Looking towards the future of Parasite Management through "host-colored" glasses

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Looking towards the future of parasite management through “host-colored” glasses

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My interest in parasite management

(Left to right) Dr. Anne Lichtenwalner, Dr. Tom Settlemire, Dr. Charles Parker, and Dr. Richard Brzozowski

Virginia Tech VT

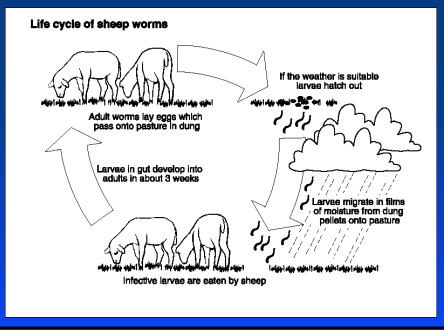
A quote to begin our discussion

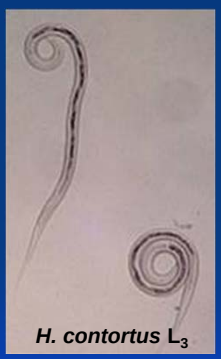
*"…after symptoms of this infection (Haemonchosis) have been seen, the time necessary for fattening lambs is greatly increased and requires the use of more expensive grains for finishing than in non-parasitized lambs…**therefore the prime requisite of economical sheep production is raising sheep that do not suffer from parasitism."***

Veterinary Helminthology (1949)

The parasites I am referring to ?

- Trichostrongylidae family
  - Includes but is not limited to:
    - *Trichostrongylus colubriformis* (small intestine)
    - *Telodorsagia circumcinta* (abomasum)
    - *Haemonchus contortus* (abomasum)
  - Worms in this family have a very similar lifecycle





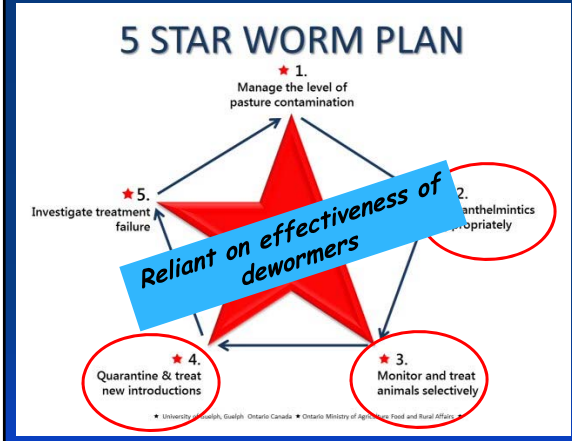
***H. contortus* L_3**

Haemonchus contortus

- "Barber-pole" worm
- Voracious blood feeders
  - 0.05ml blood/worm/day
  - 1,000 worms = 50ml blood/day
  - Results in anemia
- Seasonal
  - Year-round in warm/wet climates
    - SE US
  - Summer parasite for the rest of the US
- Very prolific
  - Females produce 5,000-10,000 eggs per day

Many parasite management strategies are focused on this critter specifically!

Pathogen-centric approach



Reduce parasitic load on pasture

Maintain anthelmintic efficacy

This type of plan in combination with FAMACHA has been very successful in mitigating parasite problems.

Dewormers are great when they work

That's not longer the story…

Resistance status	*H contortus* BZ	LEV	IVM	MOX[a]
All farms				
Susceptible	1	7	7	32
Suspected resistant	0	14	4	3
Low resistant	2	21	11	4
Resistant	43	4	24	7
Sheep farms				
Susceptible	1	6	5	19
Suspected resistant	0	6	4	3
Low resistant	2	13	6	1
Resistant	23	1	11	3
Goat farms				
Susceptible	0	1	2	13
Suspected resistant	0	8	0	0
Low resistant	0	8	5	3
Resistant	20	3	13	4

JAVMA, Vol 233, No. 12, December 15, 2008

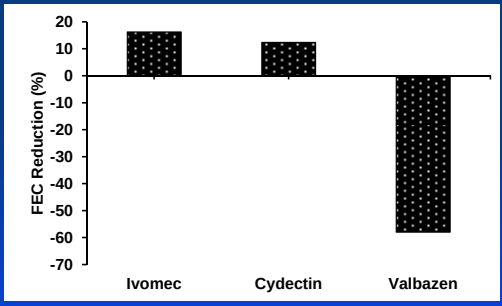
Collectively "we" got ourselves here

Due in large part to prophylactic treatment

Western states are not immune!

High school science fair project in central California

Evaluating anthelmintic resistance from 10 farms grazing sheep on irrigated pastures



We expect to see values greater than 95% (if susceptible)

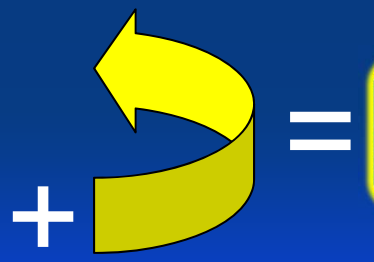
Ivomec = 16%
Cydectin = 14%

In sheep treated with Valbazen egg count increased by 56%

Maintenance of dewormer efficacy is paramount!

Don't stop using FAMACHA! If you haven't started find a training session

- Has to be a part of an integrated approach to parasite management
- Other control strategies
  - Rotational grazing
  - COWP
  - High-tannin cultivars
  - Parasite-resistant sheep



Lower parasite burden!

Defining parasite-resistance

- Very difficult to do empirically
- Let's try to define what parasite-resistant means
  - Emphasis on trichostrongylid parasites
    - Does not apply to coccidia!
  - Parasite-resistant ≠ hair sheep
    - There are cases of parasite-susceptibility in hair sheep
    - Likewise there are cases of parasite-resistance in fleeced sheep
  - Parasite-resistant sheep have lower fecal egg counts, numerically lower FAMACHA scores and perform throughout the grazing season.
    - Lower is relative to the contemporary group average, not your neighbor!
    - Parasite-resistant sheep are not devoid of parasites, they are more resistant to the effects of parasitism

Parasite management from the host perspective

Two approaches

Selection
Crossbreeding

The genetics behind resistance

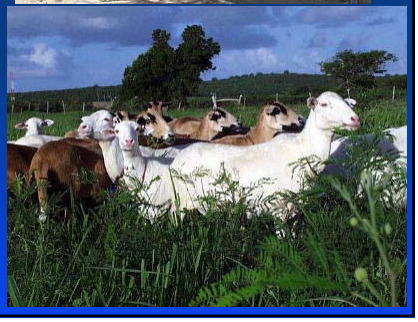
- Is parasite-resistance an inherited trait?
  - Yes
- How is parasite-resistance measured?
  - Fecal egg count
- What is the heritability of parasite-resistance?
  - 0.01 – 0.50
  - When animals that are tested have a larger parasitic load, the heritability of FEC improves
- In the Katahdin breed heritability has been reported to be near 0.5
  - Indicates that parasite-resistance has a large genetic component
  - Should respond well to selection
- Used appropriately, crossbreeding with a parasite-resistant breed should improve parasite resistance
  - Improvement can be made within breed, but will require more time

The typical culprits…in the US

What about Katahdins?

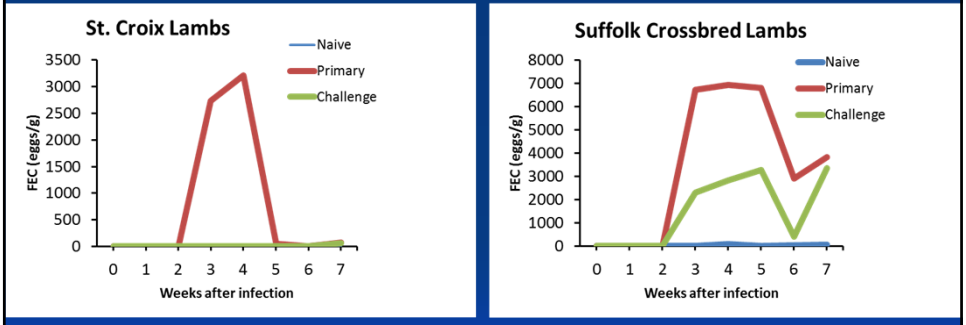
Due to their heritage they would be expected to have greater resistance than susceptible sheep, but would not be considered “resistant”

Where these sheep come from



- Grass year-round
- Perfect environment for parasites
- Why do these native sheep still exist?

Resistant vs. Susceptible



Is this difference large enough for you to begin to think about incorporating St. Croix sheep into your breeding program?

The future of genetic selection

Need the ability to identify resistant individuals without requiring that they become infected

A test that can be done at anytime regardless or age, production system, parasite exposure breed…

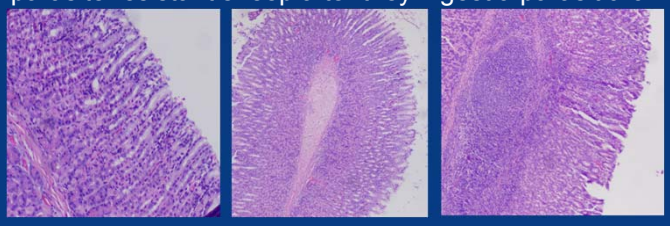
There is a small likelihood that parasite-resistance is controlled by a single gene or a simple marker

This will require that we know the precise mechanism of parasite resistance

The difference lies in immunity

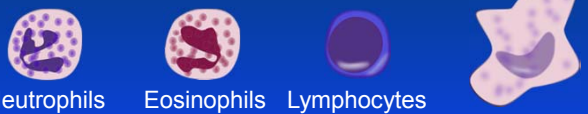
What happens in a parasite resistant sheep after they ingest a parasitic larva?

#1
They recruit cells to the abomasum



Uninfected | Susceptible Day 7 | St. Croix Day 7

These cells include:

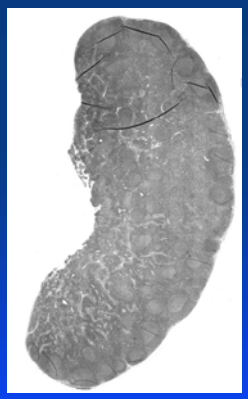


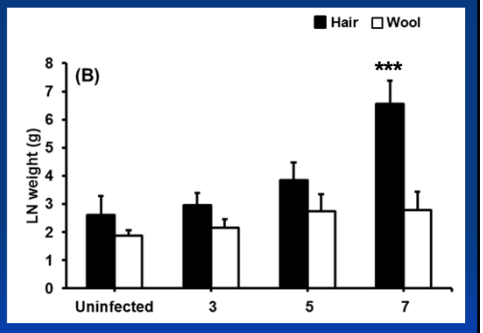
Neutrophils | Eosinophils | Lymphocytes | Macrophages

The difference lies in immunity

What happens in a parasite resistant sheep after they ingest a parasitic larva?

#2
Lymph node hypertrophy and accumulation of effector cells in the draining lymph





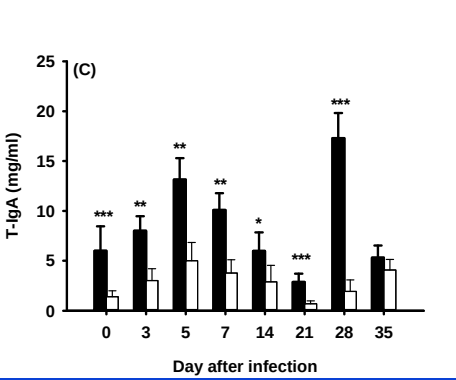
The difference lies in immunity

What happens in a parasite resistant sheep after they ingest a parasitic larva?

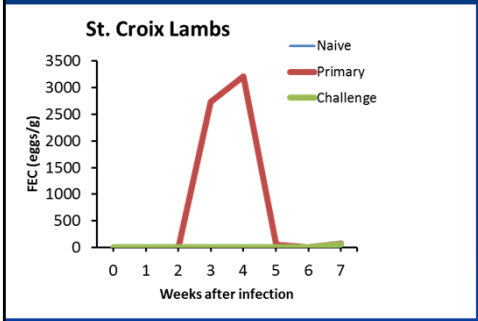
#3
Greater antibody production

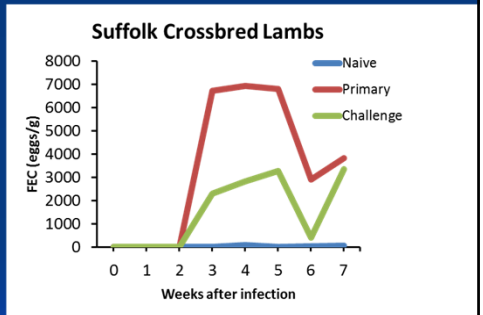
These are the immune events that we see time and time again.

The accumulation of these events in parasite-resistant sheep result in?



The difference lies in immunity





Is this difference large enough for you to begin to think about incorporating St. Croix sheep into your breeding program?

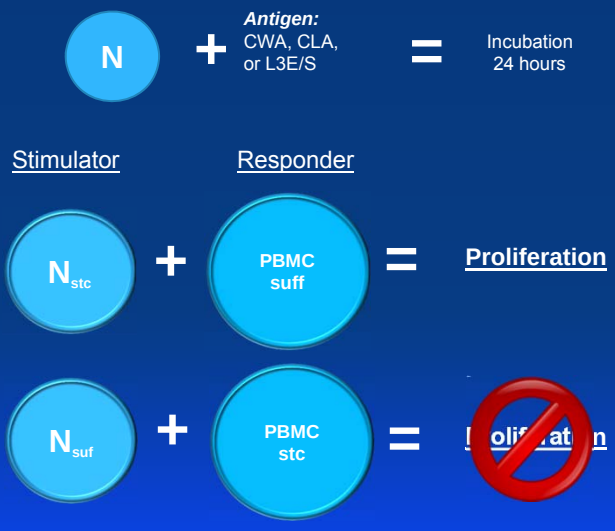
No smoking gun

With all of the differences in immunity, we have not found a key piece of evidence that would serve as a selectable marker of parasite-resistance.

Let's consider the following:

It is not that susceptible sheep are incapable of responding to parasite infection, rather that their response is blocked by either a parasite-derived mechanism or by lack of "immunological awareness."

Antigen reactivity



Immunomodulation

- Adjustment of the immune response to the desired level
- Example:

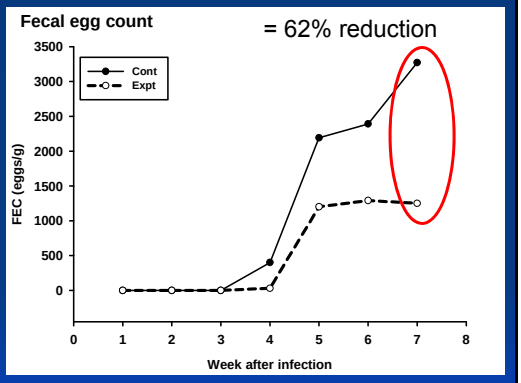
Adjuvant effect of LPS and killed Propionibacterium acnes on the development of experimental gastrointestinal nematode infestation in sheep

Parasite Immunology, 2009, 31, 604–612

Authors found that FEC was reduced by 50% at 35d in sheep receiving "immunomodulation" and infected with *H. contortus*

Dietary immunomodulation

- Suffolk crossbred wethers
- Fed a prebiotic dietary supplement for one week prior to *H. contortus* infection and continued throughout the trial



Is this what immunomodulation during a parasite infection looks like?

Mechanism of prebiotic immunomodulation

- Upregulation of early innate host immune defenses
  - Activation of macrophages
  - Recruitment of neutrophils
  - Stimulation of Mast cells, basophils
- Immunomodulation bears a striking resemblance to early immune responses of parasite-resistant sheep
- Is the reduced FEC observed during dietary supplementation a result of enhanced innate immunity?

My take on the future of parasite management

One fundamental question

How do we make these lambs

behave immunologically like these lambs?

The genetics route

Utilizing selection for FEC is commitment to a breeding program where one may not see differences for many generations.

Faster improvement can be made through the utilization of crossbreeding

- Reduced carcass size
- Seriously impact wool quality (depending on breed)
- Accurately selecting “parasite-resistant” progeny becomes difficult

A role for immunomodulation

Perhaps a solution for purebred producers

- We need to further verify the efficacy of immunomodulation on parasite reduction
- We must characterize upregulated immune activation
- Finally, we need to better understand the effects of immunomodulation before this technology is to be used on-farm

FAIR: ***Key Topic 2-3:*** Improving animal health through feed

Exciting times ahead…

Acknowledgements

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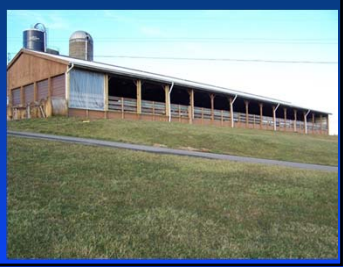

Questions ?

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http://www.growourflock.org/resources