in the neck
- 2.5 mg/kg bw or ¼ mL per 10 kg bw
- Use an automatic dosing syringe rather than repeated needle entries through the stopper
- A single dose has been shown to be effective in reducing lameness due to D nodosus (Europe)
- Meat withdrawal is 16 days for sheep don't use in lactating dairy animals

### What is the future for drug approvals for sheep?

- In a perfect world, all required veterinary drugs needed for common diseases would be approved for use in sheep
- We have had some great successes in last few years but need many more
- Veterinary Drug Directorate sees the need to facilitate veterinary drug approvals
  - Accepting drug data from other countries acceptable to Canada
     Coordinating approvals in more than one country, e.g. Metacam in Canada, Australia and New Zealand
- Threats are still monetary it costs money and costs are increasing
   Push for a funding formula like Pesticide Management Regulatory Agency (PMRA)
- Sheep Value Chain Roundtable Health Strategies Working Group continues to work with the government and veterinary pharmaceutical companies

