Decades ago, with handful of powerful antihelminitics at our disposal, it looked like a certainty that we would easily win the war against gastrointestinal parasites in small ruminants. We all envisioned the time when a healthy herd would be the norm and an animal with marked parasitism was going to be the exception. However, the bombardment of gastrointestinal nematodes with the wide range of powerful drugs has not resulted in their extinction. Instead, in certain areas of the country, a population of treatment-resistant worms has developed that can devastate herds and have extensive effect on animal production and even mortality. Table 1 lists the five most common classes of drugs used in treating gastrointestinal nematodes and brand-name examples of the drug.

The first of these drugs, Thiabendazole was introduced in 1961. For approximately 50 years we enjoyed inexpensive, effective deworming programs initiated by this drug and subsequently augmented by the introduction of Levamisole in 1970’s and Ivermectin in 1981. However, as time passed, there began to appear warning signs of a developing resistance to these medications, with ineffective treatment with Thiabendazole reported as early as 1964. Likewise, goat resistance to Ivermectin was reported before that product had even been approved for use in sheep. Over the ensuing decades, resistance to the drugs has spread in varying degrees to involve all classes of antihelmintics.

At the moment, we have the future promise of Moranpantel, an aminoacetonitrate derivative, but this drug is currently not available in the United States. Even when the drug is introduced here, estimates are that within approximately five years of introduction, resistance to the drug will develop. Additionally, Moranpantel is also significantly more expensive than the other antihelmintics currently available.

As we are faced with increasing parasite resistance of to a wide variety of drugs, management factors are playing an ever important role in the control
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug</th>
<th>Parasite</th>
<th>Approved</th>
<th>Dosage</th>
<th>Product</th>
<th>Formulation</th>
<th>Meat WDT*</th>
<th>Milk WDT*</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzimidazoles</td>
<td><em>Oxendazole</em> <em>(Safeguard, Paraquat)</em></td>
<td>Nematodes</td>
<td>No</td>
<td>Yes</td>
<td>5.0 mg/kg</td>
<td>Suspension</td>
<td>NE</td>
<td>6</td>
<td>NE In goats, approved dose of 10 mg/kg is recommended but is considered extra-label use and will require an extended WDT.*</td>
</tr>
<tr>
<td></td>
<td><em>Albendazole</em> <em>(Valbazen)</em></td>
<td>Nematodes</td>
<td>Yes</td>
<td>Yes</td>
<td>7.5 mg/kg</td>
<td>10-15 mg/kg</td>
<td>7</td>
<td>7</td>
<td>NE In goats, 10 mg/kg and WDT of 7 days in meat animals are approved for liver flukes only; 15 mg/kg is for nematodes. Do not use within 30 days of conception.</td>
</tr>
<tr>
<td>Imidazothiazoles</td>
<td><em>Ivermectin</em> <em>(Ivomec for sheep)</em></td>
<td>Nematodes</td>
<td>Yes</td>
<td>No</td>
<td>8.0 mg/kg</td>
<td>12.0 mg/kg</td>
<td>3</td>
<td>NE</td>
<td>NE Toxic side effects: salivation, restlessness, muscle fasciculation. Weighing before treatment is recommended. Use caution when using this treatment in hot weather—dehydration increases risk of toxicity.</td>
</tr>
<tr>
<td>Tetrahydroimidines</td>
<td><em>Ivermectin</em> <em>(Ivomec for sheep)</em></td>
<td>Nematodes</td>
<td>No</td>
<td>Yes</td>
<td>10 mg/kg</td>
<td>10 mg/kg</td>
<td>NE</td>
<td>30</td>
<td>0 Approved for use in lactating dairy goats.</td>
</tr>
<tr>
<td>Macrocyclic lactones</td>
<td><em>Moxidectin</em> <em>(Cydectin)</em></td>
<td>Nematodes, Arthropods</td>
<td>Yes</td>
<td>No</td>
<td>0.2 mg/kg</td>
<td>0.4 mg/kg</td>
<td>11</td>
<td>NE</td>
<td>NE Cattle injectable form is not recommended.</td>
</tr>
<tr>
<td></td>
<td><em>Eprinectin</em> <em>(Eprinex)</em></td>
<td>Nematodes, Arthropods</td>
<td>Yes</td>
<td>No</td>
<td>0.2 mg/kg</td>
<td>0.4 mg/kg</td>
<td>7</td>
<td>NE</td>
<td>NE In goats, use cattle injectable dose of 0.2 mg/kg. Use of cattle pour-on formulation is highly discouraged.</td>
</tr>
</tbody>
</table>
| Aminoacetamide      | *Morantel* *(Zolvix)*         | Nematodes | No       | No    | 2.5 mg/kg | 3.75 mg/kg | NE | NE | NE No milk withdrawal time in cattle; to be decided in other species. | Derivative

Table 1: *NE, Not Established. This constitutes extra-label use; therefore, a withdrawal time (WDT in days) has not been established. Current recommendations are available on the Food Animal Residue Avoidance and Depletion (FARAD) program website www.farad.org recommendations are available on the Food Animal Residue Avoidance and Depletion (FARAD) program website www.farad.org.
of parasitism. The two cornerstone principles of understanding modern gastrointestinal parasite control programs are understating the concepts of refugia and targeted deworming programs.

“Refugia”

Refugia is one of the most important concepts to understand when working with modern parasite control programs. It refers to those parasites both in and outside the animal that have not yet been exposed to antihelmintics. Simply stated, they are in “refuge” from the drug. This is an important concept because these genetically unexposed or drug-sensitive parasites can be used to dilute the numbers of post-treatment, drug-resistant larvae in the pasture or in the animal. In the animal, the adult worms will breed and create a mixture of both genetically drug-sensitive and drug-resistant ova. The percentages of larvae that will be sensitive or resistant depend on whether the gene for resistance is either a dominant or recessive trait in the specific parasite. This admixture of both drug-sensitive and drug-resistant larvae in the pasture will have the effect of dilution of the drug-resistant larvae by the greater numbers of drug-sensitive larvae.

“Targeted De-worming”

The best ways to preserve and increase refugia is to leave some animals untreated by limiting treatment to those animals shedding the most ova or the ones most clinically affected. Research investigations into nematode infections in herds of small ruminants have indicated that only approximately 20-30% of the animals are responsible for 70-80% of the worm burden in the herd. This worm burden is subsequently excreted into the field.

The majority of animals appears to be able to develop either resistance level or tolerance to parasite infection without significantly affecting gain or production. It became apparent that to slow development of resistance, it is important to identify the heavy shedders of ova and those individuals most affected by the parasitism. These animals can then either be targeted for specific treatment or can be culled from the herd. A combination of both diagnostic testing and clinical observation can help determine which animals or group of animals should be targeted for treatment.

Important tests to identify these animals are the Fecal Egg Reduction Test (FERT), FAMACHA scoring (see Reference Point Newsletter, spring 2012), and a general evaluation of weight loss and decreased production among the animals. Those animals that are identified as abnormal through these tests can be “targeted” and dewormed without the necessity of treating all the animals in the herd. It is important to remember that some animals may not be clinically abnormal and instead are just at a life stage more susceptible to parasitism (i.e., young kids and lambs).

If it is not practical to FERT and FAMACHA all animals, it may make sense to deworm rotating classes of animals, deworming the most susceptible groups first. This approach is not as effective as a

Figure 1: Thousands of blood filled Haemonchus contortus worms occupy the abomasal lumen.
more closely targeted one; however it should slow resistance to deworming drugs if other group refugia are available.

In contrast to a targeted approach to the use of antihelmintic drugs, many current management programs can actually inadvertently select for the development of resistant parasites. The following management practices should be avoided:

• Treating too often: Each treatment with an antihelmintic kills sensitive parasites and selects for those parasites that are resistant to the drug. While a new drug will be very effective (approximately 90% efficacy) over time, with repeated exposure to the drug, increased numbers of drug-resistant parasites will emerge. These frequently dewormed animals will then populate pastures with resistant ova and larvae. Less frequent deworming has the added benefit of a significant decrease in expenditure for antihelmintics.

• Treating the entire herd: Similar to treating too often, this practice will eliminate all the drug-sensitive parasites in a herd, effectively allowing only resistant strains to populate both animals and pastures.

• Strategic deworming: One of the changes to previous deworming concepts is to caution against the use of strategic deworming. In the past it has been common to deworm animals in the winter in the theory that there will be fewer larvae on the pasture ground at that time and decreased numbers of larvae will have been shed by the recently dewormed animals. The flaw in this theory is that the majority of the worms shed from these recently de-wormed animals, which subsequently populate the spring pastures, will be drug-resistant worms with very few refugia having survived the winter.

• Inadequate quarantine procedures: Newly purchased animals may harbor resistant parasites. These animals should be quarantined on a dry lot and dewormed with one if not two antihelmintic drugs. Pre- and post- treatment fecal egg counts (FEC) are recommended to assess the degree of resistance the new animal carries to the dewormer most commonly used on the farm. After deworming, the animal can be placed on the regular farm pastures with the knowledge that the refugia will help dilute any drug resistant ova shed by the new addition to the herd.

• Underdosing: Underdosing is a common practice that can lead to resistance. Lower than effective dosages will not adequately kill the worms and will lead to increased development of drug-resistant parasites. Typically, even cattle dosages of antihelmentics are not adequate for the treatment of sheep and goats. Topically applied drugs are also not recommended, since there is the increased possibility that the concentration of the drug in the animal will vary, effectively leading to underdosage. Long-acting antihelmintics may at first sound like a great idea, but the uncertainty of the end of the effectiveness of the drug can leave an opportunity for parasites to be exposed to sub-lethal dosage and thereby develop resistance.

Figure 2: Higher magnification of blood filled Haemonchus contortus ("Barberpole worm")
Management practices that decrease the frequency of the development of drug resistance

- Choosing the “right” antihelmintic drug: This decision should not be based on anecdotal evidence or conversation with other livestock owners; it should be an informed decision based on a fecal egg count reduction test. The test allows the right drug to be selected to decrease the number of resistant ova and developing larvae. A current recommendation for optimizing the use of antihelmintics in a parasite control program is the use of only one drug until resistance develops. More frequent rotation between multiple classes of drugs can, unfortunately, hasten the development of resistance. In cases where resistance already exists, however, the use of a combination of drugs at the recommended dose ranges may provide some benefit. In situations where there appears to be widespread resistance to a variety of drugs, a larval development assay may be indicated. This assay hatches larvae from submitted ova and determines what nematodes are present on the farm and which are sensitive to or resistant to the variety of available drug classes. Additional information on this testing can be found at http://www.sheepandgoat.com/ACSRPC/Resources/DrenchRiteAssay.html

- Use antihelmintic drugs in combination with non-drug control methods: There are a number of non-chemical management practices that can help to decrease the spread of resistant parasites within a herd. These include pasture rotation within a specific timeframe to decrease animal exposure to infective larvae, the culling of persistently infective animals with clinical signs and high egg counts, and the mixing of livestock species within the pasture. Horses, donkeys and, to a lesser extent, cattle make excellent grazers to compete for larvae, and these larvae are subsequently killed in the non-common species and decrease parasite load on a pasture as a result. Other effective non-chemical management practices include the introduction of copper oxide wire particles into the pasture soil (only moderately effective against worm in the abomasums and must be used cautiously around sheep), grazing on high-tannin forages, genetic selection for parasite-resistant breeds, and finally, pasture management (the tilling/burning of fields, etc.).

- Deworming when there are a greater number of sensitive larvae in the pastures: This management practice is the opposite of many of the earlier deworming programs. It recommends deworming only a select number of animals in the herd and then putting them on pasture in the summer to allow the non-treated eggs/larvae (refugia) to dilute the recently treated resistant ova/larvae.

Obviously, we need to have a multifaceted, targeted approach to the effective use of antihelmintics, henceforth, if we are to control parasitism in small ruminants and other livestock. The future may hold possible new drugs and combinations of drugs that will be effective for a time, but we can see that these drugs will ultimately become ineffective unless well planned, targeted deworming strategies are employed. The American Consortium of Small Ruminant Parasite Control (acsrpc.org) maintains an excellent website with a wide range of current information relating to the control of gastrointestinal parasitism.
parasites in small ruminants. The Ohio State University, College of Veterinary Medicine Extension Service (http://vet.osu.edu/extension/decision-tree) also maintains and excellent website with a helpful flow chart approach to small ruminant parasite management.

References

