

AN ABSTRACT OF THE THESIS OF

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Title: Efficacy of Morantel Sustained Release Bolus Against Gastrointestinal Nematodes in First Season Grazing Holstein Calves

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Abstract Approved:


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The efficacy of the morantel sustained release bolus (MSRB) in reducing gastrointestinal parasitism in first season grazing calves was evaluated during the summer-fall grazing seasons of 1982 and 1983 in western Oregon. Thirty-eight calves (1982) and 40 calves (1983) were randomly assigned to a control and treatment group each season. All animals in the treatment groups received the MSRB on the day of turnout onto pasture. To monitor burden of infective larvae, worm-free tracer calves (16 total in 1982 and 18 total in 1983) were introduced onto the pastures every four weeks. Mean worm burdens from tracer calves grazed with treated animals in 1982 and 1983 showed overall reductions of 86.4% (not significantly different) and 84.3% ($P < 0.01$) respectively. Ostertagia ostertagi, Cooperia oncophora, and Nematodirus helveticus were the primary nematodes recovered at necropsy. Twelve full-season tracer animals (six treated and six control) necropsied at trial termination (1982) indicated an 88.1% (P

< 0.05) overall reduction in mean worm burdens. Mean fecal worm egg counts of eggs per gram (EPG) of feces of treated animals reflected a reduction of 69% ($P < 0.05$) in 1982 and 90% ($P < 0.05$) in 1983. Based on the EPG's (1982, 1983) and the immature larvae recovered at necropsy from the final set of tracer calves (1982), infection levels were higher in the fall season. Between October 26 and December 7, 1982, the largest increase in worm counts was due to inhibited L₄ (pre-Type II) ostertagiasis. In 1982, there was a 7.9 kg weight gain advantage of control animals compared to treated animals at day 160; however, on day 202 the treated animals showed a 4.6 kg weight gain advantage over the controls. In 1983, the treated animals gained an average of 13.5 kg ($P < 0.05$) more than the control animals. All animals remained clinically healthy during the trials and no boluses were lost from treated animals. These trials demonstrated that the MSRB was an effective anthelmintic for reducing gastrointestinal parasitism in first season grazing calves and in decreasing pasture larval contamination.

EFFICACY OF MORANTEL SUSTAINED RELEASE BOLUS AGAINST GASTROINTESTINAL
NEMATODES IN FIRST SEASON GRAZING HOLSTEIN CALVES

by

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EFFICACY OF MORANTEL SUSTAINED RELEASE BOLUS
AGAINST GASTROINTESTINAL NEMATODES IN
FIRST SEASON GRAZING HOLSTEIN CALVES

INTRODUCTION

The epidemiology of gastrointestinal parasitism in first season grazing animals has been well documented in several European countries.^{45-49,70,94,95} From these studies, the epidemiological pattern has been shown to be quite consistent, with Ostertagia, Cooperia, and Nematodirus representing the most common genera. Low level initial infections are caused by the over-wintering of infective pasture larvae which are ingested by young animals when placed onto spring pastures. Although older animals develop an increasing immunity to trichostrongylid parasitism, little resistance has been demonstrated in first season grazing calves.^{5,24} Within three to four weeks after ingestion of infective larvae, fecal egg counts of untreated animals increase steadily, reaching an initial peak in mid-late summer. These eggs embryonate, hatch, and develop to infective larvae which can be ingested before the end of the grazing season, remain on the pasture to re-establish the cycle the following year, or die. Recently, a morantel sustained release bolus (MSRB)^a

^aParatect^R bolus - Pfizer Inc., Terre Haute, Indiana.

which releases morantel tartrate intra-ruminally for a minimum period of 60 days,⁷⁰ was developed to prevent establishment of initial infection by infective larvae, kill adult parasites, and later reduce egg output and pasture contamination. Consequently, MSRB treated animals should harbor less parasites, reduce pasture contamination by shedding fewer worm eggs in their feces, and be less likely to develop parasitic gastroenteritis.

The objectives of these two years of experiments in this study were to determine the epidemiological pattern of gastrointestinal nematodes in western Oregon and to determine the efficacy of MSRB in controlling worm burdens in first season grazing calves and in reducing pasture larval contamination.

LITERATURE REVIEW

Parasitic gastroenteritis (PGE) can occur in grazing cattle in either a clinical or subclinical state depending on parasite numbers and species present, developmental stage of the parasite, age and susceptibility of the host, as well as other inter-related factors.¹ Clinical signs of PGE include the usual signs of weakness, rough hair coat, anorexia, decreased weight gain, and chronic diarrhea. Occasionally death may occur due to severe nematode infections. Although O. ostertagi is the gastrointestinal nematode usually associated with bovine PGE, several other worms can cause clinical parasitism if present in sufficient numbers. Other common gastrointestinal nematodes of cattle that can cause PGE include the genera Cooperia, Nematodirus, Haemonchus, Trichostrongylus, Oesophagostomum, Bunostomum, and Chabertia.² Subclinical parasitism on the other hand often goes unnoticed because animals display no obvious signs of the disease.

Under natural conditions, parasite burdens often consist of mixed populations of nematode genera, thus the effects of the infection on the host, whether clinical or subclinical, depend on the net effect of the total parasite populations.³ Of the several nematode species in the gastrointestinal tract of cattle in Europe, Ostertagia ostertagi, located primarily in the abomasum, is the most prevalent, pathogenic, and economically significant.⁴ Numerous studies from the Southeastern and Gulf states,⁵⁻¹³ Wisconsin,^{14,15} Kansas,¹⁶ Illinois,¹⁷ Kentucky,¹⁸ Arizona,¹⁹ Montana,²⁰ California,²¹ Washington,²² Oregon,²³ and Maine²⁴⁻²⁶ (among others), indicate that O. ostertagi is the most

important nematode in the United States. These studies also reflect that parasitism is extensive and not restricted to any particular geographical region.

In 1965 British scientists classified PGE caused by O. ostertagi into three phases (Type I, Pre-Type II, Type II ostertagiasis).²⁷ Type I ostertagiasis corresponds to the classical description of clinical parasitism and is seen in Britain and other areas of similar climactic conditions from mid-summer through the end of the grazing season. This disease is seen in calves 18 to 21 days after the ingestion of infective larvae during the first grazing season. Pre-Type II ostertagiasis is the pre-cursor to Type II ostertagiasis. Type II, which causes weight loss and diarrhea, results from the maturation, up to six months later, of the pre-type II inhibited larvae. In Britain all stages of the disease are prevalent in dairy calves grazing infective pastures.⁵

When significant numbers of O. ostertagi are present in the bovine abomasum extensive pathological and biochemical changes can occur. Conditions observed in PGE include oval or circular greyish white nodular lesions on the abomasal mucosal, and hyperplasia and loss of differentiation of the abomasal epithelium resulting in a "morocco leather" appearance. The loss of differentiation of the abomasal parietal cells results in a decrease in the production and secretion of hydrochloric acid causing abomasal pH to increase from 2 to over 7.²⁷ Above pH 6 pepsinogen is not converted to pepsin and peptic digestion stops. Above pH 7 diarrhea begins within 24 hours.²⁸ Hyperplastic cuboidal cells form incomplete intercellular bridges through which plasma proteins can leak into the lumen, while

pepsinogen can enter the circulation. These blood plasma pepsinogen levels have been used by researchers to classify parasite infection as either clinical or subclinical.²⁹ Also, lowered production of plasma proteins along with the loss of plasma protein (essentially albumin) can decrease the total circulating protein levels enough to alter plasma oncotic pressure resulting in edema.^{27,28} These conditions ultimately contribute to decreased feed efficiency, poor weight gains, and other clinical signs of the disease.

Parasitized feedlot calves convert feed less efficiently than do non-parasitized calves. After treatment with an anthelmintic, treated calves displayed a mean advantage of 0.44 in feed efficiency over control animals. In addition, feed efficiency decreased more with low-energy diets than with high energy diets.³⁰

The life cycles (Figure 1) of the Trichostrongylidae are direct, with no intermediate hosts; among the various species of trichostrongylid nematodes only slight variations of life cycles occur.³ Adult female worms in the gastrointestinal tract lay eggs which may be discharged from the host in the feces. The number of parasite eggs in the feces varies considerably, dependent on the genera of parasite present, animal diet, host resistance, physiological status, and immune mechanisms.³¹⁻³⁹ These eggs discharged in the feces embryonate and hatch in the environment when favorable conditions exist. The newly-hatched first-stage larvae (L_1), feeding on bacteria present in the fecal pad develop and molt to second-stage larvae (L_2). Second-stage larvae develop further and molt to infective ensheathed third-stage larvae (L_3) which cannot feed, thus their nutrition is limited to the food reserves in their

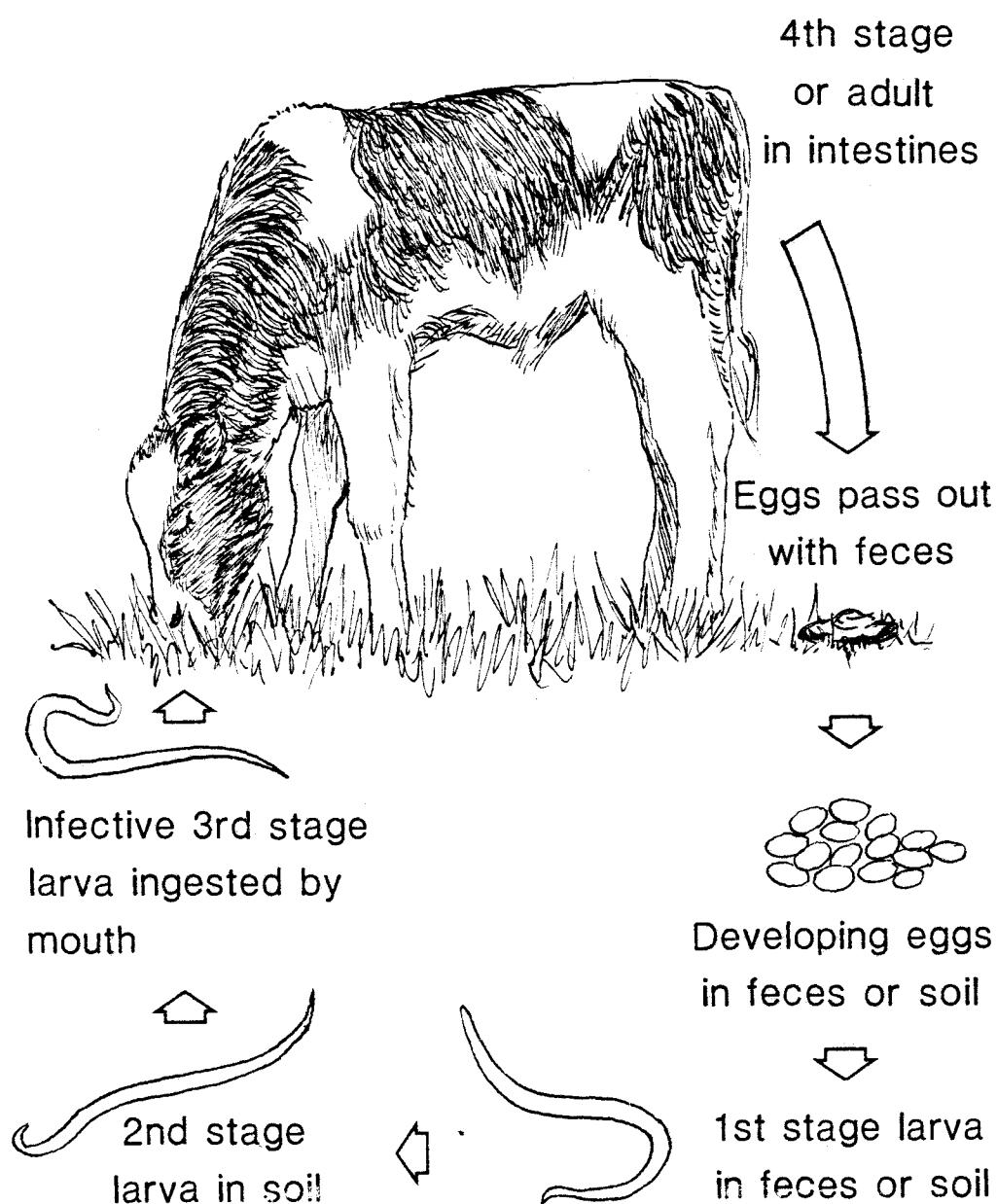


Figure 1---Life cycle of cattle gastrointestinal nematodes (Schock 1976).

intestinal cells.⁴⁰ Exposure to direct sunlight can quickly kill developing larvae.² These infective third-stage larvae remain in the fecal pad or migrate out and, if not ingested by a final host, die. After ingestion by a final host the L₃ molt into a fourth-stage larvae (L₄) which ultimately develop into adult (L₅) worms in the gastrointestinal tract. Under optimum conditions the prepatent period, the time from the ingestion of L₃ until eggs are passed in host feces, is about 21 days for the gastrointestinal nematodes.^{28,40}

In addition to the life cycle already discussed, a condition known as hypobiosis (arrested or inhibited development) occurs in certain nematode infections. In this condition the ingested infective L₃ penetrate into the intestinal mucosa, become arrested at the early fourth-stage (EL₄) and remain as such for up to six months before emerging to the mucosal surface to complete development to the adult (L₅) stage.⁴ The phenomenon of hypobiosis, has been well documented for O. ostertagi, C. oncophora, and N. helveticus in cattle.^{4,27,41,42} Although this inhibition probably occurs in other genera as well, more research is needed before any conclusions can be drawn. Arrested development has been attributed to many factors including seasonal temperature, day length, exposure to high numbers of L₃, host resistance, and nutrition.⁴³ In the Montreal area of Canada both the lowering of temperature and the shortening of day length were found to be involved in the seasonal hypobiosis of gastrointestinal nematodes.^{13,42} In New Zealand, Australia, temperate areas of the Southern Hemisphere, and in southern temperate areas of the Northern Hemisphere, stimuli to larval inhibition have not been explained.¹³

Specific times that arrested development and larval emergence occurs can vary from year to year in specific geographical areas depending upon the specific environmental conditions of that particular year. Hypobiosis has been shown to occur during the late fall season in Washington,²² Oregon,²³ Canada,^{42,44} and Europe;⁴⁵⁻⁴⁹ however, in Georgia,⁴² northern California,²¹ and Louisiana¹³ it occurs during the spring season.

Numerous studies and reviews have contributed greatly to our knowledge of the relationship of climactic conditions and the influence they have on nematode survival.^{2,50-52} Embryonation, hatching, and larval development are affected by temperature, humidity, and moisture. In 1952 Roberts et al.⁵³ found that a dry, encrusted fecal pad prevented L₃ from leaving, thus increasing larval survival time. With rainfall the fecal pad softens and the larvae are able to migrate horizontally up to 24 inches in 24 hours. Once the L₃ are freed from the fecal pad they are able to migrate vertically on the herbage, distance depending upon plant conformation. In clover L₃ were found to be evenly distributed vertically over the stems and leaves whereas in grass type plants the infective larval accumulated on the lowest blades.⁵⁴ Furthermore, Soulsby indicated that the majority of L₃ are present on the forage in the early morning and early evening when temperature and humidity are most favorable.⁵⁵

Eggs of Ostertagia spp. and Trichostrongylus spp. are very resistant to cold weather, capable of developing and hatching at temperatures below 5°C with survival as long as 20 days at -6°C. Nematodirus spp. eggs and larvae are very resistant to low temperatures and desiccation; eggs can survive exposure for 2 weeks at

-10°C. Because of their resistance to subfreezing weather both Ostertagia spp. and Nematodirus spp. are able to survive on pastures where low temperatures are common.⁵⁶ Optimum temperature for the development of nematode L₃ is between 20°C and 30°C. Below 10°C development is slower. At temperatures above 30°C development occurs more rapidly. The free-living stages of Cooperia spp., Haemonchus spp. and Oesophagostomum spp. do not survive winter pasture when subjected to subfreezing temperature.⁵¹ Temperature extremes for L₃ development of the following genera are as follows: 12.8-22.8°C,² for Ostertagia spp. and Trichostrongylus spp; 14-37°C for Haemonchus spp.; and 7-38°C for Oesophagostomum spp.³⁰ Maximum temperature for Cooperia spp. L₃ development is 36°C.⁵¹

For H. contortus and T. colubriformis a Degree-Day (temperature °C x number of days exposed) concept was described. However, with these two species it was determined that a total amount of thermal energy is needed in order for larvae to develop to their infective stages. It did not appear to matter whether the energy was obtained continuously or at intervals. As temperature increased from 20°C to 35°C less time was required for the L₃ to develop from eggs. A larger number of eggs hatched and developed to L₃ at 100% constant relative humidity (RH) than if RH was cycled between 70-100%.⁴⁰

A brief summary of the review by Kates⁵⁰ on the conditions of optimum survival for some of the gastrointestinal nematode larvae follows, beginning with the more resistant genera first. Nematodirus larvae are more resistant than Ostertagia. Optimum survival for Nematodirus larvae occurs both in cool moist, in cool dry weather, and over winter. Ostertagia larvae survives best in cool, moist weather

and over winter. Trichostrongylus larvae survival is optimum in warm, moist and cool moist weather; little chance of overwintering. Optimum survival of Cooperia larvae is in warm, moist weather; survival is minimal in cool dry weather or over winter. Haemonchus larvae survives better than Oesophagostomum larvae but both require warm, moist weather for optimum survival, with little chance of overwintering.

A variety of measures have been developed to control gastrointestinal parasitism, and, since the total eradication of gastrointestinal nematodes is not probable at this time, good management procedures and anthelmintics must attack all points of the life cycle (Figure 2).³¹ With good management and proper anthelmintic usage the potential for parasitic infection should be minimized.⁵⁷

The rotation of grazing animals on pasture as a means of controlling helminths has been recommended for many years. Through pasture rotation the reinfection cycle is interrupted by alternating grazing and resting periods, thus exposing the eggs and larvae to longer periods of adverse environmental conditions.⁵⁸ In Georgia, the level of parasitism is directly related to the intensity of grazing. More worms were recovered from cattle on heavily grazed pasture than from those on moderately or lightly grazed pastures.⁵⁹ The stocking rate of animals on pasture is directly related to the intensity of infection--as the pasture's stocking rates increase. However, controversy still exists regarding the value of this procedure because not all rotational grazing programs reduce worm population in grazing animals.^{58,60}

Numerous anthelmintics have been developed and administered both

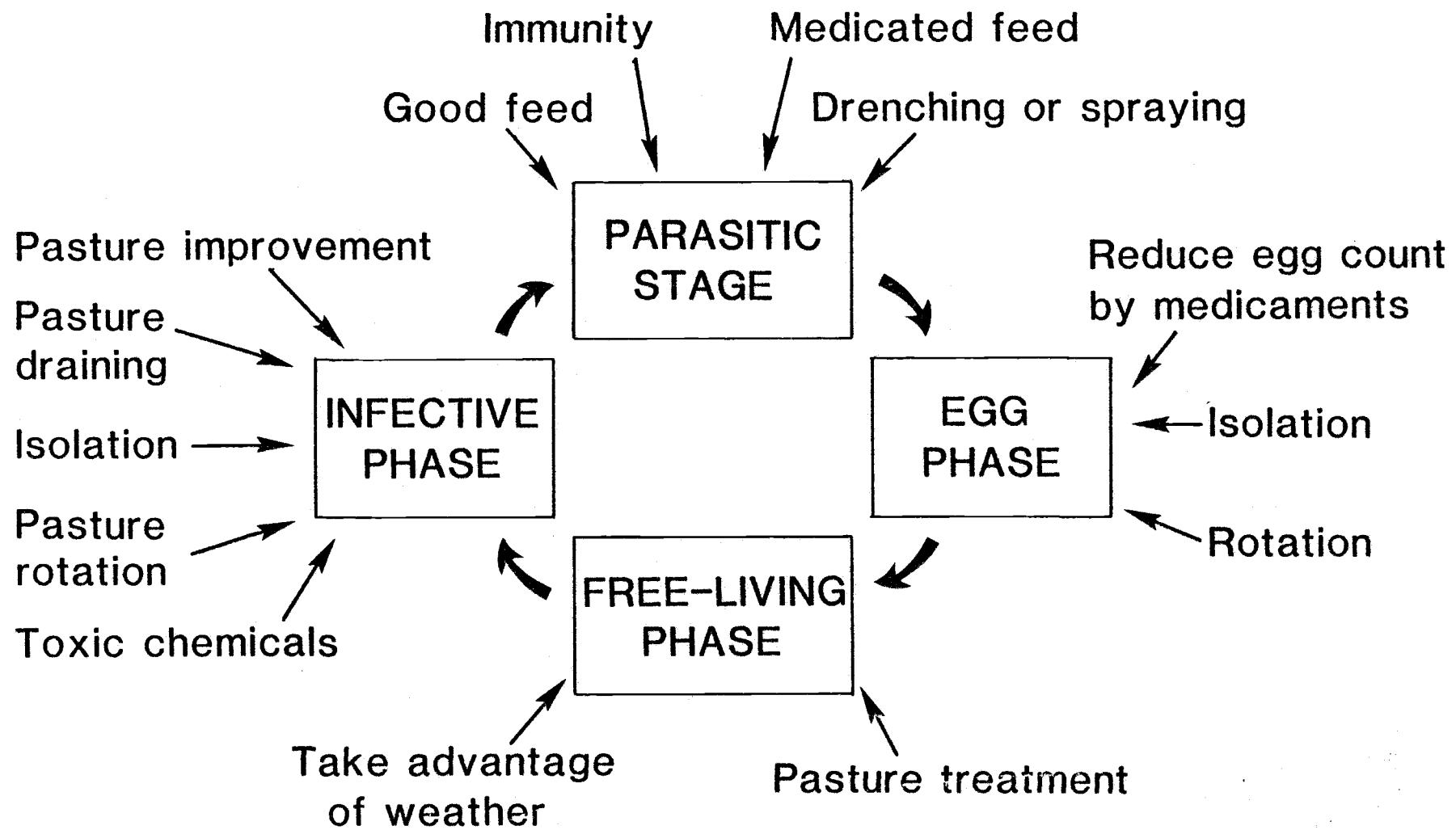


Figure 2---Means of controlling gastrointestinal nematodes by attacking all points of the life cycle (Schock 1976).

for the control and treatment of gastrointestinal parasitism. Several books and review articles concerning anthelmintics have been published.^{3,61-64}

The uses of anthelmintics have been divided into tactical and strategic approaches.⁶⁵ Tactical treatment is initiated once the clinical signs of parasitism appear, whereas strategic administration of an anthelmintic takes place before signs of clinical disease occur. Although in the past anthelmintic therapy has consisted of a tactical approach in clinically parasitized animals, an increasing amount of research has been conducted to establish the effective strategic use of anthelmintic to control gastrointestinal nematodes.

Strategic anthelmintic use was first advocated in 1948⁶⁶ but because of the lack of information on nematode epidemiology it was largely ignored.⁶⁵ In 1969, based on detailed epidemiology studies, a "dose and move" system for controlling gastrointestinal parasitism was proposed.⁶⁷ Following this method, animals are grazed in the spring on pasture until mid-summer, then dosed with a broad spectrum anthelmintic and moved to a clean pasture. This system has proven successful,^{68,69} but due to a lack of pasture availability and labor intensity it has not received universal support by livestock producers.⁷⁰

Other successful methods used to control gastrointestinal parasitism include continuous anthelmintic medication in drinking water,^{68,71} in feed supplement,⁷²⁻⁷⁴ and in molasses block formation.⁷⁵ Although these methods overcome the need for intermittent treatment, individual consumption on a daily basis has been difficult to regulate under field conditions.¹ Additionally,

paste⁷² and oral drenching⁷⁶ have been used successfully to administer anthelmintics to animals but have the disadvantage of being labor intensive.

As an alternative to the aforementioned methods of anthelmintic administration a new drug delivery system has been developed which provides a sustained but dwindling release of morantel tartrate for a minimum period of 60 days (Figure 3). The morantel sustained release bolus (MSRB) administered orally by means of a modified balling gun, consists of a stainless steel cylinder containing 22.7 gm of morantel tartrate which is continuously released through the impregnated semi-permeable membrane at each end of the bolus once contact with rumen fluid occurs. A major advantage of the MSRB is its use in the strategic control of gastrointestinal parasitism. The administration of MSRB to first season grazing calves at the time of turnout onto spring pasture prevents the establishment of ingested L₃ in the host, reduces established nematodes, and prevents PGE. By preventing the establishment of L₃ in the host the MSRB decreases worm egg excretion from the host which reduces pasture contamination throughout the early-mid grazing season. This produces "safe" pastures and improves the animal's opportunity for increased weight gains.⁷⁷ When the MSRB was administered to first season grazing calves they reflected a mean weight gain advantage of 24.5 Kg over non-treated calves.⁷⁰ From several studies conducted in Europe a 10-15 Kg mean weight gain advantage, of MSRB treated animals over control animals, can be expected at the end of the first grazing season.⁷⁸

Morantel, trans-2 [2-(3 methyl-2-thienyl) vinyl]-1-methyl-1, 4, 5, 6-tetra hydropyrimidine, discovered in 1966, is a white, water

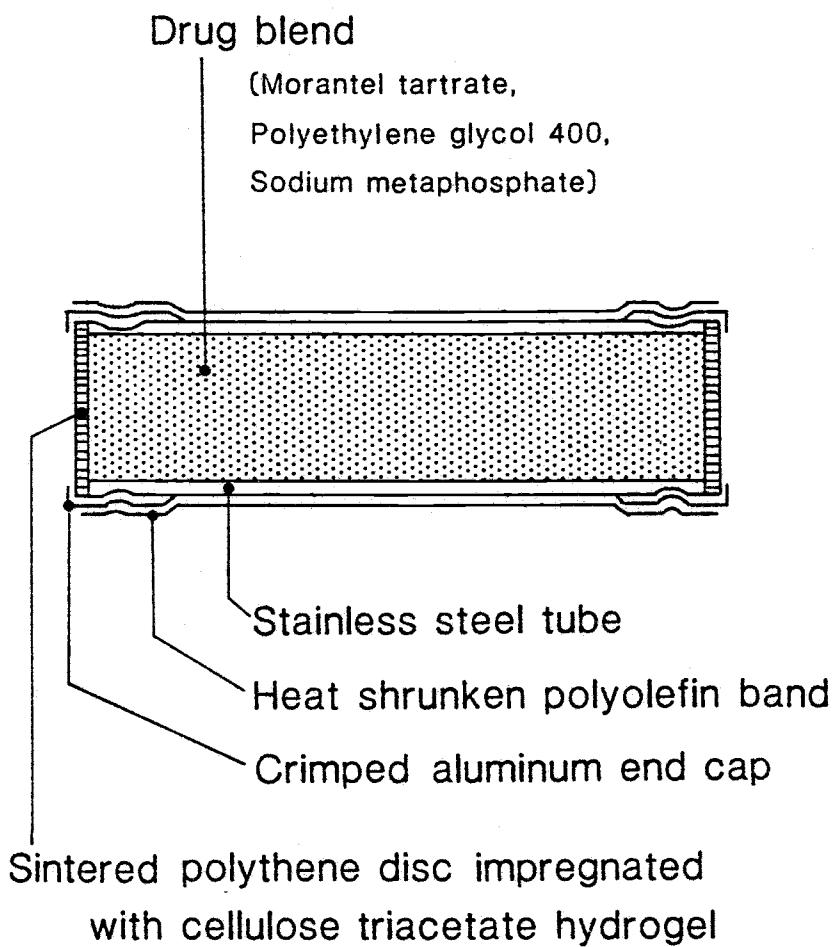


Figure 3---The morantel sustained release bolus
(Paratect bolus - Pfizer Inc.).

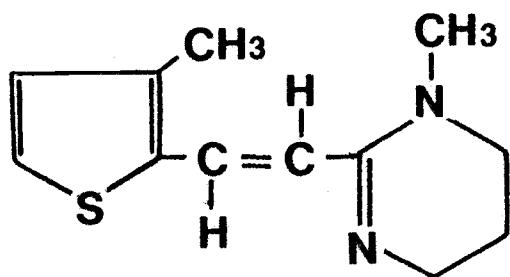
soluble, crystalline solid. It is a member of the series of thiophene-substituted tetrahydro-pyrimidine anthelmintics and is considered to be a broad spectrum anthelmintic.⁷⁹ It belongs to the same chemical group as pyrantel which has been used extensively in sheep,^{80,81} cattle⁸², and horses;⁸³ however, morantel is better tolerated.⁸⁴ Morantel differs from pyrantel (Figure 4) by a 3-methyl substitution on the thiophene ring.

The pharmacological effect of morantel, first reported in 1973, was shown to exhibit neuromuscular blocking properties much like those of depolarizing blockers;⁸⁵ thus, its action is similar to certain other anthelmintics; tetramisole and pyrantel.⁸⁶ Morantel's action differs from that of piperazine compounds which block the action of acetylcholine at the neuromuscular junction.⁸⁷ Morantel has been extensively tested with the bolus and is highly effective in preventing the establishment of infections and in removing established infections of adult O. ostertagi, T. axei, T. colubriformis, and C. oncophore.¹

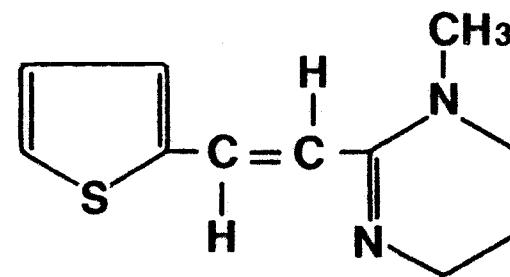
Development of anthelmintic resistant parasite strains presents a problem to treatment and control programs. Strains of H. contortus, resistant to phenothiazine have been reported^{88,89} and more recently H. contortus and trichostrongylus spp. have demonstrated resistance to benzimidazoles.⁹⁰⁻⁹² In order to prevent the buildup of resistant parasitic strains the practice of alternating anthelmintics is advocated.⁹⁰

Although the potential for resistant parasite strains to develop in response to such sustained release boluses is recognized, resistance to morantel tartrate by a single population of larvae has

not been documented during 15 years of commercial use in cattle.⁹³



MORANTEL



PYRANTEL

Figure 4---Structure of Morantel and Pyrantel (Bamgbose, Marquis, and Salako 1973).

MATERIALS AND METHODS

Animals, allocation, and pasture - Trials were conducted during the normal grazing seasons of 1982 and 1983 using first season grazing Holstein calves raised in total confinement at the Oregon State University dairy barn. In Trial 1 (1982), 38 (26 females and 12 castrated males) animals were equally allotted by computer^b to control and treatment groups according to age, sex, and body weight. Body weights averaged 210 kg for the control animals and 211 kg for the treated animals. At trial termination, the male calves used as full season tracer animals, were necropsied for worm counts. The trial was conducted on a 9.7 ha., ryegrass pasture which was grazed by infective dairy cattle the previous season. Because of excessive growth, the pasture was harvested for hay prior to allowing the groups to graze. The pasture was equally divided by a double-strand electric fence. All animals were provided free choice textured 16% protein dairy feed (averaging .96 kg/animal/day) throughout the trial and baled oat/ryegrass hay (averaging 1.2 kg/animal/day) starting July 28. Water and mineral blocks were available to both groups. In mid season 1982 (July - August) during a drought period the pastures received inadequate and uneven irrigation due to limited water delivery systems (see Discussion).

In Trial 2 (1983), 40 animals were equally allocated to control and treatment groups and assigned to the same respective pastures as

^bPfizer Inc., Terre Haute, Indiana.

the control and treated groups of Trial 1. Body weights averaged 231 kg for the control animals and 232 kg for the treated animals. Irrigation and pasture grass harvesting were not necessary (see Discussion). The animals were provided free choice oat/ryegrass hay (averaging 1.1 kg/animal/day) and textured 16% protein dairy feed (averaging .91 kg/animal/day) beginning at trial initiation.

Anthelmintic - By means of a modified balling gun, the MSRB, as described by Jones⁷⁰, was given to all animals of the treated groups at the time of spring turnout onto pasture, May 18, 1982 (Trial 1) and May 3, 1983 (Trial 2). Bolus retention was monitored periodically and at trial termination using a metal detector.^c When treated animals were necropsied at trial termination (1982), boluses were recovered.

Fecal samples - Rectal fecal samples were collected at the start of each trial, biweekly from all animals in Trial 1, and monthly from all animals in Trial 2. Determination of the number of parasite eggs per gram (EPG) of feces was by a modified flotation-centrifugation method. Five grams of feces were placed in a graduated cylinder and the volume brought to 50 ml with tap water. The water and feces were transferred to a screw-capped bottle which was then shaken. One (1) ml of the suspension was pipetted into a 15 ml glass centrifuge tube that had a ground glass rim. The tube was filled with enough saturated NaCl solution (specific gravity 1.19 at room temperature) to allow a slight bubble at the opening when topped with a No. 1, 18 mm cover glass. After centrifugation for 4-5 minutes at 100 Xg, the

^c Transfrisken All Metals Detector Model 6030,
Federal Laboratories, Inc., Saltsburg, Pa. 15671

cover slip was gently removed and transferred to a microscope slide for egg enumeration at 10X. Because of the 10-fold dilution, the number of eggs found were multiplied times 10 to report the actual number of EPG of feces.

Tracer animals - Parasite naive (supported by negative fecal exam) tracer animals were raised from birth in confinement (on concrete) at the Oregon State University dairy barn. In Trial 1, pairs of tracer calves were introduced to each pasture on May 18, July 13, September 7, and October 26 while in Trial 2 three tracer calves were placed on each pasture on May 3, July 25, and September 12. After grazing the respective pastures for three weeks, the tracer animals were housed inside on concrete for three weeks at the Oregon State University Veterinary Medical Animal Isolation Laboratory (VMAL) and then necropsied for worm counts.

At necropsy, the abomasum, small and large intestines were ligated and removed from the animals, and separated. After separation, the abomasum was opened longitudinally and the contents were collected by hand stripping the mucosal surface three times. A 5% aliquot of the abomasal contents was washed with tap water through a 12 inch-400-mesh (37.5 μ aperture) Newark^d stainless steel sieve. This material was referred to as the abomasum content. Immediately after stripping, the abomasum was placed into a tray, covered with 0.85% NaCl (saline), and soaked for 4-6 hours in a 37.5°C incubator. After removal from the incubator, the abomasum was again stripped and washed; the saline solution along with tap water rinsings of the

^d USA Standard Sieve Series A.S.T.M. Designation E11
Newark Wire Cloth Company, Newark, New Jersey 07104

vigorously rubbed abomasum were strained through the 400-mesh sieve. This material was referred to as abomasum incubate.

The small and large intestine contents were processed similar to the abomasum contents. A 5% aliquot of these contents was washed through either a 400-mesh sieve (small intestine contents) or a 100-mesh sieve (large intestine contents).

All sieved samples were preserved in 70% alcohol-iodine solutions. Dissecting microscopes were used in the visual recovery of worms which were then stored in 10% formalin until differentiated (observation with compound microscopes) into genera and species.

Plasma pepsinogen values - Blood samples were collected from all animals in both trials at the time of pasture turnout and monthly thereafter. Blood samples were drawn into 10 ml sterile evacuated tubes containing sodium heparin (Becton Dickinson).^e Plasma pepsinogen levels, expressed as milli-international units of tyrosine, were determined by the procedures described by Hirschowitz.⁹⁶

Mean weight gain - Individual live weights were recorded at the trial site using a portable electronic scale^f on all principal animals at the start of each trial, biweekly during Trial 1, and monthly during Trial 2.

Meteorological data - Continual relative humidity in % and temperature in °C were recorded using a hygro-thermograph^g at the

^e Becton Dickinson Tubes. Division of Becton Dickinson and Company, Rutherford, N.J. 07070

^f SENSTEK Model LCD-U Control/Display Unit and Model 4000U Weigh Bars, SENSTEK Agricultural and Industrial Electronics, Saskatoon, Saskatchewan, Canada

^g Hygro-Thermograph Recording Relative Humidity Air Temperature Model 544, Friez Instrument Division, Bendix Aviation Corporation, Baltimore, Maryland.

trial site, whereas the total daily rainfall in mm was recorded at the Oregon State University climatic field laboratory located approximately 12.5 km from the trial site.

Herbage dry weight - Herbage samples were collected at two-week intervals from each pasture during Trial 1 starting May 18 and ending October 27. On each sampling day, vegetation from 14 one m² areas in each pasture was clipped to ground level, collected, and consolidated in plastic containers, one for the control and one for the treated pasture. From each container a representative 250 gm wet herbage sample was dried in a 56°C hot air oven for 14 days, then weighed and recorded as dry herbage.

Statistical analysis of data - Average daily gain (ADG) and plasma pepsinogen levels were subjected to Bartlett's test on homogeneity of variances and the Shapiro-Wilk W-tests for normality.⁹⁷ Both tests were accepted at the .01 level; hence transformations were not required and a one-way analysis of variance (ANOVA) utilizing the BMDP-90 program^h, using between treatments and animals within treatments was performed. The individual animal worm egg counts at each data collection interval (days on test) were subjected to homogeneity of variance and normality tests. From these tests it was determined that a log₁₀ (EPG + 10) transformation should be used. The normality test, however, failed so the Kruskal-Wallis test, using the ranks in BMPD-3S was used on the log₁₀ (EPG + 10) transformation.

Since only two tracer animals (1982) and three tracer animals

^h Digital Computer Program from Health Sciences Computing Facility Department of Biomathematics, School of Medicine, UCLA, 1979.

(1983) from the control and treated pastures were used in each sampling interval-treatment combination, the normality tests on tracer worm counts could not be run. The homogeneity of variance test failed at the .001 level, but the transformation \log_{10} (worm counts + 10), stabilized the variances of tracer worm counts. A two-way ANOVA (BMDP-2V) was used to test treatments. The worm counts at trial termination were analyzed with a one-way ANOVA using the BMDP-2V model.

RESULTS

Mean fecal EPG counts of the control and treated animals from Trial 1 and Trial 2 are shown in Figures 5 and 6. In Trial 1, both control and treated animal EPG's were negative at day zero. Positive EPG's were first observed at six weeks (control) and eight weeks (treated) after grazing had commenced. Mean EPG counts of the control animals increased progressively to an initial peak of 22 on September 21 before declining to 16 on October 18. This decrease was then followed by a subsequent rise to a maximum level of 37 EPG on October 25. In comparison, the average EPG counts of the treated animals remained lower than in the control animals on each sampling date. Mean EPG counts of the treated animals peaked at 9 on September 21, fell to 3.2 on October 5, and then reached the highest level of 19 on October 25. When Trial 1 was terminated on October 25, 84% of the control animals and 58% of the treated animals were shedding nematode parasite eggs.

Throughout Trial 2, the mean EPG counts of the treated animals remained low, ranging from 0 on May 31 to a high of 7.5 on October 4. Control animal fecal EPG counts increased from 1.1 at trial initiation to 59 on July 26, then decreased to 36.3 by September 20, and subsequently increased to 60 at trial termination. At the end of Trial 2, 68% of the control calves were shedding nematode parasite eggs whereas only 55% of the treated calves were passing nematode eggs in their feces.

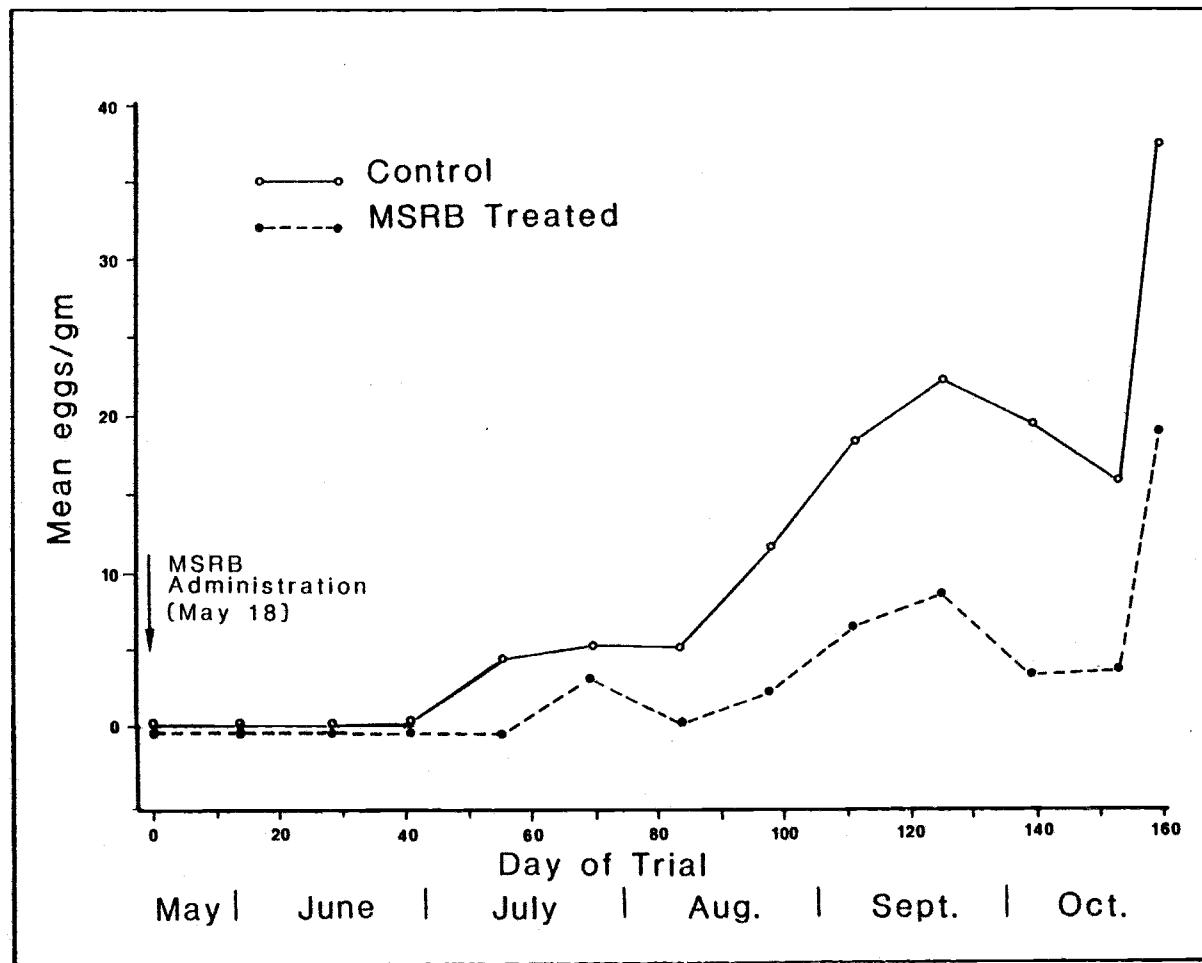


Figure 5---Mean fecal egg counts of MSRB treated and control calves during the 1982 grazing season.

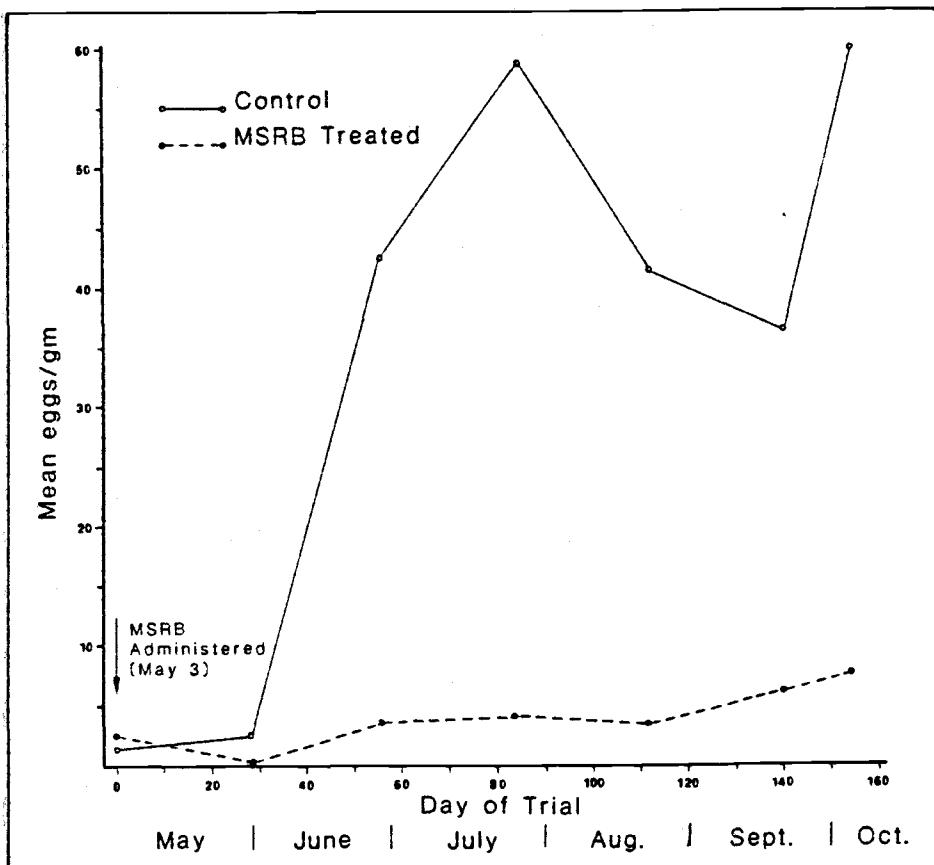


Figure 6---Mean fecal egg counts of MSRB treated and control calves during the 1983 grazing season.

The mean counts of parasites recovered from the control and treated tracer animals and the efficacy level of the MSRB in reducing pasture larval contamination of various nematodes are shown in Table 1 (1982) and Table 2 (1983). During 1982, compared to controls, the overall mean parasite reduction in tracer animals from the treated group pasture was 86.4% (not significantly different), ranging from 100% for mature *Oesophagostomum* to 0% for mature *Trichuris*. The parasitic burdens of mature *Cooperia oncophora*, *Ostertagia ostertagi*, and *Nematodirus helveticus* were decreased 85.3%, 77.4%, and 72.9% respectively while the reduction of immature *O. ostertagi* and *N. helveticus* was 88.8% and 77.6%.

On days 42 and 98, low levels of nematodes were recovered at necropsy from tracer calves of both the control and treatment groups. Thereafter the parasite burden increased steadily, reaching the highest levels on day 203 of 94,870 in the control group and 10,850 in the treated tracer animals. On day 154, *N. helveticus* was the primary parasite present (72.6%) in the control group tracer animals whereas in the treated group tracer animals *O. ostertagi* (68%) was the predominant species. When the final set of tracer animals was necropsied (day 203), *O. ostertagi* was the primary parasite present in both the control (91.7%) and treated (89.8%) tracer animals.

Ostertagia ostertagi, *C. oncophora*, *N. helveticus*, and *Trichuris* were recovered from both groups of animals whereas *Oesophagostomum* was found on day 203 in only one tracer animal of the control group.

During 1983, *O. ostertagi*, *C. oncophora*, and *N. helveticus* were the only nematodes recovered from the tracer calves of the control and treated groups. The parasite burden in the tracer calves on the

TABLE 1 - Mean parasite count from tracer animals

Location/Parasite present at necropsy	Control animals (n = 2) [†] (Day)						Treated animals (n = 2) [†] (Day)						Percent reduction*
	42	98	154	203	total	42	98	154	203	total			
Abomasum													
<i>Ostertagia ostertagi</i>													
adults	40	0	130	10910	11080	120	10	90	2280	2500	77.4		
4th stage	30	0	40	76060	76130	20	0	1030	7460	8510	88.8		
<i>Nematodirus helveticus</i>													
adults	0	0	0	0	0	0	0	10	0	10	‡		
4th stage	0	0	0	0	0	0	0	0	0	0	...		
Small Intestine													
<i>Cooperia oncophora</i>													
adults	0	0	30	1940	1970	0	20	20	250	290	85.3		
4th stage	0	0	0	0	0	0	0	0	10	10	‡		
<i>Nematodirus helveticus</i>													
adults	0	0	510	5095	5605	0	260	530	730	1520	72.9		
4th stage	0	0	20	830	850	0	0	70	120	190	77.6		
Large Intestine													
<i>Nematodirus helveticus</i>													
adults	0	340	0	0	340	0	0	0	0	0	100		
4th stage	0	0	0	0	0	0	0	0	0	0	...		
<i>Oesophagostomum sp</i>													
adults	0	0	0	35	35	0	0	0	0	0	100		
4th stage	0	0	0	0	0	0	0	0	0	0	...		
<i>Trichuris sp</i>													
adults	0	10	0	0	10	0	20	0	0	20	‡		
4th stage	0	0	0	0	0	0	0	0	0	0	...		
Total parasite burden	70	350	730	94870	96020	140	310	1750	10850	13050	86.4		

* Percent reduction = [(mean no. of parasites in the control animals - mean no. of parasites in the treated animals)/mean no. of parasites in the control animals] x 100.

† n = the number of animals necropsied.

‡ Average parasite burden increased in treated animals.

TABLE 2 - Mean parasite count from tracer animals

Location/parasite present at necropsy	Control animals (n = 3) (Day)				Treated animals (n = 3) (Day)				Percent reduction \$
	41	126	174	total	41	126	174	total	
Abomasum									
<i>Ostertagia ostertagi</i>									
adults	1587	5953	5920	13460	173	200	313	686	94.9
4th stage	0	0	47	47	0	20	0	20	57.4
<i>Cooperia oncophora</i>									
adults	0	0	7	7	0	0	0	0	100
4th stage	0	0	0	0	0	0	0	0	...
<i>Nematodirus helveticus</i>									
adults	0	20	20	40	0	20	20	40	0
4th stage	0	0	0	0	0	0	0	0	...
Small Intestine									
<i>Ostertagia ostertagi</i>									
adults	33	40	0	73	0	0	0	0	100
4th stage	0	0	0	0	0	0	0	0	...
<i>Cooperia oncophora</i>									
adults	340	2767	5973	9080	0	0	313	313	96.6
4th stage	0	0	60	60	0	0	27	27	55.0
<i>Nematodirus helveticus</i>									
adults	500	3593	5580	9673	320	1307	3440	5067	47.6
4th stage	0	60	7173	7233	0	0	73	73	98.9
Large Intestine									
<i>Ostertagia ostertagi</i>									
adults	0	0	7	7	0	0	0	0	100
4th stage	0	0	0	0	0	0	0	0	...
<i>Nematodirus helveticus</i>									
adults	0	0	0	0	13	0	0	13	‡
4th stage	0	0	13	13	0	0	0	0	100
Total parasite burden	2460 [†]	12433	24800	39693	506 [†]	1547	4186	6239	84.3*

* Statistically highly significantly less than for controls ($P<0.01$).

† A significant ($P<0.05$) residual difference of 7% in pasture infectivities at trial initiation as a result of the preceding year's Paratect Bolus treatment program.

‡ Average parasite burden increased in treated animals.

§ Percent reduction = [(mean no. of parasites in the control animals - mean no. of parasites in the treated animals)/mean no. of parasites in the control animals] $\times 100$.

|| n = the number of animals necropsied.

treated group pasture was 84.3% ($P < 0.01$) of that of the control group pasture. A high level of efficacy was recorded for Ostertagia (96%) and Cooperia (96%) while the removal of nematodirus was 69%. On day 41, O. ostertagi (66%) was the predominant parasite present in the control tracer animals in contrast to N. helveticus (66%) which was predominant in the treated tracer animals. By day 174, Nematodirus was the most common genus recovered from the tracer animals of both the control (51.6%) and treated (84.4%) groups.

Data on parasites recovered at necropsy from control and treated principal trial animals (1982) and the efficacy levels of MSRB against them are given in Table 3. Nematodirus helveticus was the principal parasite present in both the control (56%) and treated (76%) groups. Cooperia and Ostertagia represented 28% and 15% of the parasite burden in the control animals while in the treated animals the levels decreased to 11% and 8%. Only small numbers of Trichuris were recorded; however, all but one animal from each group showed infection. Overall parasite reduction in the treated animals was 88.1% ($P < 0.05$), ranging from 97% for immature Ostertagia and Nematodirus to 14% for mature Trichuris. High percentages of reduction were recorded for adult Cooperia (96%), Ostertagia (90%), and Nematodirus (82%).

The mean plasma pepsinogen levels recorded from animals in Trial 1 and Trial 2 are shown in Figures 7 and 8. In Trial 1, the mean plasma pepsinogen values remained consistently lower in the treated animals throughout the grazing season and at trial termination the control group reflected an 18% increase in mean plasma pepsinogen levels ($P < 0.05$). In Trial 2, the mean plasma pepsinogen level of

TABLE 3 - Mean parasite count from control and treated animals at trial termination

Location/parasite present at necropsy	<u>Control animals (n = 6)‡</u>	<u>Treated animals (n = 6)‡</u>	<u>Percent reduction§</u>
	(Day) 162	(Day) 161	
Abomasum			
<i>Ostertagia ostertagi</i>			
adults	634	63	90.0
4th stage	999	33	96.7
Small Intestine			
<i>Cooperia oncophora</i>			
adults	2953	123	95.8
4th stage	0	0	...
<i>Nematodirus helveticus</i>			
adults	5133	941	81.7
4th stage	900	27	97.0
Large Intestine			
<i>Trichuris sp</i>			
adults	97	83	14.4
4th stage	0	0	...
Total parasite burden	10716	1270	88.1*

* Statistically significantly less than for controls ($P < 0.05$).

§ Percent reduction = $\{(\text{mean no. of parasites in the control animals} - \text{mean no. of parasites in the treated animals}) / \text{mean no. of parasites in the control animals}\} \times 100$.

‡ n = the number of animals necropsied.

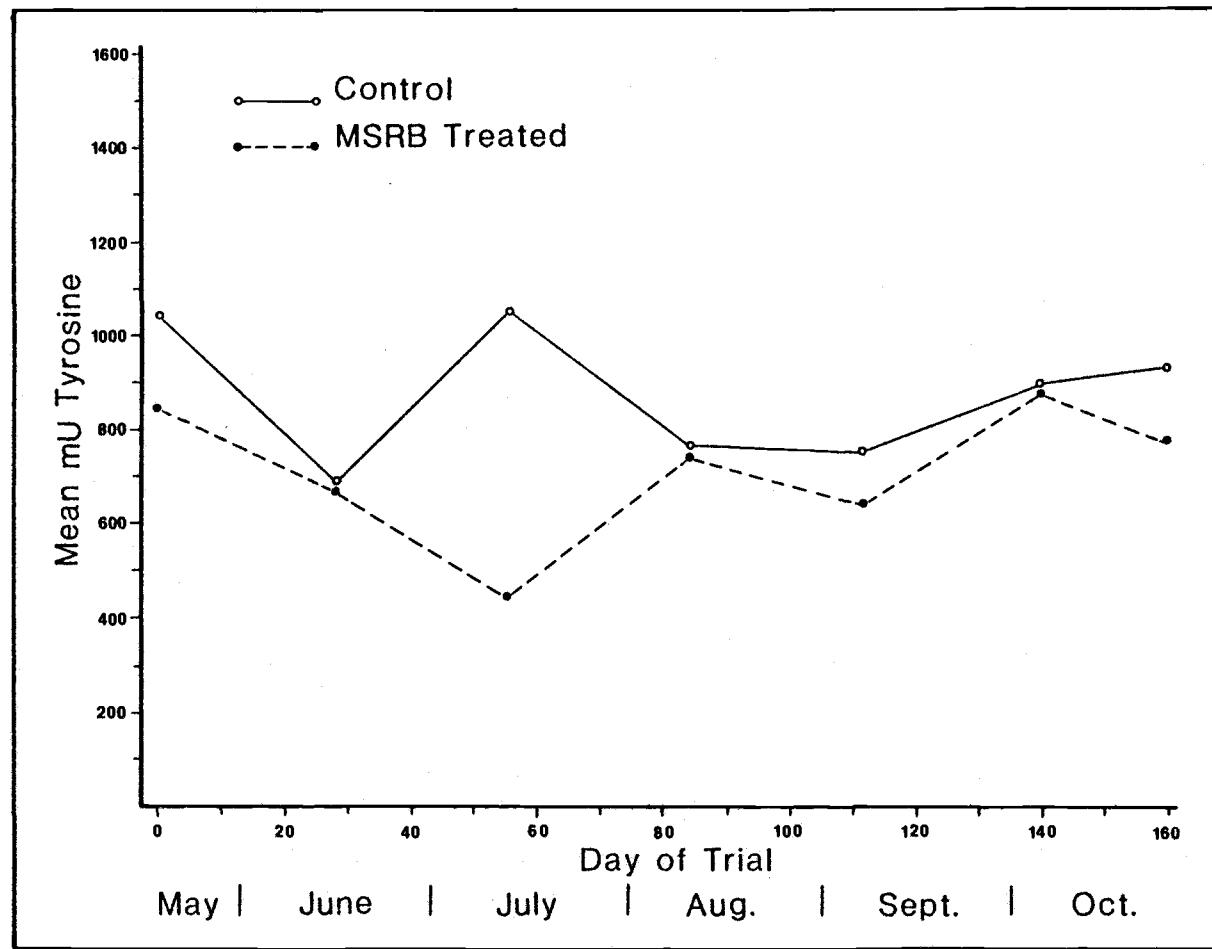


Figure 7---Mean plasma pepsinogen levels of MSRB treated and control calves during the 1982 grazing season.

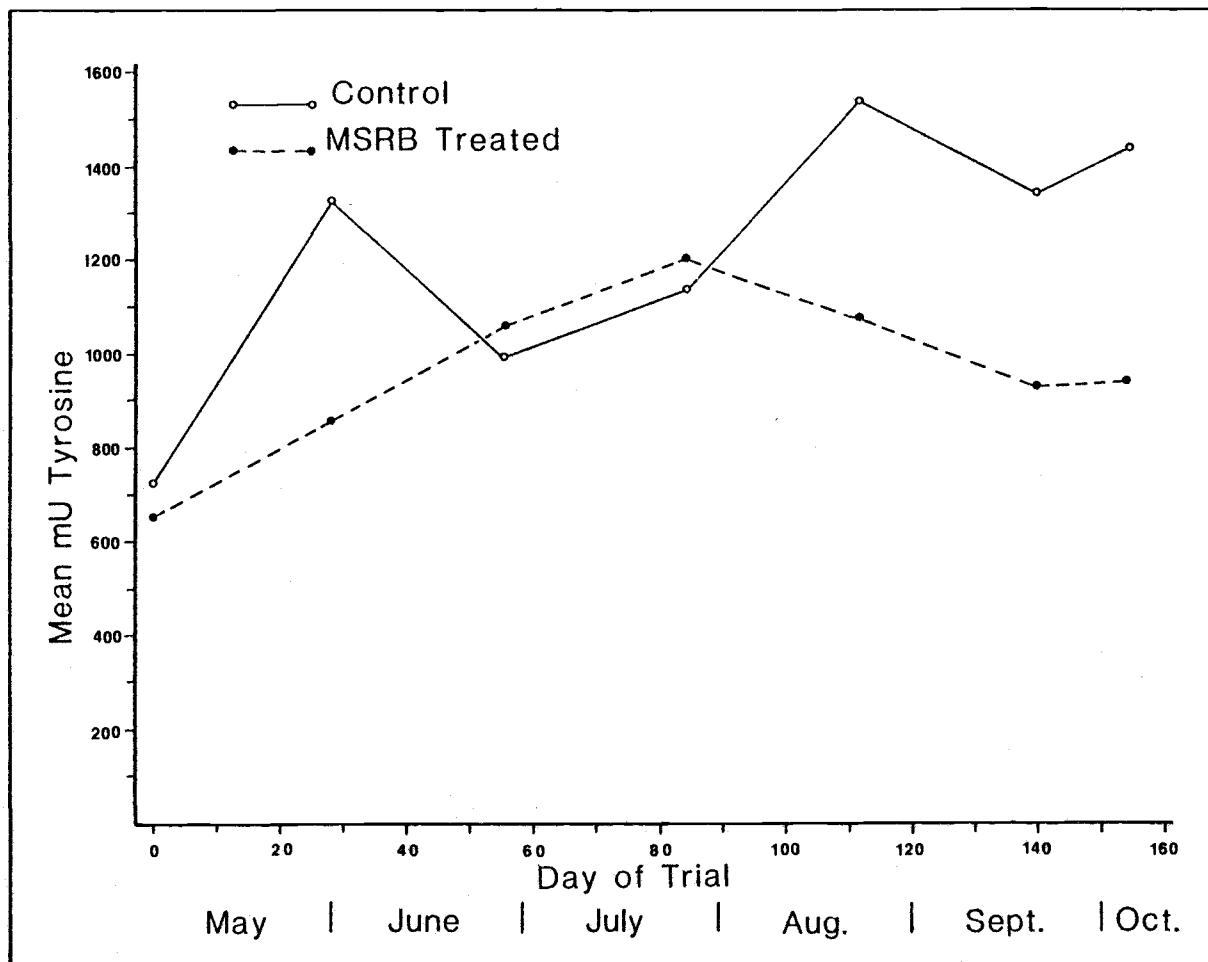


Figure 8---Mean plasma pepsinogen levels of MSRB treated and control calves during the 1983 grazing season.

the control group increased from 727 at trial initiation to 1330 in late May, then decreased to 979 in late June before reaching a high of 1541 in late August. In contrast, mean plasma pepsinogen levels in the treated group increased steadily from 657 at trial initiation to a high of 1201 in late July, then decreased to 943 at trial termination. Control animals reflected a 22% increase in mean plasma pepsinogen levels ($P < 0.01$).

The early season mean weight gain advantage of treated animals in Trial 1 was not sustained (Figure 9). By late July, the control animals gained weight more rapidly and on day 160 they had a 7.9 kg mean weight gain advantage over the treated animals; however, by day 202, the treated animals again showed a mean weight gain advantage of 4.6 kg.

The mean weight gains of animals in Trial 2 are shown in Figure 10. Throughout the grazing season, the treated animals consistently outperformed the control animals and at trial termination the treated group reflected a 13.5 kg mean weight gain advantage ($P < 0.05$).

Meteorological data recorded are presented for Trial 1 (Figure 11) and Trial 2 (Figure 12). In general, the mid-grazing season of 1982 was warmer than that of 1983. Average monthly temperature recordings were higher in June (1.6°C), July (2.2°C), and September ($.67^{\circ}\text{C}$), 1982, while they were the same in August. Also during Trial 1, the rainfall totals for July and August were 11 mm and 7 mm respectively compared to 1983 when the rainfall totals for July and August were 65 mm and 56 mm, respectively.

Dry herbage weight in gm/250 wet herbage of the control and treated pastures recorded during Trial 1 is shown in Figure 13. Dry

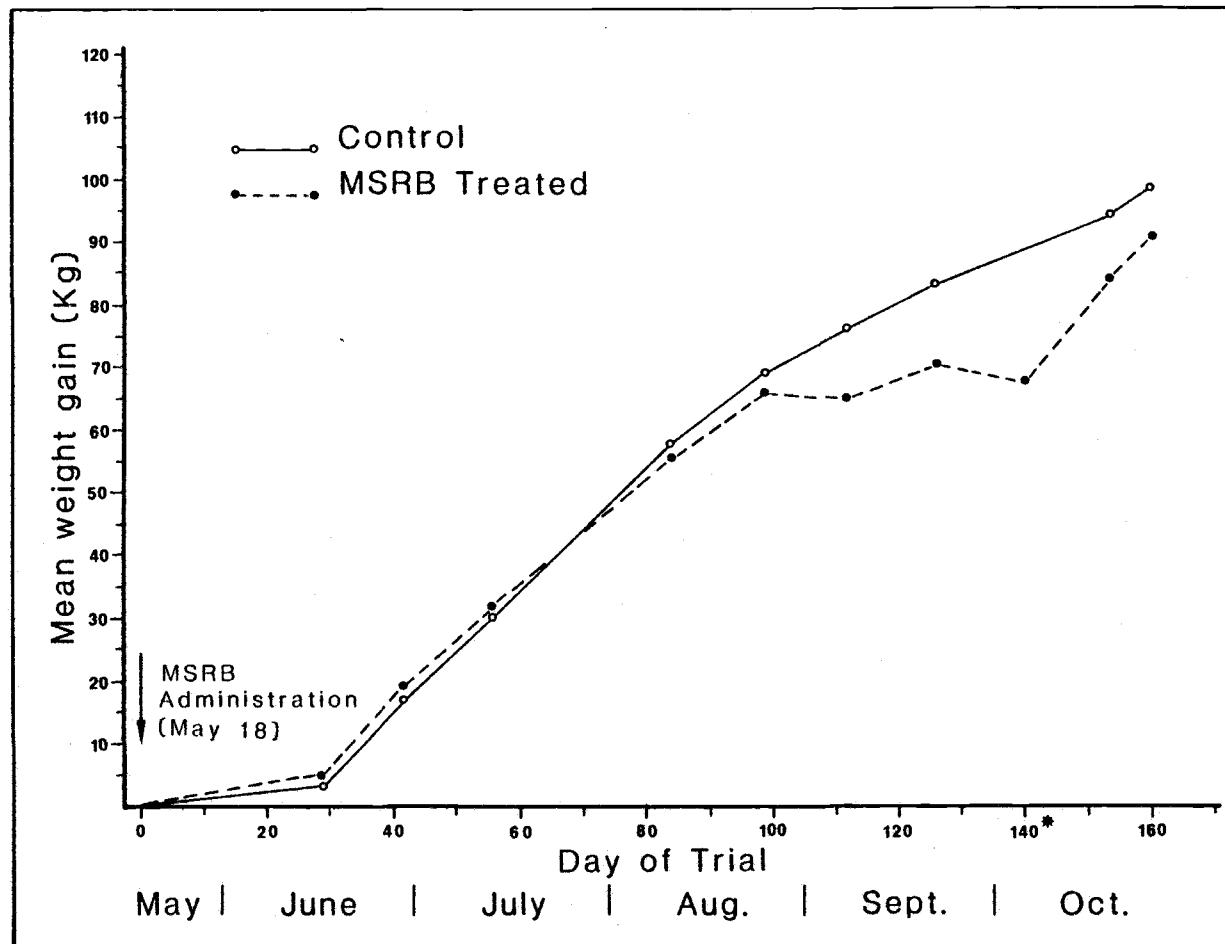


Figure 9---Mean live weight gain of MSRB treated and control calves during the 1982 grazing season. *Control weights not recorded due to mechanical scale failure.

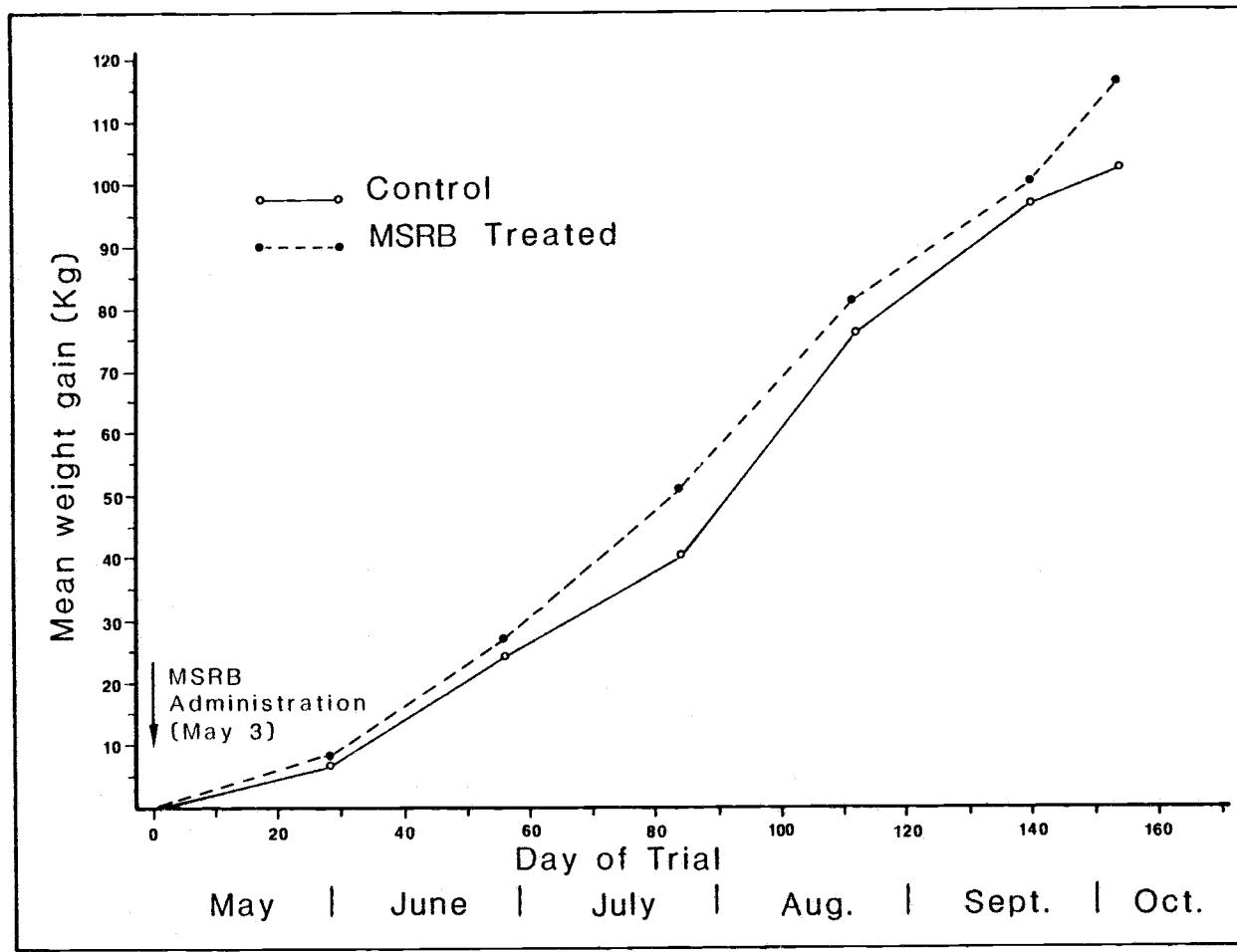


Figure 10---Mean live weight gain of MSRB treated and control calves during the 1983 grazing season.

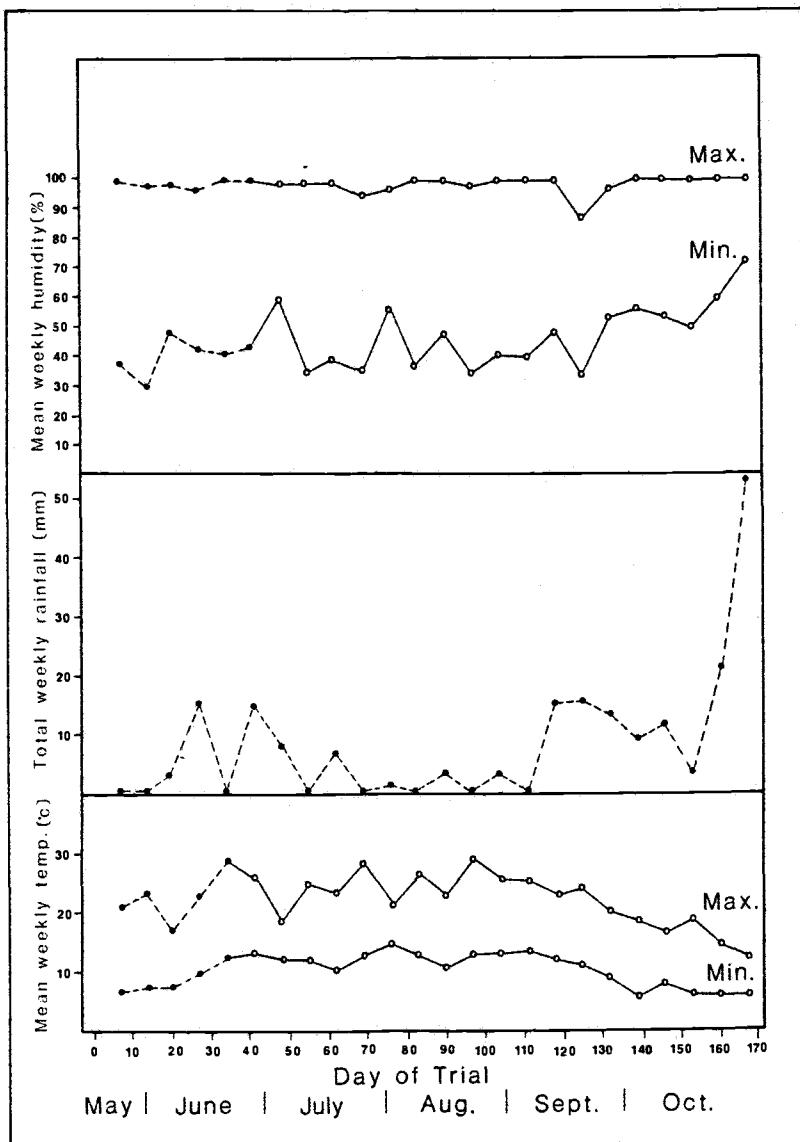


Figure 11---Weekly total rainfall; mean weekly maximal and minimal temperature and humidity recorded during the 1982 grazing season.

— Data was recorded at the Oregon State University climatic field laboratory located approximately 12.5 km from the trial site.
 — Data was recorded at the trial site.

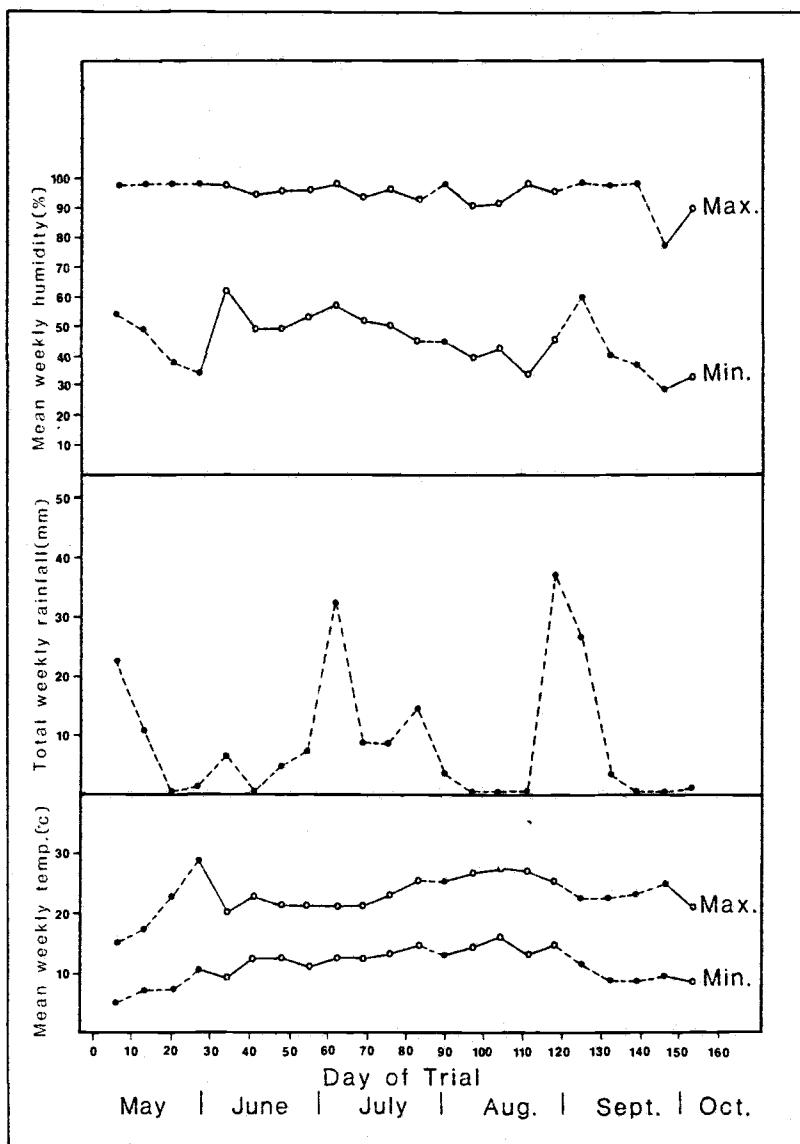


Figure 12---Weekly total rainfall; mean weekly maximal and minimal temperature and humidity recorded during the 1983 grazing season.

→ Data was recorded at the Oregon State University climatic field laboratory located approximately 12.5 km from the trial site.
 ← Data was recorded at the trial site.

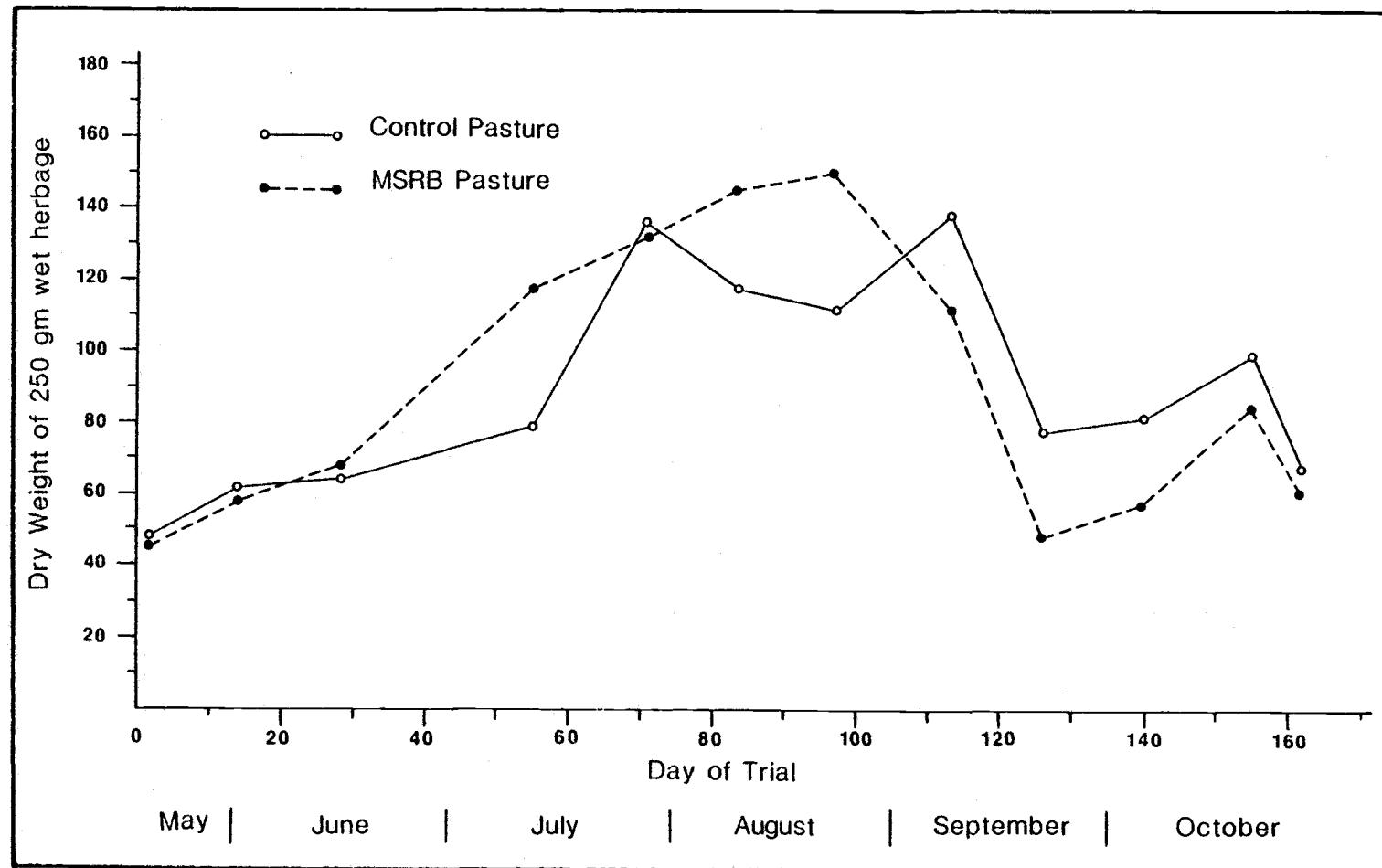


Figure 13---Dry weight of 250 gm wet herbage from the MSRB treated and control pastures during the 1982 grazing season.

herbage weight of the control pasture increased to an initial peak of 136 gm in late July, then declined to 111 gm in late August, and later increased to a high of 138 gm in early September. In contrast, the dry herbage weight of the treated pasture steadily increased to a high of 150 gm in mid-August, then declined to 57 gm in September, and then increased again to 83 gm in late October.

DISCUSSION

The results of the trials conducted during the 1982 and 1983 grazing seasons demonstrated that the morantel sustained release bolus administered to first season grazing calves at the time of pasture turnout was highly effective in reducing gastrointestinal burdens of Ostertagia ostertagi, Cooperia oncophora, and to a lesser degree Nematodirus helveticus. The overall reduction in worm burdens observed at necropsy in the tracer calves grazed on the treatment group pasture was 86.4% (not significant) in 1982 and 84.3% ($P < 0.01$) in 1983 while the 1982 treated full season animals slaughtered reflected a decrease in worm burdens of 88.1% ($P < 0.05$) compared to the full season tracer calves. These results were consistent with several European studies.^{45-49,94,95} The mean worm burden reduction (86.4%) for the 1982 tracer calves was not significant because at the 154 day necropsy, 1750 worms were recovered from tracer calves grazing the treatment pasture whereas only 730 worms were found in the control tracer calves (Table 1). The efficacy of the Paratect bolus program on decreasing host and pasture worm burdens had not been fully established by mid-season. However, the final set of tracer calves grazing the treatment pasture, necropsied on day 203, did contain substantially fewer (84,020) worms than the control tracer calves. This substantial difference in host worm burden illustrates the full effect of MSRB which suppressed egg output during the early grazing season and greatly reduced the host level of worm infection during the

later part of the season. There was little activity of the bolus against Trichuris sp. during the 1982 trial (Table 3).

To determine the number of infective larvae ingested throughout the grazing period and to estimate the time of larval inhibition, tracer calves were allowed to graze for three weeks, confined for three weeks, then necropsied for worm counts. Parasites recovered from the 1982 tracer pairs reflected that relatively few infective larvae were ingested prior to October 26 (Table 1); however, between October 26 and November 16, there was a substantial increase in worm burden, most of which was O. ostertagi. This suggests that fall infections are more important than spring or summer infections and that pre-Type II ostertagiasis occurs during the late fall season in western Oregon. This data is in agreement with other trials in specific geographic areas of the United States,^{22,23} and those in Canada,^{42,43} and Europe;⁴⁵⁻⁴⁹ this is contrast to the spring season inhibition observed in Georgia,⁹⁸ northern California,²¹ and Louisiana.¹³ Unfortunately, late season tracer calves were not a part of the agreed protocol for the 1983 trial so the 1982 late fall season inhibition was not confirmed for this specific trial in 1983. However, fall season larvae inhibition in beef cattle in western Oregon has been confirmed (Dr. Gary L. Zimmerman, unpublished data).

Although fecal egg counts do not specifically indicate the actual level of worm burden in each animal,^{99,100} they do show approximate burdens and are helpful in demonstrating epidemiology of gastrointestinal parasitism. Of particular importance was the level of increased pasture contamination observed in the control pasture over successive grazing seasons. During the 1983 trial (Figure 6),

the initial infection from pasture contamination from the previous grazing season was quite apparent in control animals 28 days after pasture turnout. The mean EPG count from the control animals (1983) peaked sooner and reached higher levels than did the 1982 control calves (Figure 5). In contrast, the mean EPG counts from the 1983 treated group were lower than those observed from the 1982 treated calves. The overall decrease in worm egg output in the treated animals in 1982 was 69% ($P < 0.05$) while in 1983 it was 90% ($P < 0.05$), thus the bolus significantly reduced the level of pasture contamination. The flotation-centrifugation method used in these studies to determine fecal egg counts can detect as few as 10 EPG, whereas the McMaster method is only capable of detecting levels greater than 50 EPG. Therefore, had we used the McMaster¹⁰¹ technique, we would have found no EPG in 1982 (Figure 5) and only minimal EPG in the 1983 (Figure 6) control group on sample days 84 and 154.

The reduction of pasture contamination attributable to the morantel sustained release bolus was further demonstrated by the initial set of 1983 treated tracer calves, which reflected a 79% ($P < 0.05$) reduction in worm burden. Subsequent tracer animals during 1983 continued to demonstrate the effectiveness of the bolus in reducing pasture contamination (Table 2).

Blood plasma pepsinogen levels have been used for estimating the level of parasitic infections and the severity of abomasal damage. Pepsinogen levels below 1000 mU/l are considered normal in calves from temperate climates while levels above 3000 mU/l indicate clinical ostertagiasis and severe abomasal damage.^{5,27} In comparison,

pepsinogen levels between 1000-1990 mU/l represent subclinical infections whereas levels from 2000-2990 mU/l reflect significant abomasal damage and animals display a reduced live weight gain.²⁹ By using these criteria, data from both trials (Figures 7 and 8) reflect that most animals in both of our trials had a subclinical level of parasitism. No treated animals from either trial exceeded the critical level of 3000 mU/l plasma, and only two control animals from Trial 2 exceeded that level.

Subclinical parasitism frequently goes undetected in dairy calves and little evidence exists which provides information on the importance of anthelmintic treatment of such low levels of worm burdens in calves and whether or not it would be economically justifiable to treat such animals. It is interesting to note that during 1983 the bolus treated group demonstrated a 13.5 kg ($P < 0.05$) mean weight gain advantage. These results indicate that reductions in weight gains caused by subclinical infections can be minimized by the use of the morantel sustained release bolus at the time of pasture turnout. This study supports research in New Zealand¹⁰² and in Ohio¹⁰³ where the administration of an anthelmintic to subclinically infected Angus steer calves and Holstein heifer calves, respectively, (based on egg counts) was shown to improve weight gain and be economically feasible.

The unexpected mean weight gain advantage of the control animals over the treated animals at day 160 in 1982 can be partially attributed to the increased dryness of pasture herbage (Figure 13), inadequate and uneven irrigation procedures, and the lack of supplemental hay. Because of an equipment shortage, both pastures

were not irrigated adequately and evenly. The control pasture received more water through irrigation, thus providing better forage for grazing, and by late July the control animals surpassed the treated group in mean weight gain. To help overcome this problem, both groups were fed supplemental hay after July 28. Drier pasture conditions were caused by 103 mm less rainfall during July and August (1982) and higher monthly mean temperatures in June (1.6°C), July (2.2°C), and September ($.67^{\circ}\text{C}$) as compared to those of 1983. Because of the numerous studies that have demonstrated the efficacy of MSRB, weight loss cannot be explained by inefficacy of the anthelmintic.

Although the control animals had a 7.9 kg mean weight gain advantage over the treated calves at day 160, it was not sustained. After day 160 of the trial, both groups were placed onto dry lot conditions, receiving equal hay and concentrate rations. On December 6 (day 202), all animals were reweighed; the treated animals reflected a 4.6 kg mean weight gain advantage over the control animals.

In the present trials it was not possible to study the long-term effects of MSRB administered at the time of pasture turnout on weight gain, calving interval, milk production, and maturation of the pre-Type II Ostertagiasis. In Austria, weight gains were shown to be highly significant in MSRB treated calves during their first season of grazing, but no difference in weight gain was demonstrated following treatment at the time of pasture turnout during the second grazing season. However, the weight gain advantage obtained during the first season was largely maintained, and MSRB treated animals reached breeding weight 19 days earlier than the control group. Consequently MSRB treated heifers began lactating 3 weeks earlier than control

animals. A significant difference in milk yield was not obtained during the first lactation in the MSRB treated heifers.⁴⁵

Even though the results of our study demonstrated the effectiveness of MSRB in reducing pasture contamination at the beginning of Trial 2 (Table 2), one can see that by day 203 (Table 1) tracer calves grazing the treated pasture were harboring a considerable quantity of 4th-stage O. ostertagi. With the onset of favorable conditions the following spring, these inhibited larvae have the potential to emerge and develop into adult worms capable of laying eggs and contaminating the pasture. To more completely control parasitism in these calves the arrested stage of larvae as well as all adult worms need to be removed. Termination dates of December 7 in 1982 and October 4 in 1983 allowed us to determine approximate dates that hypobiosis occurred. Strategic removal of cattle from pastures prior to the fall EPG rise and subsequent pasture contamination could prevent these fall infections and thus the pre-Type II Ostertagiasis. Since our data suggests that pre-Type II Ostertagiasis occurs in western Oregon after mid-October, two possible approaches exist to control the worm burdens. One method could be to administer a second MSRB in September prior to the initiation of hypobiosis. Presumably this should prevent the establishment of inhibited larvae. The normal management practice in Western Oregon is to remove dairy calves from pasture about November 1 and place them onto dry lot. Therefore, the MSRB would be continually releasing the anthelmintic during the time of the fall infection possibly preventing the establishment of arrested larvae. A second approach could be to treat the calves routinely at the time of removal from pasture with a single dose

anthelmintic capable of removing inhibited larvae from ruminants.¹⁰⁴⁻¹⁰⁷ More research is necessary before any recommendations can be made in regards to either the efficacy of such treatments or if they would be economically advantageous to the livestock producer.

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