EFFECTIVE PARASITE CONTROL FOR COW-CALF PROGRAMS - AN UPDATE ON EFFECTIVE ANTHELMINTIC USAGE

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Parasite control is necessary for optimal cow-calf performance. By deworming, nematode parasites are reduced in numbers perhaps by 95-99% with use of an effective anthelmintic drug per treated cow or calf. In mother cows, this should maximize reproductive potential, milk production and desirable weight maintenance. Treatment of cows before being moved to a "rested" pasture will reduce contamination and transmission to parasite-naive calves. Treatment of calves at a later time in the grazing period will improve growth performance.

Deworming should be an integral part of the overall herd health program. Too often, parasite control is eliminated from a program or not used. Yet subclinical parasitism has been shown to depress performance when not negated by effective anthelmintics and appropriate timing of their administration. When other factors such as nutrition, weather conditions (temperature, precipitation) and forage are in a steady state, the benefits of an effective anthelmintic are especially evident.

Scheduling of Anthelmintic Administration

In the U.S., spring calving may be from January-April but hopefully confined to 2 months of that period. Cows, late winter and fall calves and yearlings usually are dewormed prior to summer pasture turnout (April-May). Late spring calves should be treated in late June-early July.

Because of the hypobiotic larval (eL_4) phenomenon of *O. ostertagi* with subsequent massive emergence of L_5, schedules necessitate late spring-early summer deworming of early spring calves and yearlings in the warmer temperate zone of the U.S. and in the fall at weaning time for replacement heifers and calves to be backgrounded, especially in the colder temperate zone where hypobiosis occurs over winter. Cows also should be dewormed in the fall to reduce worm parasite levels.

Selection of an Effective Anthelmintic

What are the important considerations for selection of the anthelmintics of choice? They should include (1) efficacy against target parasite species; (2) spectrum of activity for other species; (3) stages of parasite affected and degree of parasite activity; (4) safety or therapeutic index of the dewormer and its contraindications; (5) retention of the drug's metabolites in meat and milk with awareness of withdrawal times; and (6) approved formulations and routes of administration [1]. Resistance has not been a factor in the U.S.

For cattle worldwide including the U.S., *Ostertagia ostertagi*, the abomasal worm, has been considered the target species of the parasitic gastroenteric (PGE) complex and has been used to test efficacy of recently approved anthelmintics. Because *Ostertagia* destroys gastric glands, anorexia due to a dysfunctional stomach results in inappetence, poor digestion, and generalized edema with the possibility of septicemia. This etiology then is one that may be expressed as clinical to subclinical parasitism, the latter especially observed in temperate areas, with less than expected weight gain of calves and of weight maintenance of cows and even inordinate weight loss with peripheral edema and pale mucous membranes. Economic losses follow. Other aspects of this parasite species are larval stages dormant in the gastric glands. Emergence causes metaplasia and pathophysiologic responses. An ideal anthelmintic for this target species must then be larvicidal as well as adulticidal and be active against dormant as well as active stages. Efficacy for removal of *Ostertagia* may approach 100% with the anthelmintics of choice.

Spectrum of activity could include other nematode species in the PGE complex such as *Cooperia*, *Nematodirus* and *Bunostomum*, the respiratory tract nematode *Dictyocaulus*, the cestode *Moniezia*, the liver trematode *Fasciola*, and ectoparasite species. In some geographic areas, one or more of these may be considered target species in addition to *Ostertagia*. Certainly ectoparasites such as biting and sucking lice

are important in causing debilitation and economic loss. Also, fixed combination dewormers broaden the spectrum of activity to remove additional target species.

In addition to *Ostertagia*, larval or immature stages of other parasite species can cause acute to chronic disease leading to blood loss anemia (*Bunostomum*), nodule formation in the gut wall (*Oesophagostomum*), and liver parenchymal damage and hemorrhage (*Fasciola*). Larvicidal anthelmintics are desirable to suppress these prepatent infections. The larvae and immature helminth parasites serve as replacements for the adults when removed by senescence or treatment. Thus, a two-fold action results by reducing clinicopathologic effects and thwarting establishment of a reproductively-active second generation.

Untoward or toxic effects induced by the dewormer are undesirable, even when efficacious as parasiticides, e.g., organophosphates may be tolerated poorly by the host and could result in aberrant behavior, incoordination and even death. Contraindications with drugs in the same chemical family or related ones, pregnancy, disease and depression must be considered prior to administration. The more recent generations of anthelmintics are well-tolerated and have little if any effect on the fetus or the female reproductive tract. These are safe for the host and do not cause abnormal behavior.

Metabolites of anthelmintics may be retained in muscle, fat, blood, etc. Are there desirable effects for the target host? Do these retained metabolites have any undesirable effects on the human consumer? Or, on other animal species which contact urine or fecal excreta with anthelmintic metabolites present in them? Food safety is currently a topic of high priority for consumers, environmentalists and hopefully producers. Knowledge of withdrawal times prior to slaughter or milk collection is mandatory.

The following section lists FDA-approved anthelmintics and their formulations, dose levels and routes of administration. Approval is based on field and laboratory trials conducted by sponsoring pharmaceutical companies which develop, test and market anthelmintics. Marketing recognizes convenience of routes, scheduling of administration and cost effectiveness. Formulations traditionally have been solutions, suspensions, powders, and granules administered as injectables, tablets, boluses, drenches and pour-ons or as premixes or as medicated feed. Sustained release devices are being developed which may allow for continuous or programmed administration. These may be intrareticular, intraruminal, or dermal and are in the pioneering stage in the U.S.

List of FDA-Approved Anthelmintics for Beef Cattle

A description of FDA-approved anthelmintic drugs is presented alphabetically by class of compounds [1]. Their mode and spectrum of activity, dose level and mode of administration, possible adverse reactions and therapeutic indices are included:

Avermectins are obtained from fermentation products of *Streptomyces avermitilis*. Antimicrobial activity is insignificant but some have anthelmintic and ectoparasiticide properties. Ivermectin (Ivomec^{R}, Ivomec^{R} Pour-On - MSD Agvet Div. of Merck and Co., Inc., Rahway NJ 07065) is the only avermectin approved and marketed as an anthelmintic for cattle. It stimulates release of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter causing paralysis and slow death of target parasitic nematodes and arthropods. Tapeworms, flukes, and coccidia do not possess GABA so that ivermectin is ineffective. GABA is only present in the CNS of mammals, therefore healthy cattle would be unaffected by ivermectin because of the blood/brain barrier.

The spectrum of activity at the recommended dose level of 200 mcg/kg includes the PGE complex of *Haemonchus placei, Ostertagia ostertagi* (adults, active and dormant infective larvae), *O. lyrata, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata, C. pectinata, Nematodirus helvetianus, N. spathiger*, and *Oesophagostomum radiatum*; the lungworm *Dictyocaulus viviparus*; and the cattle grubs *Hypoderma bovis* and *H. lineatum*, sucking lice *Linognathus vituli* and *Haematopinus eurysternis* and scabies mites *Psoroptes ovis* and *Sarcoptes scabiei* var. *bovis*.

Modes of administration include a 1% solution for subcutaneous injection in the neck region or a 0.5% pour-on given along the dorsal midline. Each ml ivermectin/50 kg bwt provides 200 mcg/kg. Doses of more than 10 ml of the injectable should be divided between two sites.

Injection sites occasionally may swell with discomfort. As a grubicide, proper timing of treatment by geographic region is indicated to avoid bloat, paralysis and possible death due to disintegration of grubs in esophageal and spinal cord sites. Toxic signs appear only at doses greater than 30x the recommended

dose. Breeding performance is not affected at recommended dose levels. Cattle must not be treated within 35 days of slaughter.

Ivermectin does appear in the feces and has an effect on fly larvae thereby suppressing emergence of adult horn flies. It may appear in run-off from feedlots with fish and other aquatic forms possibly affected.

Four benzimidazole carbamate anthelmintics are approved and marketed for cattle. All inhibit fumarate reductase in the parasite thereby blocking mitochondrial function and depleting glycogen reserves.

Albendazole (Valbazen^{R} - SmithKline Beecham Animal Health, Exton PA 19341) differs from other benzimidazoles in being a flukecide (adult *Fasciola hepatica*) at 8 weeks post-infection. It also is efficacious in killing larval and adult stages of *Ostertagia ostertagi* and *Haemonchus placei* (and *H. contortus*), *Trichostrongylus axei* and *T. colubriformis, Bunostomum phlebotomum, Cooperia oncophora* and *C. punctata, Nematodirus helvetianus* and *N. spathiger, Oesophagostomum radiatum, Dictyocaulus viviparus* and *Moniezia*. The recommended dose is 10 mg/kg as an 11.36% suspension in an oral drench. There are no overt toxic effects @ 4.5x the recommended dose and @ 2.5x no significant effect on fetuses or calves at birth, but should not be given during the first 45 days gestation as an adequate margin of safety at breeding or early gestation has not been established. Withdrawal is 7 days prior to slaughter.

Fenbendazole (Panacur^{R} - Hoechst Roussel Agri-Vet Co., Somerville NJ 08876) was FDA-approved initially in 1983 @ 5 mg/kg as an effective adulticide for the PGE complex and *Dictyocaulus*. Subsequent approvals listed larvicidal activity of most gastrointestinal nematodes @ 5 mg/kg and inhibited L_4 *O. ostertagi* and *Moniezia* spp @ 10 mg/kg. Fenbendazole is available in several formulations with differing withdrawal times prior to slaughter; these include a 10% suspension and a 10% paste (multidose cartridge) with a withdrawal period of 8 days and feed grade formulations available as a block @ 5 mg/kg for a 3-day consumption period and an 11-day withdrawal following the last treatment and a 20% premix @ 5 mg/kg in complete feed for a one day treatment or used in crumbles, pellets and cubes or as a free-choice mineral mix to be consumed over a 3-6 day period with a withdrawal of 13 days.

Oxfendazole (Synanthic^{R} - Syntex Animal Health, W. Des Moines IA 50265) was FDA-approved in 1990 @ 4.5 mg/kg for removal and control of adult *Haemonchus placei* and *H. contortus,* adult and L_4 (active and inhibited) *Ostertagia ostertagi,* adult *Trichostrongylus axei*, adult *Oesophagostomum radiatum*, adult *Bunostomum phlebotomum*, adult and L_4 *Cooperia oncophora, C. punctata,* and *C. mcmasteri*, adult and L_4 *Dictyocaulus viviparus*, and *Moniezia benedini*. Oxfendazole is a 22.5% (225 mg/ml) suspension administered orally by calibrated dose syringe or intraruminally with an intraruminal injector. There are no contraindications given. Withdrawal prior to slaughter is 7 days.

Thiabendazole (TBZ^{R} - MSD Agvet, Div. of Merck and Co., Inc., Rahway NJ 07065) is the progenitor of the benzimidazole carbamates, being introduced in the early 1960's. The recommended dose level is 66 mg/kg in a 43% paste, 2 g or 15 g boluses, 3.3% cubes and a suspension for *Haemonchus* spp., *Ostertagia* spp, *Trichostrongylus* spp and *Oesophagostomum radiatum* and 110 mg/kg for severe infections of these and for *Cooperia* spp. Cattle should not be treated within 3 days of slaughter. Thiabendazole is safe at 20x the therapeutic level even for debilitated cattle and very young animals and is safe for pregnant cattle.

Clorsulon (Curatrem^{R} - MSD Agvet, Div. of Merck and Co., Inc., Rahway NJ 07065) is a benzenidisulfonamide which inhibits glycolytic pathways of trematodes. When administered as an oral drench at 7 mg/kg, it has greater than 99% efficacy against adult *Fasciola hepatica* and 94% against the immature stage over 8 weeks post-infection. Chlorsulon can be used in conjunction with other anthelmintics and is approved as part of a fixed combination drug with ivermectin. There is an 8-day withdrawal period.

Levamisole (Tramisol^{R} - American Cyanamid Co., Princeton NJ 08540; Levasole^{R}, Totalon^{R} -Pitman Moore, Washington Crossing NJ 08560) is an imidazothiazole, initially FDA-approved in the late 1960's and is available as a subcutaneous injectable (phosphate salt), oral gel (hydrochloride salt), bolus and a soluble powder for drenching or as a pour-on. It is highly effective against adults of the PGE complex and *Dictyocaulus viviparus* and loss against immature stages. There is a narrow margin of safety with slight muzzle foaming in cattle given 2x the subcutaneous injection dose recommended. Swelling may also occur on occasion at these sites. There is no contraindication in pregnant cows. Withdrawal is 2 days for oral administration, 7 days for injection and 9 days for the pour-on.

The class tetrahydropyrimidine is represented in the U.S. by morantel tartrate (Rumatel^{R} -Pfizer, Inc., NY, NY 10017) and is available as an oral bolus or medicated premix @ 9.68 mg/kg to remove adult

Haemonchus spp, *Ostertagia* spp, *Trichostrongylus* spp, *Cooperia* spp, *Nematodirus* spp and *Oesophagostomum radiatum*. Morantel is contraindicated for severely debilitated cattle.

References

1. Corwin, R.M. 1992. Anthelmintic Therapy. Current Veterinary Therapy: Food Animal Practice 3:667-672.

Summary

Several anthelmintic drugs are FDA-approved and available for use in beef cattle in the U.S. The most recently approved dewormers have been found highly efficacious against adult and larval (including dormant) stages of the target species *O. ostertagi* with a broad spectrum of activity against the PGE complex, the lungworm *Dictyocaulus*, the adult tapeworm *Moniezia* (benzimidazoles), immature (8 weeks post-infection) and adult *F. hepatica* (albendazole, clorsulon) and ectoparasites (ivermectin). A fixed combination dewormer (ivermectin + clorsulon) for internal nematode, trematode (*F. hepatica)* and arthropod parasites is also approved. These drugs have been observed to be safe when administered at approved dose levels. There is increased awareness of and technologic capability to monitor metabolites retained in blood plasma, muscle and milk, and in excreta. For beef products used for human consumption, food safety has become of paramount interest. A variety of formulations and routes of administration has allowed for convenience of usage to reduce labor intensity and to better suit available working facilities.