Smart Drenching: Preserving the Integrity of Dewormers

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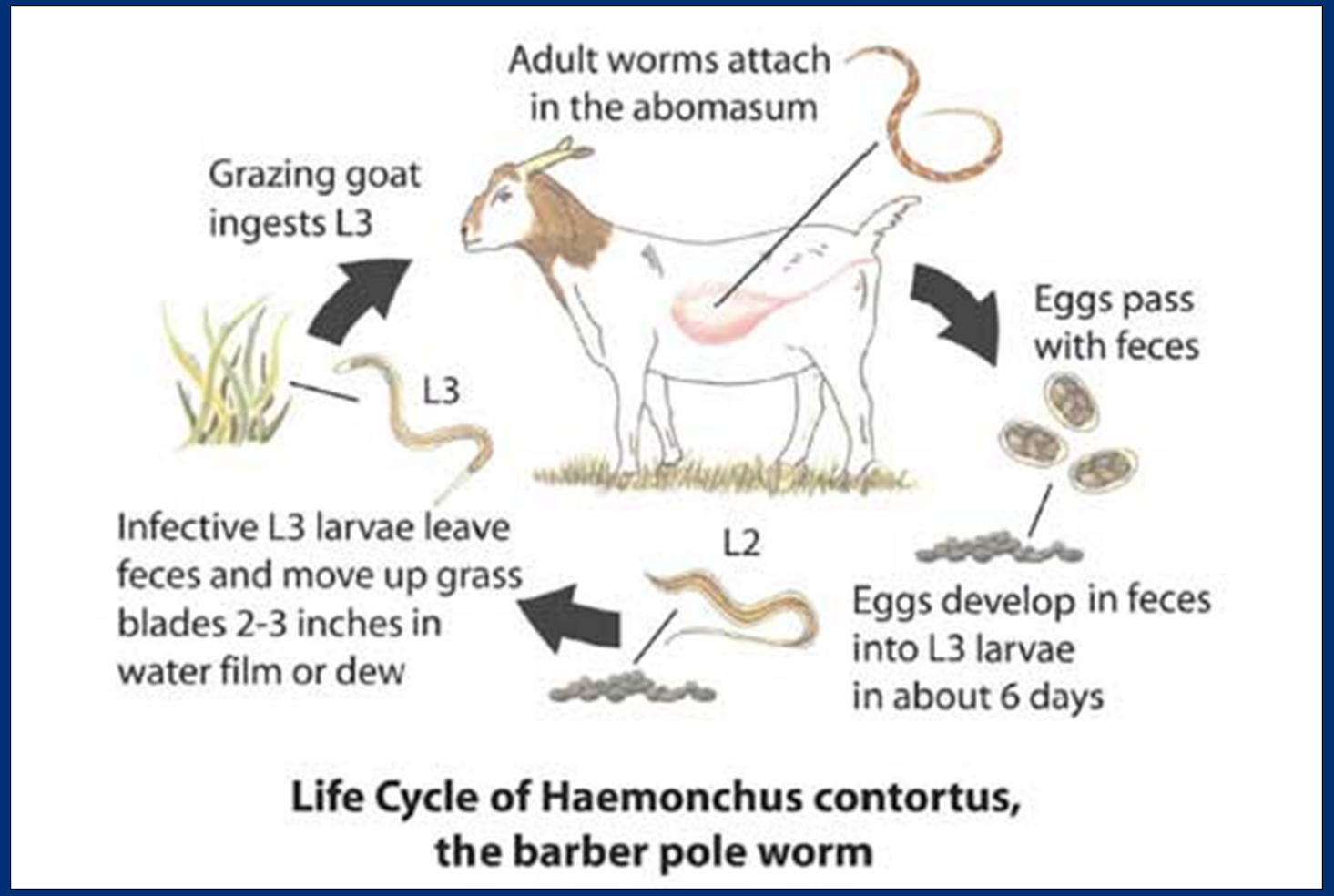
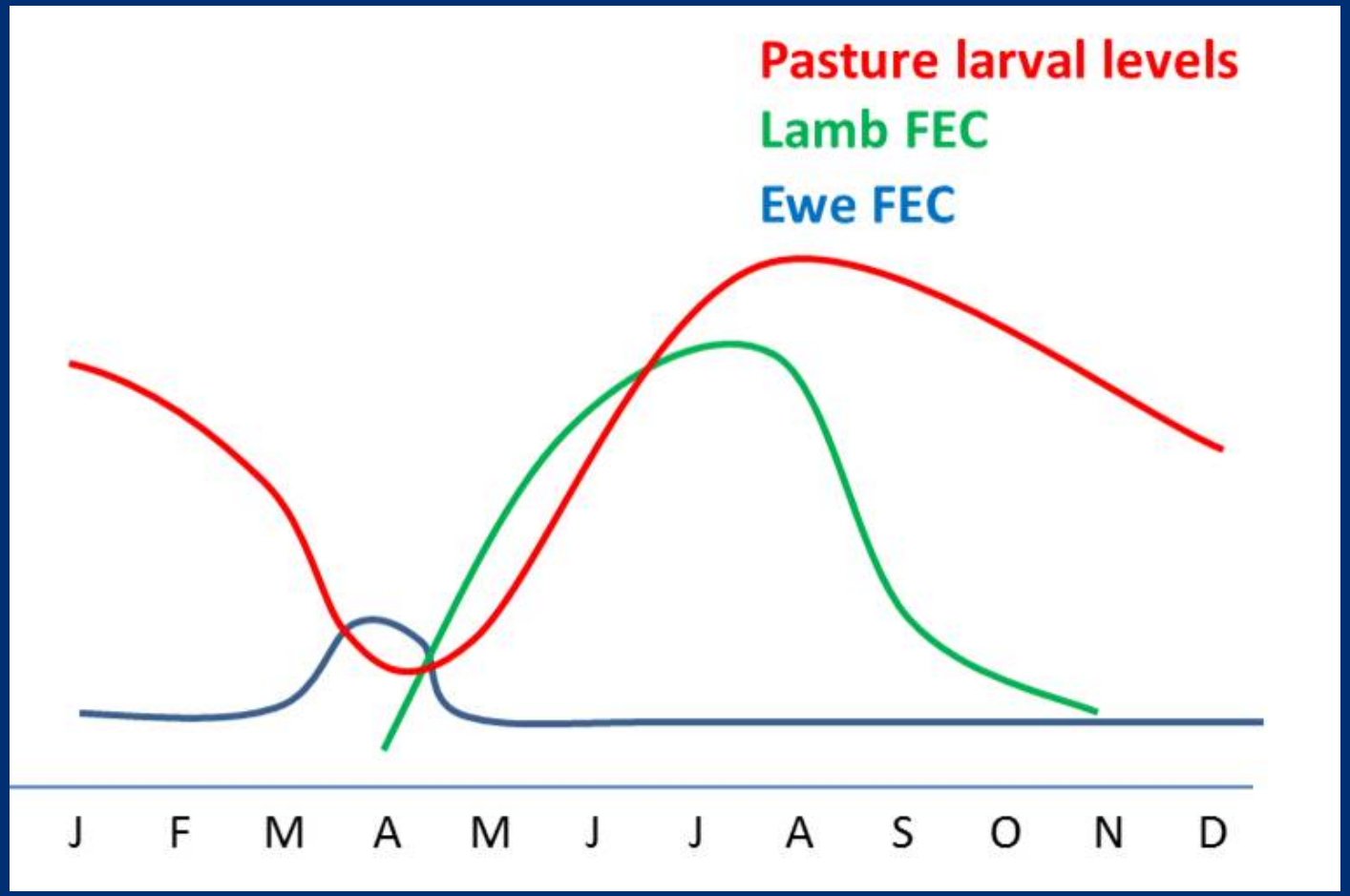
Typical Direct Life Cycle



Life Cycle of Haemonchus contortus, the barber pole worm

Worm Seasonality



Dewormers: Brief History

- Modern broad spectrum anthelmintics (dewormers)
  - Control emphasized their use in a strategic manner
    - Treating all animals in the population
    - Concentrated treatments at times of the year when infection was high
      - Helping to reduce pasture contamination immediately post-treatment for about 3-4 weeks
    - Effective dewormers = reasonable strategy
  - Several new classes of dewormers were introduced in succession (1960s-1980s)
    - Benzimidazoles (TBZ; Safeguard/Panacur, Valbazen), imidizothiazoles (Prohibit, Rumatel) and then macrocyclic lactones (Ivomec, Dectomax, Cydectin, LongRange)
      - Macrocyclic lactones offered an extended period of activity
    - Different modes of action
    - Thought was that we would have adequate control for years to come, and new classes of dewormers would continue to be developed

Dewormer Resistance

- Populations of worms developed resistance to these dewormers
  - First to benzimidazoles and then very rapidly to the macrocyclic lactones
    - First diagnosed in sheep infected with *Haemonchus*, and most severe in small ruminants
  - Diminished use of imidazothiazoles after Ivomec was first introduced
    - Resistance slowest to develop
  - Reports of resistance appeared in the 1960s (benzimidazoles)
    - Increased over the next decades
    - Widespread resistance (especially macrocyclic lactones) common into the 1990s and early 2000s

Dewormer Resistance

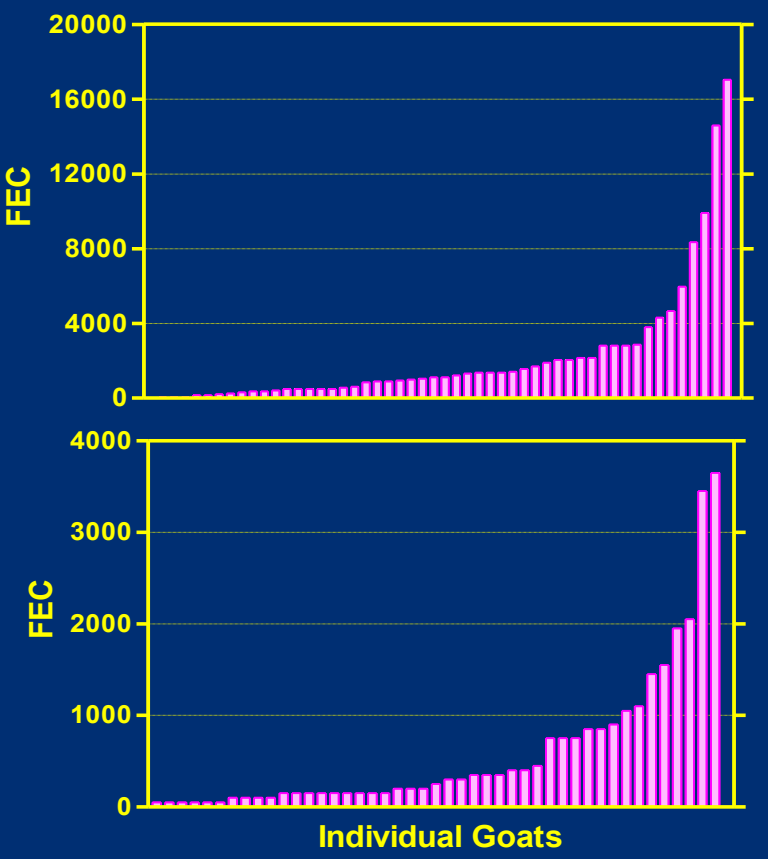
- Factors that effect the development of resistance
  - Deworming all animals in the population
    - Eliminates the susceptible worms, but leaves resistant worms to start populating the environment to compete with susceptible worms (i.e., refugia)
  - Deworming more often than necessary
    - Decreases the refugia even further - resistant population expands
  - Deworming at times of low environmental refugia
    - Allows resistant worms that survive the deworming to rapidly dominate the worm population
  - Underdosing
    - Sublethal dose permits “partially” resistant worms to survive and reproduce that otherwise would be killed with a full dose
- As resistant populations became more predominant, dewormers failed
  - Sole and frequent use of dewormers = unsustainable control.

New Hope?

- Recent introduction of Zolvix (Amino-Acetonitrile Derivatives, AAD)
  - New class of dewormer with a different mode of action
  - Promise for revitalizing control if used in a sparing manner to maintain a refugia
  - However, multiple reports of resistance have already appeared
  - Not approved for use in the US at this time
- Mention – Flukiver/Startect (Canada)
- Most recent concept is using dewormer combinations
  - Premise - combining dewormers with different modes of action will increase overall efficacy
    - Indeed the case - several combinations registered in Australia and New Zealand
  - Likely will not be sustainable as worms become multiple-resistant

Targeted Selective Treatment (TST)

- Developed primarily for small ruminants (first sheep and now goats)
- Key strategy for sustainability
  - Target those animals that need deworming
  - Leave a part of the population not dewormed to provide refugia
- TST based on the fact that not all animals in a population harbor similar numbers of worms
  - The minority of the population harbors the majority of the worms
  - Targeting those animals for deworming should alleviate clinical disease in those animals
  - Leave the animals that are not clinically affected to provide the much needed refugia
- Concept has been effective in computer simulation models and field trials
- Unfortunately, this will not stop resistance from developing
  - Increase the time frame in which this will happen
  - Extend the useful life of dewormers



TST

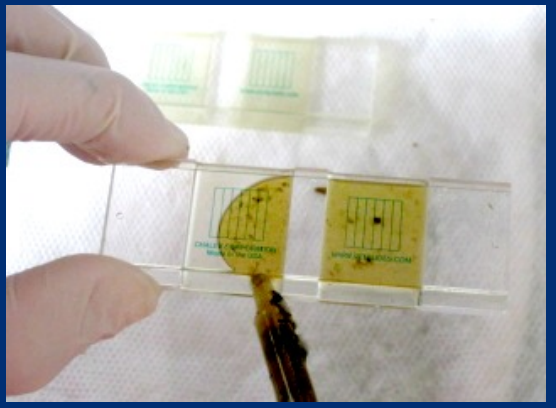
- How do we achieve TST?
  - Animals needing deworming have to be identified
  - Not that easy and can be expensive
- Fecal egg count (FEC) has been used extensively to monitor the worm infection cycles
  - Indicates when dewormings are needed
  - With large populations a sample of animals are selected and the whole population is treated based on the FEC trend
- For TST, all the animals have to be processed to determine those that need to be dewormed
  - Collecting and processing fecal samples
    - Time consuming to collect, expensive, and laboratory processing also takes time
  - If the predominant worm of concern is *Haemonchus*
    - FAMACHA system

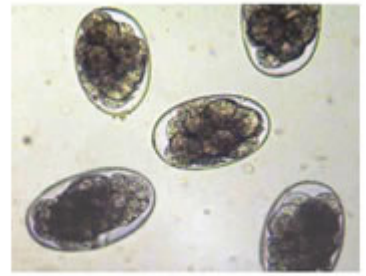
FAMACHA

- Developed (South Africa) as on-farm means to identify anemic animals
  - Blood feeding *Haemonchus* only
- Deworming can be administered immediately
- Based on the relatively good correlation between the color of the ocular mucous membranes and blood packed cell volume (PCV)/FEC
- Anemic animals, usually most heavily infected are the only one dewormed
  - Leaves the rest of the flock/herd to provide refugia
- Occasionally, some animals are anemic for another reason and harbor few worms
  - Deworming these ‘false positives’ has minimal effect on the overall objective of maintaining refugia

Fecal Egg Count/Short-term Weight Gain

- *Teladorsagia/Ostertagia* and/or *Trichostrongylus*
  - FAMACHA not appropriate and FEC may be the best approach
    - Time/labor constraints are a factor
- Another alternative is based on short-term weight gain
  - All animals have electronic ear tag that that is scanned as they enter an automated electronic scale
  - Current weight compared with previous weight
  - Animal that have not met weight gain goals cut to alternate pen and dewormed
  - Animals that have met weight-gain goals returned to pasture without deworming
  - The equipment is expensive
    - Only applicable to an operation that has sufficient numbers of animals to justify the investment





Other TST

- Observe animals on a regular basis
  - Pick out the ones that are not doing well (depressed, lethargic, anorectic, bottlejaw, etc.) for deworming
  - May be sick for some other reason, so treatment may include/ require something other than dewormers
  - May fail to identify some animals in need of deworming until the clinical situation is severe
- Selectively deworming based on age and/or production parameters
  - Older animals usually harbor fewer worms than younger ones
    - Leaving them not dewormed to provide refugia
  - Dairy animals - deworm only the high producers
- These approaches make sense and have been used with success
  - Accept that some animals that need deworming may not receive it, while others that may not need deworming do receive it

Proper Dose/Drenching Technique

- Ensure proper dose is delivered
- Proper technique when drenching ruminants is very important
  - Critical that the full dose lodges in the rumen
  - If drench is delivered to the buccal cavity, rather than over the back of the tongue into the pharynx/esophagus
    - Can stimulate closure of the esophageal groove with much of the drench bypassing the rumen
      - Faster drug absorption
      - Shorter duration
      - Efficacy is reduced

Host Physiology - Maximize Efficacy

- Restrict feed intake for 24 hours prior to treatment
  - Once in the rumen, the duration of drug effect is largely dependent on the flow-rate of the digesta
    - Decreasing digesta transit leads to an increase in drug contact with worms and increased efficacy

Proper Drug Dosage/Administration

- Goats metabolize anthelmintic drugs much more rapidly than other livestock
  - Rule of thumb -- goats should be given a dose 1.5 to 2 times higher than for sheep or cattle
    - Levamisole 1.5 X
    - All others 2X
- Administer all drugs orally
  - Pour-ons are absorbed poorly
  - Injectibles have long residual - resistance
- Combinations
  - Combination (2-4 anthelmintics) products currently used in Australia/NZ are being pursued for FDA approval in US

Do Not Buy Resistant Worms

- All new additions should be quarantined and aggressively dewormed upon arrival
  - Deworm with at least 2 anthelmintics with different mechanisms of action (different class)
    - Albendazole and levamisole, for example, upon arrival
  - Should remain in quarantine for 10 - 14 days
    - Perform FEC to confirm that no eggs are shed
  - If quarantine is not possible:
    - Treat with at least 2 anthelmintics and confine to pens for a minimum of 48 hours following treatment

Non-Drug Alternatives

- Copper oxide wire particles (COWP)
  - Effective against *Haemonchus*
  - Marketed for treating copper deficiency
  - Effect on *Haemonchus* is an extra advantage, especially when administered at times when *Haemonchus* is present
  - Caution - sheep are very susceptible to copper toxicity, so COWP should be used judiciously
- Herbal dewormers have been promoted, but there is no scientific evidence that any of them are effective against worms
  - May have some nutritional/metabolic function benefit and make the animal feel better and look better temporarily

Non-Drug Alternatives

- Condensed Tannin Containing Plants
  - Sericea lespedeza
    - Forage that grows relatively well in SE US
      - Establishment as pasture may fit some operations
      - Hay, meal, pellets, etc. may be suited for many other operations
      - Sims Bros. (simsbrothers.com)
    - Has effect on *Haemonchus*
      - Female worms lay fewer eggs
        - Reduced pasture contamination
      - Kills some worms

Concerns

- Smart drenching (TST) will leave a proportion of the animals in a population not dewormed and subject to potential clinical, but mostly subclinical infection
  - Concerns that knowingly leaving these animals not dewormed might be considered inhumane
  - What are the ethical issues?
- Also, subclinical infection does impact productivity which is the bottom line for producers
  - What is the trade off?
- Alternatively, using dewormers that are ineffective is a waste of money
  - Leads to the same production loss or ethical concerns as not deworming
  - This is a real concern
- Testing for resistance is rarely done, and surveys in many areas of the world show very high prevalence of resistance
  - Use of ineffective or poorly effective dewormers is commonplace

Conclusions

- Dewomer resistance is with us to endure and manage
- With resistance and few new drugs, sustainability must be a consideration
- Probably need to accept some level of reduced productivity
- Changes need to be made to improve sustainability
- Rapidly heading to a time when few if any effective dewormers will be available
- Parasitologists, veterinarians and animal scientists are constantly investigating new aspects of using dewormers smartly that will aid in the quest to provide sound advice that will help producers remain profitable in the face of continuing worm constraints?