

PHENOTHIAZINE-SALT MIXTURES AS AN ANTHELMINTIC FOR SHEEP

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Since Harwood and associates (1939) of the Bureau of Animal Industry demonstrated the efficiency of phenothiazine in removing various species of nematodes, the efficiency of this chemical for removing intestinal parasites of sheep has been confirmed by many other investigators. The Illinois Experiment Station reported in 1941, 1942a, and 1942b, favorable results as judged by Stoll counts following the treatment of sheep, goats, and horses for strongyles. At the Illinois Station phenothiazine had been administered to parasitized lambs in gelatine capsules, boluses, liquid, blackstrap molasses, and soya bean pellets.

Since the effectiveness of phenothiazine has been demonstrated in removing nodular worms, stomach worms, and bankrupt worms of sheep, attempts have been made to simplify the methods of administering the drug to them. One of the most popular of the suggestions has been the incorporation of the chemical with salt and offering the mixture as a lick. Habermann and Shorb found phenothiazine-salt mixtures in proportions of from 1:9 to 1:14 to be effective in reducing the larval counts in fecal cultures. The average daily consumption of phenothiazine was at least 0.5 gram per sheep. Earlier, Shorb and Habermann pointed out that daily administration of 0.5 gram doses of the drug completely inhibited the development of all nematode larvae with

the exception of *Strongyloides papillosus*. Viable larvae again appeared in the fecal cultures 48 hours after withdrawal of the drug. The egg count was not at any time reduced. Gordon arrived at essentially the same conclusions. Britton, Miller, and Cameron in an uncontrolled observation with 830 ewes and lambs reported a definite anthelmintic effect of a 1:15 phenothiazine-salt mixture. In a second and more comprehensive report involving controlled experiments, the same authors again reported favorably upon a 1:15 phenothiazine-salt mixture as a practical and effective anthelmintic for sheep. A 1:9 phenothiazine-salt mixture, according to Thorp and Keith, reduced the numbers of nematode ova in the feces of parasitized sheep. The elimination of ova remained low as long as the mixture was fed. Foster and Habermann recommend the use of mixtures containing from 9 to 14 parts of salt to one part of phenothiazine in the control of ovine nematodes. They caution, however, that the use of phenothiazine in salt should be regarded as a preventive rather than a therapeutic procedure.

This paper is an attempt to outline two years work (1943, 1944) at the Dixon Springs Experiment Station, Pope County, Illinois, to study the effectiveness of phenothiazine-salt mixture in controlling ovine nematodes on pasture.

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PLAN

In the 1943 tests approximately 600 mature western ewes, maintained at the Dixon Springs Experiment Station, were made available for the experiment. Early in January the sheep were brought in from pastures for dry lot feeding. They were divided at random into three lots of 196 ewes each. Each ewe was dosed with two ounces of a 50 percent suspension of phenothiazine in molasses and water. They had been dosed similarly for the preceding several months. Mixed hay (mainly lespedeza and grass) was fed to all lots, together with one pound of shelled corn and one-fourth pound of soybean oil meal daily per head. Beginning January 15 a 1:14 phenothiazine-salt mixture was made available to the ewes in Lot 3. They were also provided with a mineral mixture of equal parts limestone and bone meal. Lots 1 and 2 had access to a mixture of salt, limestone, and bone meal.

Lambing occurred in the three lots during February, March, and April. The experimental treatment of these lots of ewes and lambs was planned as follows: Lot 1, the control group, was to be maintained without further phenothiazine medication. Lot 2 was to be dosed with phenothiazine, one ounce per ewe, one-half ounce per lamb, at the beginning of the pasture season and thereafter maintained upon a 1:14 phenothiazine-salt mixture. Lot 3 was to be maintained continuously, both in the dry lot and at pasture, on the 1:14 phenothiazine-salt mixture. In order to limit losses however, it was planned to treat the sheep in any lot with a therapeutic dose when and if parasitism became marked.

The degree of parasitism was to be estimated by fecal examinations for

the presence of nematode ova and by autopsy examinations of representative ewes and lambs at time of marketing. The rate of gain and general condition were to be determined by inspection and periodic weighing.

The pastures ranged from one hundred to three hundred acres in size. Because of an unusual amount of rain during the spring and early summer growth of forage was excellent and ample. With one exception the pasture for each lot was changed once a month.

FECAL EXAMINATIONS AND POST-MORTEM INSPECTION

At the beginning of the pasture season and continuing at monthly intervals throughout the spring and summer fecal specimens were collected from a random selection of 25 ewes and 25 lambs in each lot. A similar collection had been made from the ewes in Lot 3 early in January. Preliminary observations (floatation) showed nematode ova to be present, and a two-gram portion of each fecal sample was preserved with 2cc. of 25 percent formalin. The specimens were then returned to the Department of Animal Pathology Laboratory at Urbana for determination of the nematode ova present according to the Stoll technique. At the time of slaughter the intestines from representative animals were observed for the presence and the relative numbers of parasites and parasitic nodules. The abomasum was opened and a portion of the contents removed and preserved in formalin for nematode examination.

RESULTS

Clinical Observations and Relative Gains

The ewes, together with their lambs, were turned to pasture April 25. The system of pasture rotation is set forth in Table 1.

TABLE 1.—PASTURE ROTATION AMONG THE THREE LOTS OF EWES AND LAMBS

Time of pasture	Pasture				
	Elam Lot	South Lot	Phelps Lot	Wells Lot	Experiment 8 Lot
April 25–May 26.....	3	2	1
May 27–June 28.....	1	3	2
June 29–August 3.....	3	1a 1b	2	1c

During the first month on pasture none of the sheep developed clinical manifestations of parasitism. It was expected however that the pasture occupied by the sheep in Lot 1, the untreated group, would become contaminated and that this pasture, subsequently occupied by the second lot, would serve to test the effectiveness of a 1:14 phenothiazine-salt mixture in protecting ewes and lambs from parasites when exposed to infection. The sheep and lambs of Lot 3, maintained continuously upon phenothiazine-salt mixture since January, were never exposed to similar infestation during the pasture season, although at the end of the first month on pasture they were placed on the pasture previously grazed by animals of Lot 2.

At the end of the second month on pasture, the ewes and lambs in Lot 2, given access to 1:14 phenothiazine-salt mixture but maintained for four weeks upon a contaminated pasture, had developed marked clinical manifestations of parasitism. The sacrifice of two ewes and one lamb from this group confirmed the diagnosis. All ewes and lambs in this lot were treated with phenothiazine and placed on clean pasture. Both ewes and lambs in Lot 1 also showed evidences of parasitism but

not to the same degree as those in the second group. Lot 1 was divided into three groups as follows:

Group a—20 ewes and their 20 lambs were untreated.

Group b—62 ewes and 35 lambs were drenched with phenothiazine, one ounce per ewe, one-half ounce per lamb.

Group c—105 ewes and 107 lambs drenched as Group b and offered a 1:9 phenothiazine-salt mixture.

The ewes and lambs in Lot 3, maintained upon a 1:14 phenothiazine-salt mixture but not placed upon a pasture recently occupied by heavily parasitized, untreated sheep, remained in good condition. Their pasture was not changed after May 27 at which time they were put in the pasture occupied the previous month by sheep of Lot 2. The gains for the various pasture periods are given in Table 2.

Examination of the data in Table 2 indicates that both ewes and lambs in Lot 3, maintained continuously upon 1:14 phenothiazine-salt mixture, made satisfactory gains. As will be noted in Table 1, they followed Lot 2 in the pasture rotation and were kept on this same pasture until August 3. On the other hand,

TABLE 2.—AVERAGE INDIVIDUAL GAINS MADE BY EWES AND LAMBS BY PERIODS
MAY 27 TO AUGUST 3—68 DAYS

Period	Lot 1			Lot 2		Lot 3	
	Group	Ewes lbs.	Lambs lbs.	Ewes lbs.	Lambs lbs.	Ewes lbs.	Lambs lbs.
May 27-June 27.		+1.1	+5.7	-2.9	-7.9	+2.8	+11.5
June 28-August 3.	a	+14.5	+4.9	+8.7	+8.0	+20.2	+16.6
	b	+20.0	+17.4				
	c	+17.4	+17.6				

TABLE 3.—LOGARITHMIC AVERAGES OF NEMATODE OVA DETERMINATION

Lot	Date of Collection				
	1-15	4-27	5-27	6-28	8-3
1 Ewes.		4,600	225	180	190
2 Ewes.		2,800	52	20	24
3 Ewes.	4	165	91	32	11
1 Lambs.			37	3,300	3,900
2 Lambs.			22	1,036	274
3 Lambs.				793	48

the gains shown for Lot 2 were very unsatisfactory. Lot 2 was given the same phenothiazine-salt mixture but followed the untreated sheep of Lot 1 in the pasture rotation. The gains made in Lot 1 were also unsatisfactory; however, the sheep of Group b and c did make satisfactory gains after treatment.

EGG COUNTS

In Table 3 is given a summary of the nematode ova contents of the fecal specimens as determined by the Stoll technic. Twenty-five fecal samples were collected at monthly intervals from the ewes and from the lambs in each lot. The results given in Table 3 are the logarithmic averages (nematode ova per gram of feces) of each series of 25 samples.

The nematode ova determinations of fecal samples as a means of estimating the degree of parasitism and as a measure of anthelmintic efficiency proved in this experiment to be of limited value. It would be deducted from Table 3, for example, that the ewes in Lots 1 and 2 initially were heavily parasitized at the time they were turned to pasture, but subsequently eliminated most of the infestation. It would be further deduced that the lambs in Lot 1 were more heavily parasitized than those in Lot 2. These deductions are not supported by observations on comparative rates of gain, mortality figures, and post-mortem examination. Just why nematode ova determinations of fecal specimens according to the Stoll technic failed to cor-

TABLE 4.—CONSUMPTION OF THE PHENOTHIAZINE-SALT MIXTURE

Period	Lot	Lambs	Ewes	Mixture	Consumption		Average daily consumption of phenothiazine
					Total	Average monthly	
					lbs.	lbs.	grams
April 25–May 26.....	2	163	187	1:14	220	0.63	0.60
April 25–May 26.....	3	157	191	1:14	200	0.57	0.54
May 29–June 28.....	2	152	184	1:14	177	0.53	0.53
May 29–June 28.....	3	158	190	1:14	130	0.37	0.38
June 29–August 2.....	1	96	105	1:9	90	0.45	0.60
June 29–August 2.....	2	150	183	1:14	225	0.68	0.60
June 29–August 2.....	3	157	190	1:14	221	0.64	0.57

relate with clinical manifestations is not clear, but probably several factors are involved. One of these would be variations in fecal moisture content. The feces of sheep on dry lot contain less water than those of sheep on pasture; and, the feces of healthy sheep are more solid than those of parasitized animals, the latter often showing profuse diarrhea. An increase in the fecal water content obviously would reduce the ova obtained per unit mass of feces in parasitized sheep. Leiper and Peters determined statistically that variations in weight are more sensitive indicators of anthelmintic efficiency than are egg counts. Our observations tend to support this conclusion.

CONSUMPTION OF THE PHENOTHIAZINE-SALT MIXTURE

During the period of observation 1,173 pounds of the 1:14 phenothiazine-salt mixture were fed to the ewes and lambs in Lots 2 and 3. Group c, Lot 1, consumed 90 pounds of the 1:9 mixture. This represents a monthly consumption of 55 pounds per 100 head of sheep, or a phenothiazine consumption of the drug per animal was 0.55 gram daily.

POST-MORTEM EXAMINATIONS

Portions of the intestinal tracts of 169 lambs from the three lots and the 20 untreated ewes in Lot 1 were examined at the time of slaughter in the packing plant. The intestines were examined for the presence and the relative numbers of parasitic nodules while the abomasum was opened and inspected for the presence of stomach worms. All examinations were necessarily qualitative in nature due to the impossibility of slowing up slaughter plant operations. A summary of these results is given in Table 5.

It is seen from the above that the lambs in Lot 3, even though making satisfactory progress, nevertheless suffered from a degree of parasitic infestation. From the large numbers of nodules found on the intestines, the lambs in Lot 2 evidently were the most heavily parasitized of the groups examined. This group made the poorest gains and suffered the greatest mortality (Table 2).

The ewes and lambs in the control group, Lot 1, as would be expected, showed marked parasitism. It is of interest to note however, that this group, although untreated since

TABLE 5.—POST-MORTEM EXAMINATION OF 189 SHEEP

Lot	Number examined	Stomach worm infestation	Nodulation on intestines		
			Free	Moderate	Heavy
1a Ewes.....	20	Moderate...	0+	4+	16+
1a Lambs.....	18	Heavy.....	0	16	2
1b Lambs.....	15	Moderate...	0	9	6
1c Lambs.....	21	Light.....	0	16	5
2 Lambs.....	20	Light.....	0	0	20
3 Lambs.....	95	Light.....	6	83	6

TABLE 6.—AVERAGE WEIGHTS OF LAMBS AT MARKET TIME AND SELLING PRICE

Lot	No. in lot	Av. lot weight	No. marketed	Av. weight of lambs marketed	Selling price, cwt.
		lbs.		lbs.	
1a.....	19	52.6	18	52.6	\$11.25
1b.....	34	64.6	15	64.6	11.25
1c.....	96	61.0	21	74.0	11.25
2.....	150	56.0	20	75.0	11.25
3.....	157	71.6	95	76.5	14.25

January, suffered less damage from parasitism than the treated ewes and lambs in Lot 2. This apparent inconsistency is explained by the system of pasture rotation used (Table 1). Also of interest is the effect the drenching with phenothiazine, Lot 1b, and the drenching plus 1:9 phenothiazine-salt mixture, Lot 1c, had on the parasitic infestation. It may be reasonably assumed that the exposure to infestation in Lot 2, one of the groups upon 1:14 phenothiazine-salt mixture, was greater than that of Lot 1. Lot 2 suffered the greater damage. The table below

gives the weights of the various lots at marketing time, August 3.

Very few of the lambs in Lots 1 and 2 were fat enough to make satisfactory carcasses. The lambs in Lot 3 carried considerable finish.

1944 STUDY

The second phase of the work at the Dixon Springs Experiment Station with the phenothiazine-salt mixture was carried on in 1944. The object of this phase was to compare the efficiency of a 1:14 and a 1:9 phenothiazine-salt mixture as an anthelmintic for ovine nematodes.

TABLE 7.—CONSUMPTION OF PHENOTHIAZINE IN A 1:9 AND A 1:14 PHENOTHIAZINE-SALT MIXTURE

Period	Mixture	No. ewes	No. lambs	Consumption		
				Total mixture	Mixture per head	Phenothiazine per head per day
May 1-June 17.....	1:9	219	247	lbs. 538	lbs. 1.15	grams 1.23
May 1-June 18.....	1:14	185	202	489	1.26	0.83

PLAN

All sheep at the Station were included in the tests. They were all given individual doses of one ounce of phenothiazine in a drench the first week in January although they had been on a 1:14 phenothiazine-salt mixture since August, 1943. The phenothiazine-salt lick was then discontinued for the remainder of the winter period. All ewes and rams were given the one ounce drench again in April before going on pasture. The lambs were not treated. They were then put on pasture and both ewes and lambs had access to phenothiazine-salt mixtures as follows:

A lot of about 200 ewes and their lambs, Lot 1, was maintained on a 1:14 phenothiazine lick. A similar lot, Lot 2, was maintained on a 1:9 mixture. The remainder of the sheep at the Station were given access free-choice to both 1:14 and 1:9 phenothiazine-salt mixtures.

However, due to the severe drouth which began early in the summer, the pastures intended for Lots 1 and 2 became very poor, and the lots were combined and offered a free-choice of 1:14 and 1:9. Thus, the free-choice lot was the only one carried throughout the grazing period.

Lots 1 and 2 were carried on 1:9 and 1:14 phenothiazine-salt mix-

tures from May 1 until the middle of June, and the phenothiazine intake is shown in Table 7.

The average daily consumption of phenothiazine per sheep as shown in this table is considerably higher than many other investigators report. The amount consumed in the 1:9 mixture was 48 percent greater than that consumed in the 1:14 mixture. The total mix consumption on the other hand shows only a slight difference. Thus, the amount of phenothiazine consumed varied directly with the concentration of the mixture.

In the group having access to both the 1:9 and the 1:14 mixtures free-choice, 1,029 pounds of the 1:9 mixture were consumed and 1,511 pounds of the 1:14 mixture were consumed. Thus, the phenothiazine intake was about the same, 114 pounds and 108 pounds respectively. The salt consumption was increased about 53 percent when the phenothiazine-salt mixture was fed compared to a 1:9 mixture.

On July 7, 1944, the lambs were weaned from the ewes and put in dry lot for feeding. Their identity was kept according to treatment during the pasture period. When they were slaughtered examination was made of the intestinal tract of the lambs. The results are shown in Table 8.

TABLE 8.—RESULTS OF SLAUGHTER EXAMINATION

93 lambs fed 1:9 phenothiazine-salt mixture:		<i>Nodules on Caecum</i>	
<i>Stomach worms (Haemonchus)</i>		45 or 48.4% free	
64 or 68.8%	free	41 or 44.1%	1—5
29 or 31.2%	light	7 or 7.5%	6—25
		0	over 25
47 lambs fed 1:14 phenothiazine-salt mixture:		<i>Nodules on Caecum</i>	
<i>Stomach worms (Haemonchus)</i>		22 or 46.8% free	
33 or 70.2%	free	23 or 48.9%	1—5
14 or 29.8%	light	1 or 2.3%	6—25
		0	over 25

An additional 109 lambs which had access to both 1:9 and 1:14 free-choice were examined for nodules on the intestines. On 59 or 54.1% no nodules were found, 42 or 38.5% showed a light nodulation of 1 to 5 nodules; 4 or 3.7% a medium nodulation of 6 to 25 nodules; and, 4 or 3.7% showed over 25 nodules per lamb.

In general these infestations are very light compared to previous years. The dry lot feeding no doubt had some bearing on this light infestation.

DISCUSSION

It is known that the administration of small repeated doses of phenothiazine to sheep, such as would be received in a salt mixture, probably exerts its major anthelmintic action not through elimination of worms from the intestinal tract, but from a suppressed development of the eggs to the infective larval form. This is clearly indicated in the observations of Shorb and Habermann and of Shorb and Gordon. It appears, therefore, that the greatest benefits should be derived from the feeding of a phenothiazine-salt mixture when sheep, relatively free from internal parasites, are placed upon an uncontaminated pasture.

Such a plan for nematode control in sheep is made more practical by recent disclosures that the larvae of these parasites do not survive as long on pastures as has previously

been thought. In the climatic conditions prevailing in the vicinity of Washington, D. C., Sarles, and Kates have shown that pastures heavily contaminated with egg-containing feces during one grazing season become largely non-infective for parasite-free lambs the following spring and summer. Using laboratory procedures only and working with *Haemonchus contortus*, Shorb, also working near Washington, failed to demonstrate over-winter survival of the larvae.

In an earlier and even more revealing article, Shorb showed the survival period of the common nematode larvae parasitic for sheep to be limited on summer pastures even in the presence of abundant shade and moisture. One such contaminated pasture apparently became non-infective for parasite-free lambs in the short space of only two months. It is shown in the same paper that eggs passed during the winter and early spring do not develop to the infective larval stage. Feed-lot infestation of sheep, therefore, except during periods of unusually warm weather, may be of negligible importance.

From the observations reported in this paper and the other papers mentioned, a practical procedure for nematode control in sheep for the northern states might tentatively consist of individual, prepasture treatment of the ewes with the thera-

peutic dose of phenothiazine and their maintenance thereafter at pasture, together with the lambs, on a phenothiazine-salt mixture in the range of 1:9 to 1:14. It is believed a therapeutic dose of phenothiazine should also be given at the end of the pasture season. For best results, the animals should not at any time be maintained upon pasture occupied by parasitized untreated sheep during the preceding two months.

SUMMARY AND CONCLUSION

A lot of 348 sheep (191 ewes, 157 lambs) maintained continuously upon a 1:14 phenothiazine-salt mixture throughout the dry lot and grazing seasons and handled as an isolated unit without contact, direct or indirect, with heavily parasitized, untreated sheep, made a total gain of 8,670 pounds from May 27 to August 3 (10 weeks). One animal died. Their progress was considered satisfactory. Post-mortem examinations of 95 lambs from this group showed internal parasites to be present. The phenothiazine-salt medication, therefore, markedly suppressed but did not eliminate nematode infestation.

A second lot of 350 sheep (187 ewes, 163 lambs) treated individually with phenothiazine at the beginning of the grazing season and maintained thereafter upon the same phenothiazine-salt mixture but placed upon a pasture occupied the previous month by parasitized, untreated sheep, made a total gain of only 10 pounds in the same period. Fourteen of these animals died and three others were sacrificed because of debility. Losses in this group undoubtedly would have been much larger if they had not been treated individually with phenothiazine and placed on clean pasture. Post-mortem examination of 20 representative lambs indicated this group to be heavily parasitized.

A third lot of 359 sheep (197 ewes, 162 lambs) which was not treated after the treatment given at the end of the previous pasture season developed marked symptoms of parasitism at the end of the second month on pasture. It was found they infested the pasture on which Lot 2 was placed the second month of the pasture season. Division of this lot and treatment with a therapeutic dose of phenothiazine of all but 20 ewes and 20 lambs in this lot caused a marked recovery and increase in the gains. Post-mortem examinations, however, showed this lot to be rather heavily parasitized.

The 1944 phase of the work compared the efficiency of a 1:9 and 1:14 phenothiazine-salt mixture in controlling ovine nematodes. The lot receiving 1:9 consumed about 48% more phenothiazine over a 48-day-period than the lot receiving the 1:14 mixture. When offered both mixtures free-choice the amount of phenothiazine consumed was about the same, 114 pounds in the 1:9 mixture and 108 pounds in the 1:14 mixture. The total consumption of the mix, however, when offered free-choice was 53% greater in the case of the 1:14 phenothiazine-salt mixture.

From the observations made during 1943 and 1944 at the Dixon Springs Experiment Station it is concluded that a 1:9 or a 1:14 phenothiazine-salt mixture markedly protected the sheep from excessive parasitism when the animals, relatively free from internal parasites at the beginning of the trial were maintained without contacting, directly or indirectly, other sheep. The same phenothiazine-salt mixture did not, however, protect sheep when they were placed upon a pasture recently contaminated by parasitized, untreated sheep.

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