Untangling conflicting messages: Optimal approaches for controlling internal parasites of cattle in the age of drug resistance

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Abstract

Anthelmintic resistance in gastrointestinal nematodes of cattle has been worsening over the past 2 decades and is now a global problem. Though the problem was originally seen primarily in *Cooperia*, which is not a highly pathogenic species, we now know that other more pathogenic species have become drug resistant as well. With no new classes of anthelmintics in the cattle product pipeline, we will need to be better stewards of the drugs we have now, as they will need to last us for a long time. Thus, there is a need to use our anthelmintics differently and smarter than in the past. In this paper we present several strategies for improving the sustainability of parasite control in cattle that will both reduce the development of resistance while maintaining good productivity. Furthermore, we should not just assume a drug works or does not work; testing using the fecal egg count reduction test (FECRT) should be performed on every farm. This is the only way to make evidence-based decisions on optimal drug choices. Optimally, the strategies promoted here should have been instituted years ago. However, it is not too late, and the sooner these strategies are implemented widely, the more successful the beef industry will be in controlling parasites both now and in the future.

Key words: cattle, internal parasites, resistance

Overview of Resistance Situation in Gastrointestinal Nematodes of Cattle

Beginning with phenothiazine in the 1950s, followed by the benzimidazoles in the 1960s, the imidazothiazole/tetrahydropyrimidines in the 1970s, and the avermectin/milbemycins (AM) in the 1980s, a new class of anthelmintics was introduced into the marketplace each decade. This arsenal of highly effective and relatively inexpensive drugs led to recommendations for parasite control that were based almost solely on the frequent and/or strategic use of anthelmintics, the goals of which were to maximize livestock health, productivity, and profitability. Though this approach was highly successful for a number of decades, we are now experiencing ever-increasing levels of anthelmintic resistance in all drug classes, involving virtually all of the most economically important parasites of all livestock species. Resistance in parasites of cattle was slower to develop than in the small ruminant and equine sectors, but over the past decade we have seen a rapid escalation in the levels and distribution of anthelmintic resistance in parasites of cattle worldwide.

Though there are some published case reports of resistance in parasites of cattle in the US,[5,6] no studies have been performed to establish the national prevalence of resistance. Thus, we do not know how severe and widespread the problem is nationally. However, studies performed by my laboratory on a number of cow-calf farms in Georgia and on stocker cattle purchased at various stockyards in the southern region suggest that AM resistance in cattle is both common and widespread. In fact, more than 90% of farms tested by us in the last 5 years have AM-resistant *Cooperia*. Resistance in *Cooperia* spp and *Haemonchus* spp are the most common, but we also have seen resistance in other species as well, including *Ostertagia*. In fact, we are seeing resistance in *Ostertagia* at levels never before seen in the US; it appears that we are in the emerging stages, and as resistance worsens, this will pose a serious threat to cattle health and productivity.

Outside the US, there is a large amount of published data indicating that resistance is becoming a very serious problem; a study in New Zealand reported that ivermectin resistance was evident on 92% of cattle farms and resistance to both ivermectin and albendazole was evident on 74% of farms.[19] More recently resistance in *Ostertagia ostertagi* has been found on numerous New Zealand beef farms.[20] Very high prevalences of resistance have also been reported in studies performed in Brazil, Argentina, and Australia.[14,16,18] *Cooperia* is consistently the species with the most resistance, but resistance in *Haemonchus* is also common. Resistance in *Oesophagostomum* and *Ostertagia* are reported less commonly, but recent evidence suggests increases in these species as well.

Historically, *Cooperia* was not considered a very important pathogen. However, over the past few decades, as a consequence of heavy use of AM drugs, the relative intensity of *Cooperia* compared to other species has risen substantially. Though *Cooperia* does not impact animal health and productivity to the degree that *Ostertagia* does, a recent study confirmed that *Cooperia* infections do have a significant negative effect on growing cattle.[17] So, although clinical disease in cattle due to *Cooperia* may be uncommon, there is little

doubt that significant production losses can result from high levels of infection. Consequently, there is little evidence to support the opinion of some that AM resistance in *Cooperia* is not a major concern.

Luckily, resistance in *Ostertagia* is not yet a major problem in most of the world. However, recent evidence suggests that this might be in the process of changing. In 2018 we found ML resistance to Ostertagia on 1 of about 8 farms tested. In another study, we demonstrated almost no efficacy of AM drugs against inhibited *Ostertagia* L4. Registration studies with these drugs reported 95-99% efficacy against this stage. The virtual complete loss of efficacy is quite concerning. Should avermectin/milbemycin resistance emerge at high levels in *Ostertagia*, the problem of resistance in cattle parasites will reach a new level of importance and concern, as *Ostertagia* is a highly pathogenic species that can produce not only production loss, but also severe clinical disease and occasional deaths.

The problem of anthelmintic resistance also needs to viewed with an eye to the future. No new classes of anthelmintic have been introduced for use in cattle since ivermectin in 1981, 35 years ago. Other second generation AM drugs have provided some improvements since then, but AM resistance demonstrates a class effect; resistance to any 1 AM drug tends to confer resistance to all AM drugs. Additionally, no new novel classes of drugs have become available in the US over this time. The new drug monepantel (Zolvix®; Elanco) is sold throughout much of the world for sheep, but this drug has not yet been approved for use in the US, and it is unknown when or even if it ever will be. Currently there are no other new anthelmintic prospects in the late-phase pipeline, thus, we are left in a situation where it could be a long while before a new anthelmintic class is sold for cattle. This makes it important that the efficacies of currently available products are protected as much as is reasonably possible.

Given this situation, the problem of anthelmintic resistance in parasites of cattle should not be ignored. Clearly, there is a great need for new research to address this issue, but waiting for this research before acting is not advisable. It is recommended that anthelmintic resistance in parasites of cattle be considered a major threat to cattle productivity, and that steps be taken to mitigate the potential problems resistance can cause. Because almost no research has been done in this area, no one can say for sure what are the best approaches to reduce the rate with which anthelmintic resistance evolves in cattle. However, it would seem logical to follow some of the recommendations for sheep, which are based on sound research. To do nothing seems irrational and short-sighted.

Strategies for Mitigating the Problem of Anthelmintic Resistance in Cattle

There are several approaches that have proven effective in reducing the rate with which resistance develops in sheep nematodes: 1) using drug combinations (2 or more active compounds from different drug classes administered at the same time), 2) leaving a percentage of the flock untreated (e.g. the heaviest 10%), 3) treating selectively based on some measure of parasitism or growth rate, and 4) not treating the ewes and only treating the lambs.[1,10,11] However, cattle are not sheep – thus some will be more difficult to implement in cattle, and some may be less effective in cattle. Still, some of these are easily adapted for cattle and are likely to be effective. For instance, not treating cows will not provide as much benefit as not treating ewes. This is due to differences between the species of importance and host-parasite interaction. In sheep, both ewes and lambs share the same parasite species in similar proportions, and periparturient ewes have relatively high EPG. Thus not treating the ewes provides a source of refugia of the same species that infect the lambs. However, there is no periparturient rise in EPG in cattle, thus the relative level of egg shedding in cows remains low so long as nutrition is adequate. Furthermore, cows usually have very good immunity to *Cooperia*, and are predominantly infected with *Ostertagia*, whereas calves are infected with both *Cooperia* and *Ostertagia*. Consequently, not treating cows will not have a major impact on the resistance levels in *Cooperia*. Still, this practice may be quite beneficial for slowing the development of resistance in *Ostertagia,* which is of growing concern. Quite simply – if *Ostertagia* develop resistance at high levels, the cattle industry will suffer great economic losses, and the health and welfare of cattle will suffer. Thus, implementation of any practices that can reduce this likelihood is a good idea, so long as it does not cause significant productivity losses now.

I have often heard people say that cattlemen will not leave some animals untreated since this goes against what they have been told for years, and goes against their common sense of what is best for maximizing productivity. This may sound reasonable at first, but how many of these same cattlemen are currently using anthelmintics that are poorly effective without knowing it? Based on my experience in testing cattle farms for resistance, this may be the majority of farms. So – yes, they are treating all animals with the full associated costs, but they are not getting a highly effective result, and in some cases getting almost no benefit. I have tested several farms that had 0% reduction in FEC, and the cattleman had not suspected resistance at all prior to the test. Studies in sheep have clearly demonstrated that the production cost of subclinical parasitism as a result of using an anthelmintic product that is less than fully effective due to resistance can greatly exceed the cost of routine testing of anthelmintic efficacy.[13] Cattle farmers would thus be much better off in the present, and have greater sustainability for the long term, if they used effective anthelmintic treatments and left some animals untreated. Testing the efficacy of drugs with a FEC reduction test (FECRT) is the best way to make sure they are using effective drugs. The reluctance of most cattlemen to test for anthelmintic resistance is not rational from an economic perspective.

Recent research has also demonstrated quite clearly that the use of anthelmintics in combination is a beneficial practice. In fact, in Australia and New Zealand there are few products sold as single actives; most products contain 3, 4, or 5 different anthelmintic classes (note that they have some anthelmintic classes that are not available in the US). There are 3 major benefits to using drugs in combination: 1) one gets an additive effect with each drug used, thus the efficacy of the treatment increases, sometimes dramatically (Table 1). 2) Provides broad-spectrum efficacy; resistance is species and drug specific, thus a second (or third) drug may kill any species resistant to the first drug. This will then return the broad-spectrum result that one aims to achieve (and that is specified on the product label). 3) By achieving a higher efficacy, there are fewer resistant survivors, thus there is a greater dilution of resistant worms by the susceptible portion of the population. For example, if 2 drugs each with 90% efficacy are used in rotation, then each time cattle are treated 10% of the worms (resistant) survive. In contrast, if the 2 drugs are used in combination then the efficacy would be 99%; this yields 10X fewer resistant survivors (first drug kills 90%, second drug kills 90% of the remaining 10%).

Thus, cattleman should perform a FECRT to determine which drugs are effective and then knowing this, they should optimally use 2 drugs in combination. Additionally, they should leave 10 to 20% untreated (selected from best looking animals; upper quartile) to provide un-treated refugia. Using this new approach, they will be getting a highly effective treatment in most of the herd, which will greatly diminish egg shedding thus reducing subsequent pasture contamination and re-infection. And by leaving some animals untreated they will be sustaining a drug-susceptible refugia, which will dilute out the small number of resistant worms that survive the treatment, thus maintaining a predominantly drug-susceptible worm population. The production loss in the 10% that are untreated is likely to be small because these were in the upper quartile of animals before the treatment, and so their growth was apparently not being heavily impaired by parasites. Studies in sheep comparing productivity of groups where both traditional and targeted selective treatment programs were used demonstrated no significant differences in growth of lambs.[4,8] Using effective drugs (and preferably combinations of drugs) and managing refugia by leaving some animals untreated is highly likely to improve overall herd productivity, and the susceptibility of the worms to the drugs will be sustained much longer into the future. This approach is likely to be even more effective when using new long-acting formulations. Research is needed to investigate this issue more fully.

Table 1. Impact of using anthelmintics in combination on the efficacy of treatments. Note the increase in efficacy is due to an additive effect.

Drug 1 (%)	Drug 2 (%)	Drug 3 (%)	Combination (%)
80	80		96
80	80	80	99.2
90	90		99
90	90	90	99.9
60	95		98
60	60	95	99.2
99	99		99.99

In summary, given the current situation, it is recommended that cattle farms not assume high efficacy of their treatments and rather they should test for drug resistance using the FECRT. Doing so will allow farms to make future treatment decisions based on the knowledge of which drugs are effective and which are not. Failing this, they should assume they have resistance and move immediately to the use of anthelmintic combinations. It is also important to appreciate that resistance develops slowly over many years and is undetectable during this time, but then suddenly reaches clinically detectable levels rapidly. Because the last phase of resistance development can happen quite quickly, the FECRT should be repeated every few (2-3) years. Currently there are no published standards for performing the FECRT in cattle, so there are different things being recommended by different veterinarians and parasitologists. This is a problem because an improperly designed or analyzed FECRT can result in erroneous conclusions. Thus, it is important that clear guidelines for the FECRT in cattle be established; such guidelines are currently in preparation by the World Association for the Advancement of Veterinary Parasitology (WAAVP). Nevertheless, the recommendations recently published by this author[7] should closely resemble the final published protocol, thus I recommend following those procedures until official WAAVP guidelines are published.

Recommendation for Control of Gastrointestinal Nematodes in Cattle

There is no such thing as a 1-size-fits-all parasite control program. Parasite control programs must be tailored to the farm – differences in climate, weather, type of cattle, grazing management, cattle/milk prices, etc., will impact decisions for what constitutes the optimal control program for a farm. Selection of drugs may be based on many factors, the most important of which are: label efficacy against the targeted species/stages, what the expected prevalence of anthelmintic resistance is in your region, whether drug efficacy testing (using FECRT) has been performed on the farm, type of cattle, time of year, cost and convenience. Gastrointestinal helminths usually do not cause clinically apparent disease in cattle, but rather produce subclinical disease that is measured as lowered productivity. When clinical disease does occur, it is most likely seen in young animals less than 2 years old. This is true for both the GI nematodes and liver flukes.

Though anthelmintics can produce important improvements in the productivity of cattle, total reliance on anthelmintics for parasite control is no longer recommended, and will not be sustainable into the future, as drug resistance becomes

a more serious problem. There are numerous anthelmintic products currently available for use in cattle. Many of these drugs are both highly effective and convenient to administer, making treatment of parasites easier than ever. However, many of these drugs are expensive and may not be working at the levels they did in the past; money can be lost to unnecessary or ineffective drug treatment just as easily as to parasites. And there is always the risk of losing the ability to effectively control parasites in the future should anthelmintic resistance develop due to heavy use of these drugs. With this is mind, it is important to distinguish treatment from control. Treatment with an effective drug kills those parasites infecting animals at the time of treatment (and for a short period after treatment if the drug has residual activity). However, depending upon many factors, removal of these parasites may or may not have a significant health and/or economic benefit. On the other hand, control of parasites implies developing strategies to prevent cattle from becoming infected with economically and/or clinically important levels of infection. This most often relies on the strategic use of anthelmintics at times of the year when treatments will have the greatest benefit. This brings parasite control into the realm of cost-benefit decision-making and requires knowledge of the epidemiology of the important parasites. However, strategic control when used optimally, places strong selective pressures for the development of anthelmintic resistance. Thus, strategic control should be used together with resistance-mitigating strategies outlined above.

The clinical disease syndrome produced by gastrointestinal nematodes is referred to as parasitic gastroenteritis. This can be a very serious disease that is characterized by weight loss, diarrhea, submandibular edema, and anemia. It is caused by a variety of nematodes infecting the abomasum and intestine (primarily of the family trichostrongylidae), but *Ostertagia ostertagi* (abomasum) historically has been the most important. Other common species include *Haemonchus placei* (abomasum), *Trichostrongylus axei* (abomasum), and *Cooperia* spp (small intestine). Less common and important genera are *Oesophagostomum* and *Nematodirus*, but these too can cause diseases if present in high enough numbers.

Historically, *Ostertagia ostertagi* was the most common, pathogenic, and economically important parasite of cattle throughout most of the temperate world. In contrast, *Cooperia* spp were not viewed as being a very important parasite of cattle. However, this view is changing; emerging avermectin/milbemycin (macrocyclic lactone) resistance in *Cooperia* spp, particularly *C. punctata*, is raising concerns regarding the pathogenic potential and economic impact of this parasite species. And *Haemonchus placei* is known to be pathogenic if infections reach certain thresholds, and resistance to this species is also on the rise.

Immunity to GI nematodes is slow to develop and requires several years of grazing to reach adequate levels. Therefore, when developing appropriate parasite control programs it is important to consider the age and use of the cattle. Healthy cows (older than 3 years) that are in good body condition and on a good nutritional plane tend to have fairly strong immunity to GI nematodes. In this class of cattle, when otherwise healthy, clinical disease from GI parasites will almost never be seen. However, subclinical reductions in production are still likely. On the other hand, young recently weaned calves in their first year at grass are highly susceptible to parasitism. The potential for high fecal egg counts (>500 epg) combined with the production of a large amount of feces due to their increasing body size, make this group of animals at greatest risk for production loss and clinical disease.

Favorable climatic conditions for hatching of nematode eggs and development of trichostrongylid larvae include moisture and moderate temperatures ranging from 40 to 85°F (4 to 29°C). Temperatures beyond either extreme are often fatal (too high) or inhibitory (too low). During hot times of the year moisture then will be the limiting factor that determines the magnitude of infective larvae development. In contrast, once the infective L3 stage is reached, a different set of climatic conditions are favorable for continued survival. L3's persist longest under moist, cool conditions and are rapidly killed by high temperatures, freeze-thaw cycles, and desiccation. Thus, optimal periods of transmission will vary among regions of the USA. This will then impact the optimal times for administering anthelmintics.

Anthelmintic Therapy in Cattle

There are 3 primary classes of anthelmintics available for use in treatment of helminth infections in cattle: 1) benzimidazoles (BZ), 2) imidazothiazoles/tetrahydropyrimidines (I/T) also referred to as membrane depolarizers, and 3) avermectin/milbemycins (AM) (also referred to as macrocyclic lactones and macrolide endectocides). All 3 major anthelmintic classes are broad spectrum nematocides, but effectiveness against other groups of parasites varies widely. Cattle are typically infected with multiple species of helminth parasites that differ in their susceptibilities to the different anthelmintic drugs, but most of the commonly used drugs are effective against the most economically important species, unless resistant. This is important because some species of parasites are much more pathogenic than others, and therefore are much more important to target with treatment. It can generally be assumed that virtually all cattle will benefit from an effective anthelmintic treatment; but the magnitude of the health and cost benefit is related to the timing of treatment in relation to the parasite transmission dynamics and the management system. Appropriate meat and milk withdrawal times must be followed for all anthelmintics administered to food-producing animals, and anthelmintics not labeled for use in dairy cattle should not be administered to dairy cattle of breeding age or older.

Classes of Anthelmintics

Benzimidazoles (BZ): benzimidazoles are broad-spectrum nematocides, with albendazole also having activity

against tapeworms and flukes, and fenbendazole being effective against tapeworms and Giardia. Many BZ kill larval stages of nematodes as well as the adults, but often larval efficacy is lower than for adults. In some cases increasing the dose and/or duration of treatment (e.g. treat for multiple days) will increase efficacy against larval stages. BZ also have moderate to good activity against hypobiotic (arrested) larvae of Ostertagia, but this efficacy is considerably lower than that seen with the avermectin/milbemycin drugs. BZ are very safe; the toxic dose is 10 to 100 times the therapeutic dose, depending upon the drug. Fenbendazole is approved for use in lactating dairy cattle. BZ must be administered orally only, but are available in numerous formulations such as feed premix, bolus, drench, paste, mineral/protein block, and pellets. Albendazole is teratogenic in mice but little evidence of teratogenocity exists in ruminants. Nevertheless, there is a label warning to not use in cows during the first 45 days of gestation. Though drug resistance is reported, the serious problem of BZ resistance seen in parasites of small ruminants and horses has not yet emerged as a problem in cattle. This may be due largely to the fact that BZ have been used much less frequently in cattle than the avermectin/milbemycin drugs over the past 30 years. BZ drugs are non-persistent and rapidly metabolized; however, a rumen reservoir and gut recycling leads to prolonged gut levels of BZ in ruminants (but still short duration, <24 hr). Because of this, efficacy can be improved by restricting feed intake for 24 hr before treatment. This increases digesta residence time by decreasing digesta transit rate, which in turn increases drug availability and contact time of drug and parasite.

Membrane Depolarizers (Nicotinic agonists): this group is comprised of 2 chemically unrelated groups of drugs having very similar mechanisms of action. These drugs act as cholinergic (nicotinic) agonists causing paralysis of worms. Levamisole (imidazothiazole) is a broad-spectrum nematocide, but has no effect on any other groups of parasites, and is not effective against hypobiotic (arrested) *Ostertagia* larvae in cattle. Similar to the BZ, this drug is very short acting, but may have added benefits as an immune stimulator by potentiating T-cells, and stimulating phagocytosis in monocytes. Safety can be an issue with levamisole; toxicity appears at 3-5 X the therapeutic dose. Overdose of levamisole resembles organophosphate poisoning, with transient ataxia, salivation/muzzle foaming, and muscle fasciculations as common symptoms. Levamisole also may potentiate organophosphates, especially in Brahman cattle. Because of this, it is best to not use levamisole in debilitated animals or in animals also being treated with organophosphate insecticides, but levamisole is considered safe in pregnant cattle so long as it is dosed appropriately. Morantel (tetrahydropyrimidines) is a broad-spectrum nematocide that is approved for use in lactating animals. In contrast to levamisole, morantel is very safe and gentle with no contraindications for debility, pregnancy, or age. Presently, morantel is available only as feed premix for cattle making accurate and uniform dosing a little more challenging.

Avermectins/Milbemycins (AM, Macrocyclic lactones, Macrolide endectocides): avermectin/milbemycins are derivatives of naturally occurring antibiotic-like compounds secreted by soil-dwelling bacteria of the genus Streptomyces; presumably as a defense against bacterial feeding soil nematodes. Drugs in this group are broad spectrum, being effective against most nematodes and arthropod parasites. They have excellent efficacy (>99%) against both adult and larval stages of virtually all trichostrongyle parasites including arrested (hypobiotic) larvae, if resistant. Efficacy against *Nematodirus* spp and *Trichuris* is often less than that for most other worm species, but still should be >90% if the parasites have not developed drug resistance. AM resistance has been reported in all major species of parasites infecting cattle, but is most prevalent in *Cooperia* and *Haemonchus*. AM drugs have excellent efficacy against most ectoparasites and fly larvae (myiasis), although drugs in the avermectin group (ivermectin, eprinomectin, doramectin) are more potent against arthropod parasites than those in the milbemycin group (moxidectin). AM drugs are highly lipophilic and provide residual activity against reinfection of many parasites for periods of time that vary depending upon the worm species.

Though commonly administered as pour-ons with a dose of 0.5 mg/kg, the bio-availability is superior when administered orally or by injection at a dose of 0.2 mg/kg. Though very convenient, and thus popular with cattlemen, pour-ons are a very poor way to administer an anthelmintic. It is well established that pour-on formulations produce high variability in plasma drug concentrations between animals, due to both allo- and self-licking.[2,9] In fact, drug exchange can be quite high; in 1 study untreated animals ingested up to 27.4% of a pour-on dose.[2] In another study, 4 calves were treated with ivermectin pour-on and housed together with 6 untreated calves. Percent reduction in FEC of the untreated calves ranged from 0% (1 heifer) to approximately 95% (1 heifer), with intermediary values from approximately 30% to 80% in the other 4 untreated animals.[3] In addition, haircoat type and length, soiling of haircoat, and poor application technique can all lead to reduced efficacies not related to drug resistance. Because of these delivery and pharmacokinetic (PK) issues, the pour-on route is less forgiving to dosing errors and this often leads to reduced efficacy, even when resistance is not present. For example, poor efficacies were observed following administration of a pour-on formulation of doramectin in Highland calves, whereas subsequent treatment with injectable doramectin yielded 100% reduction in FEC.[15] Furthermore, a recent study in New Zealand demonstrated superior efficacy when AM drugs were administered orally as compared to injectable and pour-on routes.[12] Though oral administration is the least convenient, it generally provides the best efficacy because that is where the worms are. There is little metabolism of AM drugs as

most of the drug is excreted unchanged in the feces. However, currently there are no oral AM products sold for cattle.

Considerations for Treatment and Control of Gastrointestinal Nematodes in Cattle

As mentioned above, there is no such thing as a 1-size-fits-all parasite control program, and parasite control programs must be tailored to the farm. Nevertheless, there are some general recommendations that will apply in most situations. Beef cows in poor body condition due to suboptimal winter nutrition should be given a treatment in the late winter. This treatment is usually best given just before calving, but of course optimal timing will vary depending on the time frame of calving. Once new grass growth begins to occur, a return to improved nutrition will allow the cow's immune system to take back control, and the cow will limit its own worm burden. In dairy cows there is no consensus on whether treatment is economically justified. The more time dairy cows spend grazing, the more likely a treatment at calving will be of economic benefit. However, cows housed in confinement systems where they have little access to pasture may not gain much benefit from treatment. Due to the high cost of deworming 1500 lb (680 kg) dairy cattle, confinement operations may optimally do an on-farm study to determine if deworming is beneficial. This is easily accomplished by matching pairs of cows and milking heifers based on age, production and calving date, and randomly deworming 1 within the pair, and leaving the other untreated. Then after a year, milk production data can be compared to see if deworming led to a significant increase in milk production.

Stockers and replacement heifers are at the greatest risk for production loss from parasites, and use of anthelmintics will be important to their health and production. However, optimal strategies for applying those anthelmintic treatments will vary greatly, depending on the management and grazing system. Thus, it is not possible to provide a general recommendation. In general, strategic treatments, resistance-mitigating approaches, and sound pasture management must be used together.

Finally, it should be understood that any recommendation given will not be uniformly accepted by all parasitologists and veterinarians who work with cattle. There is no single best worm control program, and there is plenty of room for disagreement among experts; the best and most cost-effective strategy will differ from region to region and farm to farm, depending on many factors. And what is optimal today will not be optimal tomorrow. Constant vigilance to changes in the host-parasite-environment dynamic (including the emergence of drug resistance) is required. Finally, as noted above, the risk/problem of anthelmintic resistance must be considered. Drug resistance is not something that only happens to one's neighbors; it is extremely common and worsening all the time.

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