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A comparison of several anthelmintics for the control of internal parasites of sheep

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A COMPARISON OF SEVERAL ANTHELMINTICS FOR THE CONTROL OF INTERNAL PARASITES OF SHEEP

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Foreword

Despite careful pasture management, parasites can become a real threat to profitable sheep production. Thus, even the best grazier must at times resort to some drug to relieve his flock of parasites. Reliance upon such drugs must be even greater at lower levels of management or under adverse conditions which disrupt even the soundest management.

Anthelmintic drugs thus have become a necessity for profitable sheep production, particularly in the humid grazing areas. A steady improvement in anthelmintic efficacy has been experienced with the addition of each new drug to the shepherd's shelf. To the long-used copper-sulfate and nicotine sulfate combination was added phenothiazine. Now, one of the most recent additions, thiabendazole, promises to make the sheepman's arsenal against parasites more effective than ever.

The work described in this bulletin represents the cooperative efforts of several people. The initial trials conducted in the 1960 grazing season were largely the work of Dr. E. R. Ames (Merck, Sharpe and Dohme) and Mr. C. J. Cunningham, Jr. During the 1962 trials, the contributions of R. W. Harvey and R. L. Reynolds are noteworthy. During these trials, Dr. J. A. Welch and Dr. N. O. Olson provided supervision and direction.

The extended ewe treatment trial begun in 1960 and presently continuing has been the responsibility of Dr. J. O. Heishman and Mr. C. J. Cunningham, Sr.

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SUMMARY

A series of field trials using commercial farm flocks were conducted to determine the comparative anthelmintic efficacy of phenothiazine, copper sulfate and nicotine sulfate, and a new drug, thiabendazole. The results of these trials may be summarized as follows:

1. The most practical and effective dosage level of thiabendazole was about 50 mg/kg of body weight.

2. Under conditions in which flocks were heavily parasitized, thiabendazole was the most effective of the different materials studied.

3. When the level of infection in lambs was low and parasitism was not a major problem, any of the anthelmintics used gave satisfactory results.

4. The particle size and purity of phenothiazine influenced its effectiveness against internal parasites of sheep.

5. Thiabendazole was found to be effective against the major sheep internal parasites and was particularly effective against immature forms of parasites.

6. One flock of ewes has received regular thiabendazole treatment since 1960. During a period of over three years each ewe received about 65 doses which contained the equivalent of about 140 gms of thiabendazole. During this time no evidence of toxicity was observed, nor was there any indication that a tolerance to thiabendazole had developed.

A COMPARISON OF SEVERAL ANTHELMINTICS FOR THE CONTROL OF INTERNAL PARASITES OF SHEEP

G. C. ANDERSON, J. O. HEISHMAN, AND J. A. WELCH

For many years a mixture of copper sulfate and nicotine sulfate, "cunic," was the most effective control agent available for internal parasitism in sheep. Its anthelmintic efficacy is limited, however, and when the superior effectiveness of phenothiazine was demonstrated, this new drug was adopted quickly by sheepmen.

After many years of satisfactory results, it was difficult to understand why phenothiazine failed to provide its usual protection in certain flocks. The explanation for this decrease in phenothiazine's efficacy was offered, at least in part, by the work of Drudge *et al.* (1957a) which suggested that certain nematodes (*Haemonchus contortus*) developed a tolerance for phenothiazine. This original observation from Kentucky has been substantiated by the subsequent work of Drudge *et al.* (1957b), Leland *et al.* (1957), and Drudge *et al.* (1959). These reports, and an increasing number of verifying observations by flock owners on the decrease in efficacy of phenothiazine, emphasized the need for a more satisfactory means of sheep parasite control.

With this in mind, it is easily understood why the announcement of Brown *et al.* (1961) of a new anthelmintic drug, 2 (4'-thiazolyl)-benzimidazole or thiabendazole was most welcome. Early critical tests of the drug by Brown *et al.* (1961) and Cuckler (1961) indicated that it possessed a broad anthelmintic spectrum. Another important practical characteristic of the drug was its low toxicity and wide margin of safety in relation to the dose needed for effective results.

This bulletin describes a series of trials conducted with commercial sheep flocks during the 1960 and 1961 grazing seasons.[1] The objectives of these trials were to determine the most satisfactory level of thiabendazole, to determine the comparative anthelmintic efficacy of thiabendazole and phenothiazine alone or in conjunction with copper sulfate and nicotine sulfate. In addition, one of the flocks involved in the 1960 trials has continued to receive regular treatments of thiabendazole in an attempt to determine if sheep nematodes develop a tolerance for this drug.

[1] Certain aspects of this work have been described elsewhere by Anderson *et al.* (1961), Welch *et al.* (1961), and Cunningham (1962).

EXPERIMENTAL PROCEDURE

Commercial farm flocks used in this work were selected to represent a range in management practices, grazing conditions, and severity of parasitism. Before the trials were begun, phenothiazine had been used as the anthelmintic of choice by all flock owners although the regularity of treatment, method of administration (drench, bolus, or in salt) and combination with other standard materials varied as did the response or degree of parasite control.

The purposes of the 1960 trials were to determine the value of thiabendazole as an anthemintic under practical conditions, the dosage needed for most useful control, and to compare it with various forms of phenothiazine.

In trials 1 and 2 the suckling lambs in a flock were randomly assigned to receive phenothiazine or thiabendazole treatment. Very small lambs or lambs which would soon be marketed were excluded. In these trials the number of lambs used represented at least ten per cent of the flock, but not less than ten lambs per treatment, whichever was greater. All lambs and ewes in each flock grazed together regardless of treatment. Those lambs and ewes in a flock which were not involved in the trials were treated with thiabendazole each time the experimental animals were dosed.

Trials 3 and 4 were conducted with 5 five-and-a-half-month-old weaned lambs. These lambs could not be profitably marketed off their dams largely because of a heavy parasite infection which had not responded to conventional phenothiazine treatment.

During the 1961 trials six flocks were used in a series of studies to compare the anthelmintic efficacy of thiabendazole, phenothiazine, and alternating treatments of phenothiazine and a copper sulfate-nicotine sulfate mixture (cunic). Thirty suckling lambs in each of six flocks were selected for experimental use and randomly assigned to one of three treatment groups. Those ewes and lambs in each flock which were not involved in the trials were given the alternating cunic-phenothiazine treatment when the experimental animals were dosed.

In both years, fecal samples were obtained from the lambs before treatment (predose) at 7 and at 21 or 28 days following the first treatment. The effectiveness of subsequent treatments was based on fecal samples taken 21 or 28 days later.

After collection, fecal samples were placed in individually marked polyethylene bags and transported in a chilled portable cooler to the laboratory where they were stored at 36-40°F until fecal parasite egg counts could be completed.

Total fecal parasite egg counts were made using the method of Stoll (1930) with minor modifications. Eggs per gram of feces (EPG) includes all species of nematodes except *Strongyloides papillosus*. Since *Haemonchus contortus* was the predominant parasite and is a very prolific egg producer, EPG values primarily reflect infections of this parasite. Differential parasite egg counts were not made except for *Trichuris ovis* and *Nematodirus* sp. However, the presence of eggs of other genera was noted (*Trichostrongylus, Bunostomum, Oesophagostomum, Strongyloides, Moniezia, Chabertia, Cooperia,* and *Ostertagia*).

The efficacy of the anthelmintics at a designated post-treatment time is expressed as the percentage reduction in parasite eggs per gram of feces (EPG) from the predose or before treatment level as shown in the following formula:

$$\text{Efficacy} = \frac{\text{EPG at 7 days after treatment}}{\text{EPG before treatment (predose)}} \times 100$$

A similar calculation was made to determine efficacy at 21 or 28 days after treatment. Individual lamb weights were obtained before treatment and 21, 28, or 56 days after treatment.

RESULTS

1960 Trials

The anthelmintic properties of thiabendazole had been established in laboratory experiments at the Merck Institute prior to the 1960 trials (Green, 1960; Cuckler, 1961) but evaluation under commercial flock conditions had not been attempted. Thus, the primary objective of the 1960 trials was to determine the effectiveness of thiabendazole under a wide range of practical conditions and to determine the most useful dosage level.

Trial 1

The flock used in this trial had not responded to ordinary parasite control procedures. Since phenothiazine had been used regularly and did not provide adequate protection, the parasites in this flock were considered to be phenothiazine tolerant or resistant.

The results (Table 1) obtained in this trial clearly demonstrated that the regular form of phenothiazine, National Formulary (N.F.), was ineffective but the micronized material did provide suitable protection.

Of the various levels of thiabendazole used in this trial, only the 50 and 100 mg per kilogram of body weight provided adequate protection.

TABLE 1
Influence of Two Types of Phenothiazine and Different Levels of Thiabendazole on the Parasite Load of Lambs
Trial 1, Flock 5

	Characteristics of Fecal Parasite Egg Counts				
	Predose	7 Days		28 Days	
Treatment[a]	Total	Total	Per Cent Predose	Total	Per Cent Predose
	EPG	EPG		EPG	
Phenothiazine Regular[b]	2570 (700-4600)[c]	2845 (275-15300)	110.7	7157 (800-17800)	278.5
Phenothiazine Micronized	7157 (800-17800)	1203 (24-5650)	16.8	1215 (350-4200)	16.9
Thiabendazole[d] 12.5 mg	4745 (1125-9275)	2681 (400-8175)	56.5	13111 (1050-77500)	276.3
Thiabendazole 25 mg	1832 (275-4700)	187 (10-1400)	10.2	1890 (102-10250)	103.2
Thiabendazole 50 mg	2830 (275-8350)	87 (8-288)	3.1	1245 (30-4825)	44.0
Thiabendazole 100 mg	2810 (1325-5725)	14 (0-44)	0.5	280 (52-740)	9.9

[a] Ten lambs per treatment.
[b] Administered in 25-gram amounts to each lamb.
[c] All figures in parentheses indicate range in eggs per gram of feces.
[d] Treatment in mg per kilogram of body weight.

Of equal importance in terms of control was the prolonged reduction in egg passage, indicating removal of immature worms by thiabendazole.

Phenothiazine's anthelmintic efficacy is clearly related to fineness of particle size, as indicated in trial 1. Accordingly, this was considered in trial 2 although the flocks used in this trial were not as heavily parasitized as those used in trial 1, nor had phenothiazine been used as regularly.

Trial 2

The results of trial 2 are summarized in Table 2. Again, the regular form of phenothiazine (N.F.) failed to be as effective as the micronized form. Fecal parasite egg counts were higher 28 days after treatment with regular phenothiazine than they were prior to treatment. On the other hand, fecal egg counts were about 30 per cent less than the original level 28 days after treatment with the micronized form.

All three levels of thiabendazole used on the flocks in trial 2 were more effective in reducing parasite eggs per gram of feces than either form of phenothiazine. Weight gains were not materially effected, possibly because the pastures provided less than optimum nutrition.

The results of trials 1 and 2 verified the anthelmintic efficacy of thiabendazole. Of the various dosage levels used, it appeared that about 50 mg per kilogram of body weight would be the most useful in terms of effectiveness and cost.

TABLE 2

Comparative Effectiveness of Thiabendazole and Phenothiazine in Flocks with a Low Level of Parasite Infection and No Apparent Phenothiazine Tolerance[a]

Trial 2, 1960

Flock	Treatment	Lambs	Average Initial Weight (lb.)	Average Net Gain (lb.)		Eggs Per Gram of Feces				Per Cent Predose	
				28 Days	56 Days	Predose	7 Days	28 Days	56 Days[c]	7 Days	28 Days
1	Phenothiazine[b] Regular	11	71	7.5	15.9	1896 (32-4225)	197 (12-526)	1905 (60-7200)	799 (16-4250)	10	100.5
1	Thiabendazole[b] 50 mg	12	56	8.4	16.8	4152 (650-18950)	63 (4-180)	733 (20-2950)	353 (0-1250)	2	17.6
3	Phenothiazine Regular	13	74	8.5	12.5[d]	775 (378-1875)	73 (10-188)	921 (225-3725)	853[d] (275-1700)	9	120
3	Thiabendazole 100 mg	14	77	8.1	11.1[d]	1016 (275-2800)	5 (0-18)	546 (14-1800)	630[d] (146-2225)	1	54
4	Phenothiazine Micronized	15	81	3.1	6.9	760 (84-2200)	65 (0-204)	525 (34-2400)	727 (58-3575)	9	69
4	Thiabendazole 25 mg	15	73	7.5	11.5	1172 (175-3075)	74 (2-350)	450 (54-1075)	514 (36-2450)	6	38
4	Thiabendazole 50 mg	15	75	6.5	12.1	2168 (100-12300)	6 (0-52)	344 (4-898)	343 (0-1725)	..	....

[a] Based upon the observations of flock owners, condition of lambs, and EPG prior to treatment.
[b] Uniform dose of 25 gm phenothiazine per lamb. Thiabendazole given in indicated amounts per kilogram of body weight.
[c] All flocks retreated at end of 28 days except flock 3. Note flock 4 treated with micronized phenothiazine instead of regular material.
[d] Based on 6 lambs in phenothiazine treatment and 7 lambs in thiabendazole treatment.

TABLE 2b

Comparative Effectiveness of Thiabendazole and Phenothiazine in Flocks with an Apparent Phenothiazine Tolerance[a]

Trial 1960

Flock	Treatment	Lambs	Average Initial Weight (lb.)	Average Net Gain (lb.)	Eggs Per Gram Feces			Per Cent Predose	
				28 Days	Predose	7 Days	28 Days	7 Days	28 Days
5	Phenothiazine[b]	10[c]	44	2.4	2570 (700-4600)	2845 (275-15300)	7157 (1050-17800)	111	278
5	Thiabendazole[b] 12.5 mg	10	43	3.3	4745 (1125-9275)	2681 (400-8175)	13111 (1050-77500)	57	276
5	Thiabendazole 25 mg	10	50	6.1	1832 (275-4700)	187 (10-1400)	1890 (102-10250)	10	103
5	Thiabendazole 50 mg	10	47	4.8	2830 (275-8350)	87 (8-288)	1246 (30-4825)	3	44
5	Thiabendazole 100 mg	10	42	6.6	2810 (1325-5725)	14 (0-44)	280 (52-740)	1	10
6	Phenothiazine	10	40	5.3	5300 (600-16475)	556 (136-1704)	3420 (850-7750)	10	65
6	Thiabendazole 50 mg	10	43	8.2	5838 (650-12050)	151 (14-432)	349 (18-650)	3	6
8	Phenothiazine	8	84	3.4	2589 (575-5100)	356 (124-628)	3704 (1975-7200)	14	143
8	Thiabendazole 50 mg	28[d]	80	5	3143 (250-16150)	149 (4-516)	1083 (175-2300)	5	35
9	Phenothiazine	5	71	2.3	2000 (225-2750)	1114 (222-2275)	8300 (1700-13700)	56	415
9	Thiabendazole 50 mg	38[e]	77	6.0	4662 (550-10200)	65 (6-170)	3006 (1150-6250)	1	65

[a] Based upon observations of flock owners, condition of lambs and EPG prior to treatment.
[b] Uniform dose of 25 gms phenothiazine (N.F. Regular) per lamb. Thiabendazole given in indicated amounts per kilogram of body weight.
[c] Incomplete set of samples from four lambs. Values based on samples from six lambs.
[d] Average weights based on all lambs; EPG on seven.
[e] Average weights based on all lambs; EPG on five.

The information presented in Table 2 was obtained from flocks in which phenothiazine had provided reasonably satisfactory parasite control. These flocks were designated as having no apparent tolerance for phenothiazine. For comparative purposes, data from flocks considered to be tolerant to phenothiazine, because adequate parasite control could not be obtained through the regular use of this material, are presented in Table 2b.

Trial 3

Phenothiazine had been used as the major anthelmintic in flock 8 for many years. The material was constantly available in salt (1:9) and was also given periodically as a bolus or drench. Nevertheless, parasite control had not been satisfactory.

The lambs used in this trial were about five-and-a-half-months old and represented that portion of the lamb crop which could not be marketed directly off their dams. Phenothiazine had been administered regularly, with the last treatment being given three weeks before the trial was begun. The 58 head were randomly divided into two groups, 29 lambs each. The lambs in group A were randomly subdivided so that eight lambs received phenothiazine and the remaining 21 received thiabendazole. Similarly, lambs in group B were randomly subdivided so that seven lambs received phenothiazine while 22 received thiabendazole. The groups grazed adjacent bluegrass-white clover pastures. Lambs in group B were fed grain (Table 3).

Under both feeding systems thiabendazole proved to be markedly superior to the phenothiazine N.F. in reducing parasite eggs in the feces (7 days $P > 0.5$, but at 28 and 56 days $P < 0.1$). The nutritive value of the aftermath pasture was apparently low, for weight gains were hardly satisfactory. Supplementing the pasture with grain increased gains markedly and permitted the lambs to respond to parasite control treatments. Under these conditions the thiabendazole-treated lambs gained 0.1 pound more per day than the phenothiazine-treated lambs ($P < 0.5$).

Trial 4

The lambs used in this trial were from the same flock as those used in trial 3. Trial 3, it will be recalled, involved sheep that had been regularly treated with phenothiazine for many years. At the beginning of both trials 3 and 4 evidence of parasitism was apparent from the appearance of the lambs despite regular treatment. Some mortality had been experienced in the preceding six weeks and, according to the flock owner, parasitism was the cause of these losses.

TABLE 3

Effectiveness of Phenothiazine and Thiabendazole in Weaned Lambs (August 12—October 21, 1960)

Trial 3, Flock 8

Item	Treatment	Lambs	Average Initial Weight (lb.)	Average Net Gain (lb.)		Eggs Per Gram Feces			
				28 Days	56 Days	Predose	7 Days	28 Days[b]	56 Days
A. Pasture	Phenothiazine[a]	8	68	6.0	11.5	2044	519	4621	5585
	Thiabendazole	21	68	5.9	12.5	3600	55	1295	538
B. Pasture and Grain	Phenothiazine	7	62	8.5	14.3	3128	1128	3357	5350
	Thiabendazole	22	56	12.6	21.0	3800	87	871	618

NOTE: Fecal egg counts are based on all lambs in phenothiazine groups and an equal number selected randomly from thiabendazole groups. Weight gains are net and are average of all lambs.

[a] Each lamb treated with 25 gm bolus of N.F. phenothiazine containing 0.5 gm lead arsenate or with 50 mg of thiabendazole per kilogram body weight.

[b] Retreated at 28 days.

Previous fecal parasite egg counts had excluded *Strongyloides papillosus* since the pathogenicity of this parasite is considered to be relatively low, although heavy infections may be damaging. This trial was conducted to determine the relative efficacy of phenothiazine and thiabendazole in the control of *Strongyloides papillosus* and similar observations were made relative to *Nematodirus* sp. and *Trichuris ovis* since preliminary observations suggested that infections of these nematodes might be unusually high.

As mentioned earlier, regular phenothiazine treatment had been ineffective in the control of the parasite infection in this flock. Thus, in order to reduce the risk of additional losses, five instead of the usual minimum of ten lambs were randomly selected for phenothiazine treatment. The remaining lambs, 38 head, received thiabendazole. Fecal parasite egg counts were based on samples from all of the phenothiazine lambs and from five randomly selected thiabendazole-treated lambs. Weights were obtained for all lambs. All lambs grazed a red clover, lespedeza, and orchardgrass aftermath. Pastures were changed three times during the trial.

Results of this trial are recorded in Table 4. Phenothiazine in the form administered was ineffective in the control of the total parasite infections and particularly *Strongyloides papillosus.*

As in previous experiments, thiabendazole effectively reduced the fecal parasite egg counts. *Strongyloides papillosus* and *Nematodirus* sp. were susceptible to thiabendazole but *Trichuris ovis* was not. The degree of parasite control experienced was reflected in weight gains ($P < .05$).

Thiabendazole and Phenothiazine for Ewes

In the course of the lamb trials, the comparative efficacy of phenothiazine and thiabendazole for the control of parasite infections in the ewe flocks was also assessed. During the trials, all ewes in the experimental flocks were treated with thiabendazole except for ten randomly selected ewes in each flock which were treated with phenothiazine. Fecal samples were obtained from these ewes and from ten similar ewes which were treated with thiabendazole. The parasite infection in some of the ewes was so low that EPG counts were not meaningful. These counts are not included in the values given in Table 5 which are based upon the number of ewes indicated. Ewes and lambs were treated on the same day.

As would be expected, the parasite infections of the ewes were much lower than that of the lambs, although considerable variation in fecal parasite egg counts was recorded. The general character of the results presented in Table 5 are in accord with the observations made on the

TABLE 4

Effectiveness of Thiabendazole and Phenothiazine for the Control of *Strongyloides papillosus*, *Nematodirus* sp., and *Trichuris ovis* (August 12—October 4, 1960)

Trial 4, Flock 9

Treatment[a]	Lambs	Average Initial Weight (lb.)	Average Net Gain (lb.)			Eggs Per Gram Feces			
			28 Days	56 Days		Predose	7 Days	28 Days	56 Days
Phenothiazine	5	71	2.3[b]	4.0	Total:	2000	1114	8300	5875
					Range:	(725-2750)[c]	(222-2275)	(1700-13700)	(3550-8550)
					Trichuris	9	13	50	0
					Nematodirus sp.	19	0	38	....
					Strongyloides	463	600	2913	2675
Thiabendazole	38	77	6.0	8.8	Total:	4662	65	3006	503
					Range:	(550-10200)	(6-170)	(1150-6250)	(36-900)
					Trichuris	137	58	494	19
					Nematodirus sp.	0	0	0	....
					Strongyloides	1631	7	44	264

[a] Each lamb received 25 gm bolus of phenothiazine N.F. or 50 mg thiabendazole per kilogram of body weight.

[b] Each lamb retreated at 28 days.

[c] Figures in parentheses indicate range in parasite eggs per gram of feces.

TABLE 5
Phenothiazine and Thiabendazole for Control of Internal Parasites in Ewes

	Thiabendazole				Phenothiazine			
	Eggs Per Gram Feces				Eggs Per Gram Feces			
Flock	Ewes	Predose	28 Days	Per Cent Predose 28 Days	Ewes	Predose	28 Days	Per Cent Predose 28 Days
1	5	185[a] (32-386)	3* (0-6)	2	5	40 (16-98)	31 (4-80)	77
3	6	167 (46-325)	5 (0-16)	3	5	367 (104-729)	67 (8-160)	18
4[b]	5	123 (10-304)	14 (2-46)	11	5	124 (12-328)	43 (8-132)	35
5	6	1020 (56-3842)	149** (28-370)	15	6	1339 (210-5200)	3004 (325-8425)	124

[a] Figure indicates average number of eggs per gram of feces, whereas those in parentheses give the range.
[b] Micronized phenothiazine used. Regular grind material (N.F.) used in other flocks 25 gm per ewe. Thiabendazole, 2.28 gm per ewe, or 44 mgm per kg body weight.
* Significant ($P < .05$); ** significant ($P < .01$) reduction in EPG in comparison to phenothiazine treatment.

lambs. That is, thiabendazole was more effective than phenothiazine in reducing parasite infections, as indicated by parasite fecal egg counts. This effect of thiabendazole, along with its effect on the immature form of parasite, should be of value in reducing pasture contamination.

1961 Trials

Thiabendazole, phenothiazine, and alternating cunic and phenothiazine drenches were compared in six commercial flocks. The trials were begun in June and continued for two months. For use in this study, 30 lambs in each of the flocks were chosen on the basis of uniformity in size, sex, and type of birth. The lambs used averaged 60 pounds at the beginning of the trials. All other lambs and all the ewes in these flocks were treated every 21 days with alternating drenches of phenothiazine and cunic mixture.

The lambs in each flock were divided into three treatment groups of ten lambs each. Lambs in group 1 were treated with 20 grams of fine grind, purified phenothiazine in a commercially available suspension; group 2 lambs received approximately 44 mg of thiabendazole per kilogram of body weight; and those in group 3 received the alternating phenothiazine-cunic mixture treatment. The cunic mixture was administered first, with a treatment of phenothiazine following 21 days later. Cunic mixture was given again 42 days after the start of the trial. Dosage level of thiabendazole and cunic mixture was adjusted with lamb weight as shown in Table 6.

Fecal parasite egg counts included all species except *Trichuris* and *Strongyloides*.

TABLE 6

Dose Schedule of Anthelmintics in Relation to Lamb Weight

Lamb Weight	Anthelmintic		
	Phenothiazine	Cunic	Thiabendazole
pounds	*grams*	*ounces*	*grams*
44-55	20	1	1
56-68	20	1	1.25
69-80	20	1.5	1.5
81-93	20	2	1.75
94 and more	20	3	2.0

The performance of the lambs in terms of weight gain was remarkably similar for all treatments (Table 7). The uniformity in response to anthelmintic treatment within and between these flocks which represent diverse management and grazing conditions is surprising, although it should not be unexpected in terms of sound flock management reflected in the very low level of parasite infection existing in all flocks (Figure 1). Figure 1 also summarizes the effect of the different anthelmintics in reducing the parasite infection. The values presented in this graph do not include *Trichuris ovis* and *Strongyloides papillosus* eggs. Since *Haemonchus contortus* was the predominate species present, the values represented largely reflect the infection of this prolific egg producer. Each bar represents an average value for 60 lambs.

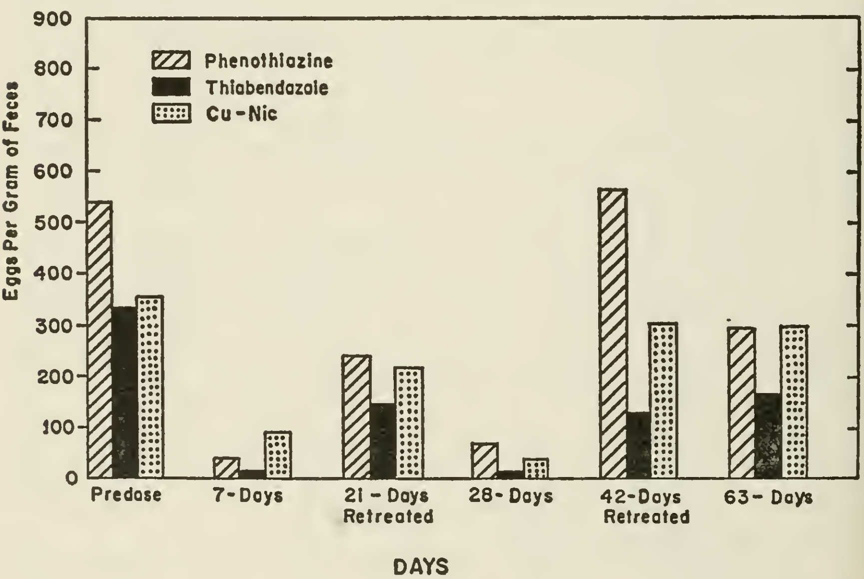

FIGURE 1

TABLE 7

Effect of Different Anthelmintic Treatments on Lamb Gains

1961 Trials

	Phenothiazine			Phenothiazine-Cunic			Thiabendazole		
		Average Weight (lb.)			Average Weight (lb.)			Average Weight (lb.)	
Flock	Lambs	Initial	63 Days	Lambs	Initial	63 Days	Lambs	Initial	63 Days
1	10	63.1	90	10	64	93	10	62	91
2	9	74.3	99	9	66	90	9	69	94
3	9	56.8	69	10	52	67	9	53	68
4	10	50.6	71.5	10	47	68	9	51	70
5	10	54.4	66	10	54	67	10	55	71
6	10	69.4	82.8	10	67.5	81.5	10	74.7	86.5
Total	58	3492	4535	59	3434	4568	57	3475	3705
Average		60.2	78.2		58.2	77.4		60.9	80.2
Average Gain			18.0			19.2			19.3

The first set of three bars represents the average EPG in the fecal samples taken before treatment and establishes the low level of parasite infection which did not increase during the trials. Although the level of infection did not permit a really critical evaluation of the three treatments, it can be seen that thiabendazole was consistently the most effective in reducing the number of eggs per gram of feces.

Athough *Trichuris ovis* and *Strongyloides papillosus* are parasites found in sheep, they are not believed to ordinarily influence lamb performance in the area represented in these trials. However, this might change under certain conditions and thus the effectiveness of the three treatments in the control of these two parasites was determined. From the results recorded in Figure 2 it can be seen that none of the treatments appeared to be effective against *Trichuris ovis.* However, in Trial 4 of the 1960 grazing season phenothiazine appeared to be effective against *Trichuris ovis.* On the other hand, *Strongyloides papillosus* was effectively controlled by thiabendazole, as shown in Figure 3, and this is in agreement with the results of trial 4, Table 4. In both trials phenothiazine was ineffective in controlling *Strongyloides papillosus.*

Continuous Use of Thiabendazole in a Commercial Ewe Flock

The regular use of an anthelmintic over a long period of time may permit the development of parasite strains tolerant to the material.

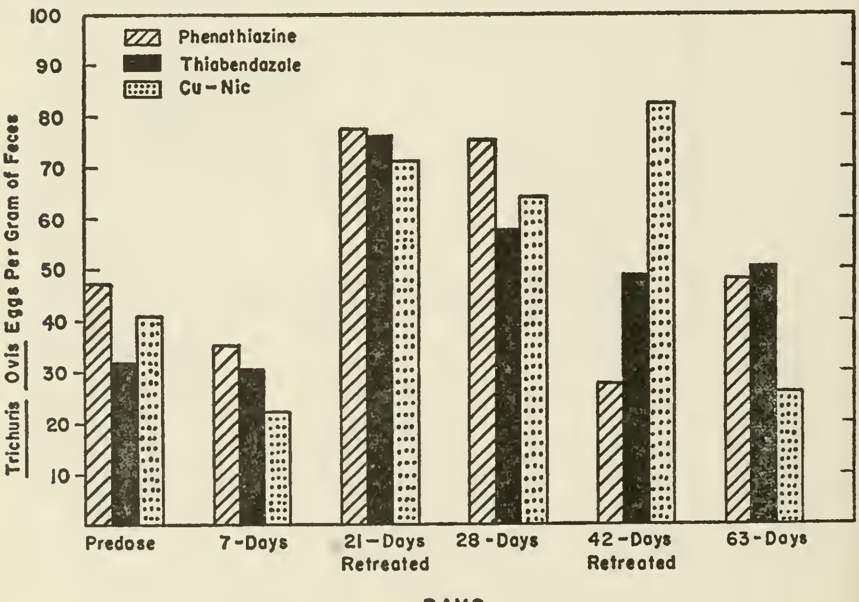

FIGURE 2

The observations of the Kentucky workers mentioned earlier suggest that this was the case with phenothiazine and the major sheep parasite, *Haemonchus contortus.*

It was with this in mind that one of the commercial ewe flocks involved in the initial 1960 trials was continued on thiabendazole. This flock of 125 cross-bred white-face ewes is managed to lamb during the early fall. Pasture rotation is practiced, with availability of feed determining change of pastures.

Beginning in August 1960, a systematic thiabendazole treatment program was begun. Every 21 days all ewes received one ounce of a commercial preparation which provided two grams of thiabendazole. On the basis of ewe weights at that time, this dose was calculated to provide 50 mg of thiabendazole per kilogram of body weight. Although a gradual increase in body weight was apparent as the trial progressed, no adjustment in treatment level was made until January 1964. As a result of the gradual increase in body weight (90 to 140 lb), the treatment level had fallen from about 50 mg per kilogram of body weight to about 30 mg. Accordingly, the quantity of material was increased to 1.5 oz or the equivalent of 3 gr of thiabendazole per ewe (44 mg/kg of body weight). At the same time, the treatment schedule was changed

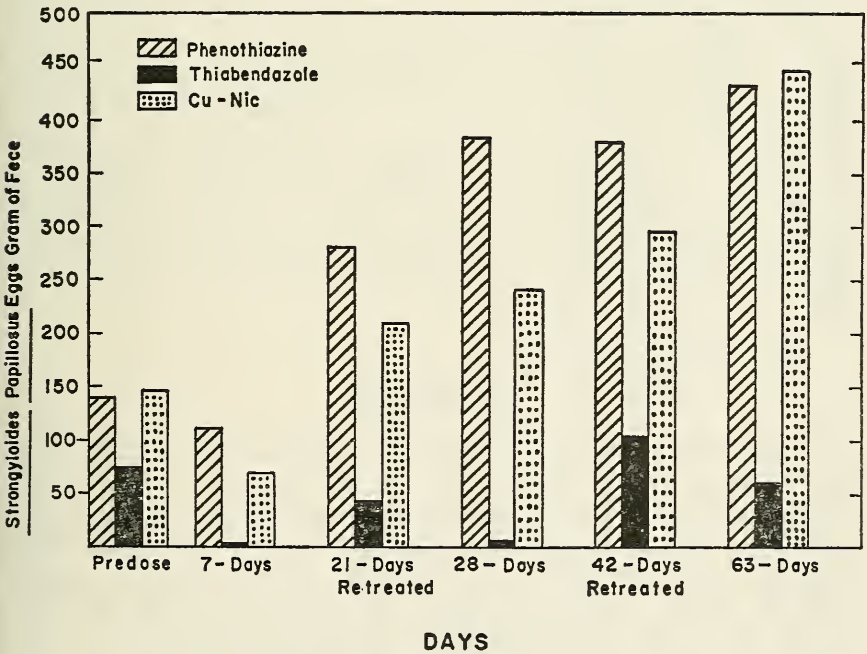

FIGURE 3

TABLE 8

Effect of Extended Thiabendazole Treatment Upon the Fecal Parasite Load of Ten Monitor Ewes

Date of Sampling and Treatment	Average Number of Parasite Eggs Per Gram Feces	Date of Sampling and Treatment	Average Number of Parasite Eggs Per Gram Feces
8-12-60 (Before treatment)	4662	9-23-63	1066
9- 9-60	3006	10-11-63	2303
10- 7-60	502	11- 1-63	2796
2-26-63	359	11-23-63	339
3-22-63	457	12-18-63	248
4-19-63	445	1-24-64	315
6- 6-63	254	2-14-64	111
6-28-63	80	5-23-64	313
7-20-63	605	8- 8-64	2394
8- 9-63	1676	12- 8-64	993
8-30-63	1528		

from every 21 days to five treatments per year to be administered in January, February, May, August, and December.

In the beginning of the study, ten ewes were randomly selected to serve as monitors of the flock's parasite infection. These ewes were individually marked and fecal samples were obtained from them at each treatment. Differential parasite egg counts were not made and thus parasite infection is estimated from the total parasite eggs per gram of feces. An account of the parasite infection of these ewes for 1963 and 1964 is given in Table 8 and Figure 4. The average number of parasite eggs per gram of feces increased each year during the late summer-early fall period, as would be expected under the conditions prevailing in the area. The results at present do not suggest any build up or sustained increase in parasite load as would be expected if a tolerance for thiabendazole developed during the period from July 1960, to December 1964.

This study is being continued.

DISCUSSION

None of the materials used in these trials caused an observable toxic reaction. During initial trials with thiabendazole, a level of 100 mg per kilogram of body weight was commonly used. In accompanying exploratory studies doses five times this level did not produce observable symptoms of toxicity. Bell *et al.* (1962) did not record signs of toxicity until 800 mg/kg were administered. Of the various treatment levels studied, that of 50 mg per kilogram of body weight (equivalent to 2.28 gm for a 100 lb sheep) appeared to be the practical and effective

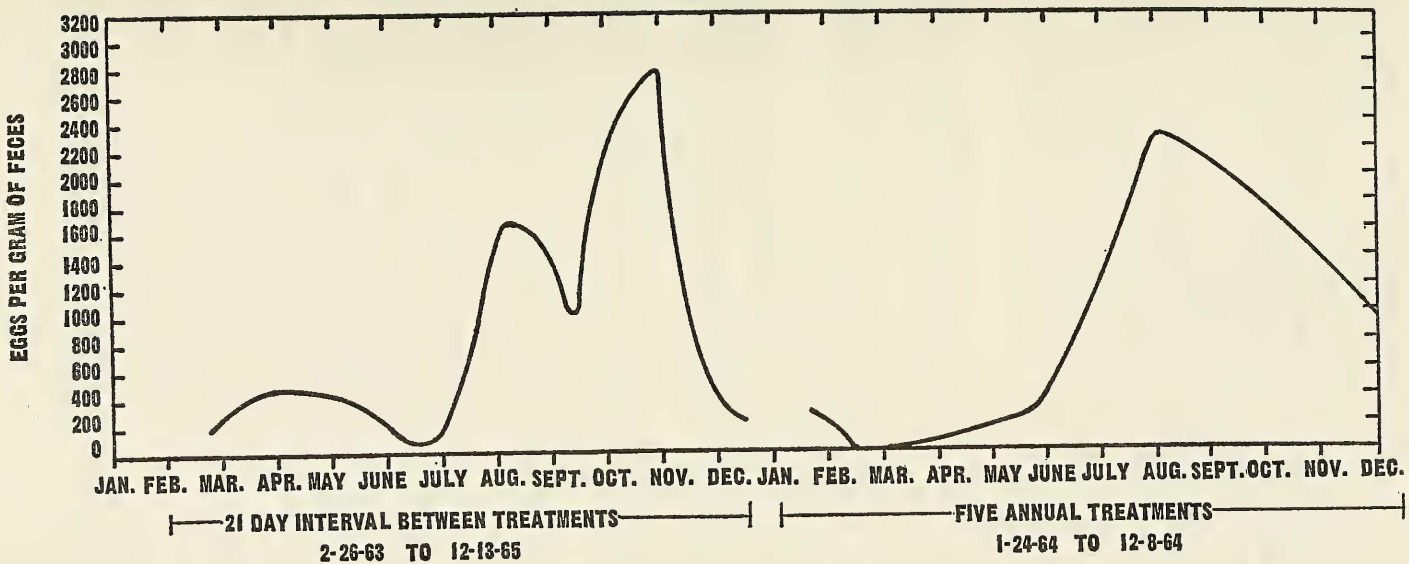
EGGS PER GRAM OF FECES
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
JAN. FEB. MAR. APR. MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR. APR. MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC.
21 DAY INTERVAL BETWEEN TREATMENTS
2-26-63 TO 12-13-65
FIVE ANNUAL TREATMENTS
1-24-64 TO 12-8-64

FIGURE 4

level of choice. The observations supporting this selection are in accord with the laboratory findings of Brown *et al.* (1961), Cuckler *et al.* (1961), and subsequent studies such as those by Reinecke (1962), Muller (1961), Gordon (1961), and Herlich (1962). Extensive use of this dosage level or its practical equivalent, 44 mg/kg, in subsequent work has clearly established its efficacy.

The effectiveness of thiabendazole against a wide range of internal parasites as described in the initial announcement by Brown *et al.* (1961) has been verified by trials conducted in every major sheep producing country. These diverse studies also affirm the effectiveness of thiabendazole against immature forms of the major parasites (Cairns, 1961; Bell *et al.*, 1962; Gordon, 1962; Drudge and Szanto, 1962; Southcott, 1963; and Gordon, 1964).

During the 1960 trials the real value of thiabendazole was apparent when the parasite infection was high and could not be controlled by phenothiazine. On the other hand, in the 1961 trials, the flocks used were only slightly infected and the three treatments were equally effective in terms of lamb gains. However, in terms of reduction in fecal parasite eggs, thiabendazole was most effective.

The variation in response to phenothiazine treatment observed in the 1960 trials can be considered from two viewpoints. First, the particle size and purity of a phenothiazine preparation influences its effectiveness, as shown by Gordon (1956) and Douglas *et al.* (1957). Secondly, in some flocks phenothiazine had been used continuously for many years and certain helminths may have developed a resistance toward it.

The low level of parasite infection in the flocks used in 1961 trials reflects to a considerable degree a favorable grazing season and management practices which discourage parasite infection. The application of proper management as a means of controlling parasite infection cannot be overemphasized. In fact, anthelmintics properly used should be a part of control management but not considered as a substitute for it.

The major reason for conducting the extended trial with ewes was to determine if the parasites infecting the ewes would develop resistance to thiabendazole. Since the beginning of this trial, the ewes have received about 65 thiabendazole treatments and have received an equivalent of about 140 gm of the drug. To this time, observations suggest that no resistance to thiabendazole has developed.

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