CURRENT APPROACHES TO INTERNAL PARASITE CONTROL IN FOOD ANIMALS

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The current concept on control of internal parasites of food animals should be just that, control. When an anthelmintic is used, individual animals are usually dewormed and then placed back into the same or a similar environment from whence they came. Even if hundreds of thousands of parasites were killed by the administration of the anthelmintic the billions of infective larvae in the environment were not and, within a short time, the animal may very well be as heavily infected as before. Some knowledge of the biology of the parasites, the specificity and spectrum of the anthelmintic, and the management and goals of the herd, flock or drove manager is necessary to control parasites.

The primary consideration is to decide which parasites to control. For example, Ostertagia and Cooperia are the predominant genera of cattle nematodes in temperate regions of the world. With populations of 3,000,000 or more Cooperia in a calf, the calf will have signs of enteritis but will probably recover. However, infections with as few as 30,000 Ostertagia is of much greater priority than that of Cooperia. The same consideration also applies to the parasites of swine and small ruminants.

Perhaps the most clear cut approach to the control of parasites in food animals is in swine where the entire life of market pigs is, at least in North America, in a confinement system. Under these conditions the transmission of parasites which require intermediate hosts or larval development in the external environment is practically nonexistent. However, those parasites which utilize an egg, cyst or are transmitted vertically can be easily transmitted in confinement systems and if sanitation and anthelmintic control are not practiced can easily reach economically significant numbers.

Daily intake of medicated feed containing pyrantel tartrate significantly reduced the prevalence of condemned livers due to ascarid migration.[1] Administering the anthelmintic in the feed or water is less stressful than other means, and if palatable it will likely be assimilated by healthy pigs in sufficient quantity to adequately treat all of the pigs within the population.

Where swine are maintained on pastures, periodic treatment with anthelmintics having an effect on both adult and larval parasites could have a distinct advantage,[2] especially when vertical transmission is the primary means of spread, treatment of sows may negate the presence of parasites in the young.[3]

More research has been done concerning the biology of various species of parasites of ruminants. The ruminant on pasture is the animal usually affected by clinical or economic parasitism. The exception to this is the situation where animals with arrested larvae within their tissues may suffer disease some period of time later after leaving the pasture where the infection occurred. The concept of arrested larval development (sometimes called hypobiosis or inhibited larvae) has increased our understanding of the survival of parasites and helps to explain apparent failures following anthelmintic treatment and outbreaks of disease at a time or place they theoretically should not occur.[4]

Arrested development of larvae may occur when there is competition for space within the host, the benevolence of the host is limited, or where environmental conditions program larvae to interrupt their development within the host. The stage of development where this occurs varies with the species of parasite involved. The arrested larvae are metabolically inactive and usually cause no damage to the host at the time they are arrested. However, this lack of activity makes them unresponsive to many anthelmintics and they are unrecognized by the host as being foreign.

Examples of arrested development to avoid unfavorable environmental conditions are those of Ostertagia ostertagi of cattle which are in arrested development during the hot dry Texas summers[5] and Haemonchus contortus which overwinters in the abomasum of small ruminants in Texas.[6] When environmental conditions become more favorable for the survival of the non-parasitic stages of the life cycle, larvae resume development. This may occur with the advent of either warmer or wetter conditions, or it may be associated with changes in the host's immunological response.

With some species of parasites, the presence of large numbers of adults within the host seems to activate a feedback mechanism which limits the number of larvae which can develop to adults within that host. When this mechanism is functioning there is a natural loss of senile worms which are replaced by similar numbers of larvae. However, if there is removal of adult worms by anthelmintics or immunologic expulsion, the larvae may develop en masse. It often appears that two or more of these mechanisms may be operating at the same time.[7] Larvae which are programmed by environmental conditions to undergo arrested development may only do so in a host which has resistance to the parasite. For instance, if larval Haemonchus which have been programmed to overwinter are ingested by a ewe they will undergo arrested development; however, if they are ingested by a parasitologically naive lamb they may develop immediately. A ewe that is genetically able to resist infection by Haemonchus contortus is unable to expel the worm during early lactation, so that Haemonchus are able to reproduce within her. By the time the ewe's ability to expel the parasite has returned, the pastures will be sufficiently laden with infective larvae and her lambs will have become infected.

In recent years anthelmintics which have the ability to kill arrested stages of various parasites have become an important part of the management strategy against those parasites which utilize arrested develop as a means for surviving unfavorable environmental conditions.[8,9] If these drugs are used against arrested larvae during unfavorable seasons there will be no larvae to emerge when conditions are once more favorable for their development and survival.

Other strategies that may be utilized are those using compounds which have an effect against the infective stages of the parasite or interfere with the parasite's ability to reproduce. These drugs may be included in a concentrate ration, with salt or mineral, for daily intake. However, unless the drug is utilized daily, sufficient parasites may survive and become an economically important problem. Another aspect to consider is that those parasites may have been selected to survive because of their resistance to the drug in question. One technique to avoid this problem may be the use of a reticular bolus which exudes anthelmintic into the animal for a prolonged period of time. A sustained release bolus utilizing morantel tartrate, for instance, has been

found to be useful in controlling parasitic gastroenteritis.[10] The use of controlled release boluses or the implanting of sustained release pellets containing anthelmintic substances may negate the need to prepare parasite free pastures for susceptible young animals. However, in view of the strong interests in having food substances free of "unnatural substances," methods of controlling parasites by the use of "natural substances" such as hormones or pheromones may be the direction of future research.[11]

The problem of anthelmintic resistance by various parasites has allowed the propagation of some parasites into considerable numbers. Resistant species of parasites also appear to increase in numbers because of lack of intraspecific competition, malnutrition, esophageal groove closure or anorexia.[12] Selection toward resistance will be more rapid if there is a large proportion of the worm population that is not killed by the anthelmintic. If there are resistant genes in the population and a dosage is given which may kill only those worms that are fully susceptible, then the next generation will contain only those worms which have the resistant gene. If, however, the level of anthelmintic is sufficient to kill all but those fully resistant to the anthelmintic then the population may become so limited that reproductive efficiency is decreased.[13] However, those worms that do escape are extremely likely to be resistant to the class of anthelmintic utilized and the rate of development of resistance to an anthelmintic is greatest when only a small proportion of the worm population escapes exposure to treatment.[14] To delay the development of resistance, alternation of classes of anthelmintics has been advocated. This strategy will be effective only if the alternation is spaced so that only one drug will be used on a generation of parasites. If rotation of anthelmintics is of shorter duration, multiple resistance to all classes of anthelmintic used will occur in a shorter time than if no alternation of drugs had been practiced.[13]

Table 1. Spectrum of efficacy of anthelmintics approved for use in swine in the United States.

Anthelmintic	Ascaris	Stephanurus	Strongyloides	Gastrointestinal nematodes
Piperazine	++	-	-	-
Coumaphos	++	-	++	++
Pyrantel	++	+	+	++
Levamisole	++	-	++	++
Fenbendazole	++	++[a]	-	++

\- no or limited efficacy
\+ some efficacy
++ acceptable efficacy
a efficacy at greater than label recommendation

Table 2. Spectrum of efficacy of anthelmintics approved for use in cattle in the United States.

Anthelmintic	Liver Flukes	Gastrointestinal nematodes	Tapeworms	Lungworms	Arrested Ostertagia
Phenothiazine	-	+	-	-	-
Coumaphos	-	+	-	-	-
Thiabendazole	-	++	-	-	-
Levamisole	-	++	-	++	+
Haloxon	-	++	-	-	-
Morantel	-	++	-	-	-
Fenbendazole	-	++	++	++	++[a]
Albendazole	++	++	++	++	++
Ivermectin	-	++	-	++	++

- \- little or no efficacy
- \+ limited efficacy
- ++ acceptable efficacy
- a efficacy at greater than label recommendation

Table 3. Spectrum of efficacy of anthelmintics approved for use in sheep and goats in the United States.

Anthelmintic	Liver Flukes	Gastrointestinal nematodes	Tapeworms	Lungworms	Haemonchus
Phenothiazine	-	-	-	-	+[b]
Thiabendazole	-	++	-	-	++[b]
Levamisole	-	++	-	++	++[b]
Albendazole*	++	++	++	++	++[b]

- \- little or no efficacy
- \+ limited efficacy
- ++ acceptable efficacy
- b resistant populations
- * sheep only

Table 4. Mechanism of action of various anthelmintics approved for use in food animals in the United States (15,16,17).

Anthelmintic	Class of Compound	Mode of Action
Phenothiazine	phenothiazine	unknown
Piperazine	piperazine	muscle hyperpolarization
Coumaphos	organophosphate	acetylcholinesterase inhibitor
Haloxon	organophosphate	acetylcholinesterase inhibitor
Thiabendazole	benzimidazole	mitochondrial reaction inhibitor
Fenbendazole	benzimidazole	mitochondrial reaction inhibitor
Albendazole	benzimidazole	mitochondrial reaction inhibitor
Levamisole	imidazothiazole	cholinergic agonist (ganglionic)
Morantel	pyrimidine	cholinergic agonist (ganglionic)
Ivermectin	avermectin	GABA agonist (post-synaptic)

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Points raised during discussion

Question: What about the usefulness of ivermectin in food animals?

Dr. Craig: With food animals, at least, we will have to look at this question in terms of economics. With ivermectin as it is right now we have the situation where we know that we can do a super job with it against arrested larvae of Ostertagia, the principle parasite of cattle in temperate areas of the world. It also has exquisite effects against such parasites as Hypoderma at very low levels. About 0.2 mg/kg will apparently kill this particular parasite. So when you are talking about certain target parasites, yes, ivermectin will have almost revolutionary effects but what are the economics going to be for some of the other parasites? Ivermectin does not have an effect against, for example, liver flukes or tapeworms. Tapeworms are probably

not all that important but liver flukes are, at least under some circumstances. So it may be the one parasite that will be the limiting factor for this particular anthelmintic and certainly there are a few more things about its activity we really need to test under field conditions to ascertain how much of a revolution ivermectin will produce.

Question: What about feeding low levels of anthelmintics and the emergence of resistance?

Dr. Craig: Reading the literature in this general area, one is left with a great deal of confusion. With the present product of the slow-release morantel bolus and the studies that have been done, at least on a short-term basis of about a year, would seem to indicate that resistance does not appear to be a problem. However, by the same token, there was some evidence that low-level use of phenothiazine, which was acting not so much as an anthelmintic per se but more as a pill for the lady worms, was cutting their ability to reproduce. There did appear to be a faster increase in resistance under some circumstances but this is not proven true in all species. This has been more the case in the equine than it has been where studies have been done in ruminants. This may be due to a lack of knowledge of the pharmacokinetics right there. We have seen this with drugs such as fenbendazole in ruminants versus other animals. We can only speculate on the problem and we really cannot make any hard and fast rules at this time.

Question: Are the economic aspects of the use of anthelmintics in food animals being studied?

Dr. Craig: The question is, "Are we investigating the economics of the use of anthelmintics in food animals?" We are attempting to do this. An example would be the several studies that we have done in the past 5-6 years looking at the use of anthelmintics in healthy stocker cattle. The normal procedure here in Texas is for ranchers to sell calves at weaning time, which is most often in the autumn. They will then go onto a small grain pasture (wheat, oats, rye, rye grass or combinations thereof) and will spend the winter there. We will find an average daily gain difference of 0.1 to 0.25 pounds per day between those calves that were dewormed before going onto the pasture and those that were not. However, we were unable to see any difference among various anthelmintics given at a time of the year which was past the time that we would have emerging larvae that were arrested and the new ones that were not in yet. We were virtually working against worms. We used thiabendazole, levamisole, fenbendazole, albendazole, morantel and in various trials one would look better than the others but there really was no difference between them. We have also done some trials with suckling calves, where the suckling calves were given an anthelmintic going into the same type of situation as their mothers. We again found a difference of about 0.25 pounds average daily gain. When you add this up over a 150 days you

have a real difference. We are presently setting up a trial in beef cattle looking at the difference between the deworming of cows, the deworming of cows and calves and the deworming of calves only. My contention is that the biggest parasite a cow owns is her calf and that the calf is the source of contamination for pastures. We will find, if we are looking at eggs per gram, that in our cows, we will maybe get them up to 20-25 egg per gram and the calves are running around with 650-1500 eggs per gram. The calf looks fine and the cow looks like hell. The cow is doing the work; she's making milk and the calf is utilizing it. We have got a little herd out here of 800 cows and we think we can generate enough numbers to get some differences that are meaningful, although the statistics on this are a bag of worms, if you want to put it that way!

Dr. DiPietro: I want to emphasize the question of milk production in dairy cows and deworming at freshening. The Agricultural Bureau of Great Britain hired a statistician to evaluate this. Because one is dealing with subclinical parasitism in those cows and multifactorial parameters, such as milk production, and the heat at that particular time of year when the cow comes fresh, it was estimated that it would take 70,000 perfectly matched cows to answer the question through one lactation.