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Some Observations on the Effect of Drenching Young Sheep with Phenothiazine

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SINCE 1938 when the anthelmintic properties of phenothiazine were first demonstrated, many papers have appeared on various aspects of its use. The effects of the drug on the parasites have been studied in considerable detail but few authors have paid much attention to body weight changes after drenching.

The action of the drug on the parasites has been studied in a number of ways. The more critical studies have been made on penned sheep carrying pure infestations with a single species of parasite. In these and the more numerous field experiments, some of the following techniques have been employed.

Where large numbers of animals are available, it is possible to compare the number of worms that remain in the treated animals with those found in similar untreated controls. The value of this method is severely limited by the wide variations that are found within groups of similar animals, though in some instances, experiments of this kind have yielded clear-cut results.

In the case of some of the larger parasites, especially those of the large intestine, the value of the anthelmintic can be measured by collecting all the faeces passed for several days after dosing, counting the worms eliminated and relating these to the number remaining after the test animal is killed.

The third method is the one most frequently used since it avoids the necessity of slaughtering the experimental animals; it consists of a comparison of the number of worm eggs passed in the faeces before and after treatment. Eggs per gram of faeces are usually estimated rather than the more satisfactory eggs per day, as the latter figure requires the collection of total daily output of faeces, a procedure which is very laborious when large numbers of animals are used. The most serious shortcomings of the method stem from the fact that there are in sheep about a dozen different species of parasite, the eggs of which can be differentiated only with difficulty. Each species possesses its own rather variable capacity for egg production and further the susceptibility to drugs varies between species and even within the same species at different stages of development. A further complication is introduced by the fact that the worms that are not expelled by the treatment may show a temporary depression of egg production over a period of 2-3 weeks and this necessitates a rather lengthy period of post-treatment observation.

It is clear that the response to drenching will vary directly with the level of the infestation, the pathogenicity of the parasite concerned and its susceptibility to the drug. The plane of nutrition and the thrift of the animal will undoubtedly also have some effect.

The purpose of the present paper is to bring together the published data on the body weight response to drenching and to present the results of further experiments carried out in New Zealand under several sets of conditions, in order to illustrate the range of effects that can be expected. No attempt will be made to assess the problem from a national point of view as the cover has been quite inadequate for this purpose. It is in fact true that many of the observations were made in areas or on properties where a definite problem existed and

sometimes the most backward animals were selected for the experiments. For this reason therefore the position as stated would tend to be exaggerated rather than otherwise.

The results presented will be confined to comparisons between drenched and undrenched animals that have been run together in the same paddocks. This, it is considered, is the only valid comparison that can be made unless paddock differences are eliminated by an elaborate and replicated experimental design. There is, of course, the criticism that the drenched animals are exposed to reinfection by running with the undrenched controls but this has been unavoidable. Only experiments with animals under 12 months of age are considered.

Overseas results cannot be applied directly to New Zealand because the environmental conditions, the range of parasites and their relative abundance may be different. A striking example of this is seen in the nodule worm (*Oesophagostomum columbianum*) which though virtually absent from New Zealand, is one of the most important parasites in America, Australia and South Africa, and it is in these countries that much of the work on phenothiazine has been carried out.

PUBLISHED DATA FROM OVERSEAS.

In the first reports on phenothiazine from Great Britain, a few data on body weight changes were given. In general they were small, 1-4lb. but in one experiment quoted by Taylor and Sanderson (1940), a 12lb. difference was recorded over a period of six weeks.

Peters, Leiper and Clapham (1941) carried out an experiment in which 18 lambs were used and 2 dose rates, 0.3 and 0.15 g. per kilo, and two different wetting agents, were compared with undosed controls. The conclusion reached was that drenching had no effect on the weight of the lambs 3 weeks after drenching. In another paper, Leiper, Peters and Clapham (1941), 12 lambs were used to compare drenching with liquid and with tablets, but using a dose rate of 1.0 g. per kilo, with undrenched controls. (This dose rate is about twice that usually recommended in New Zealand). In this experiment there was some evidence that the tablets did not break up readily and the conclusion reached from an analysis of the body weight data, was that there was no difference between the weights of the lambs dosed with liquid and the controls but those dosed with the tablets suffered a significant set-back.

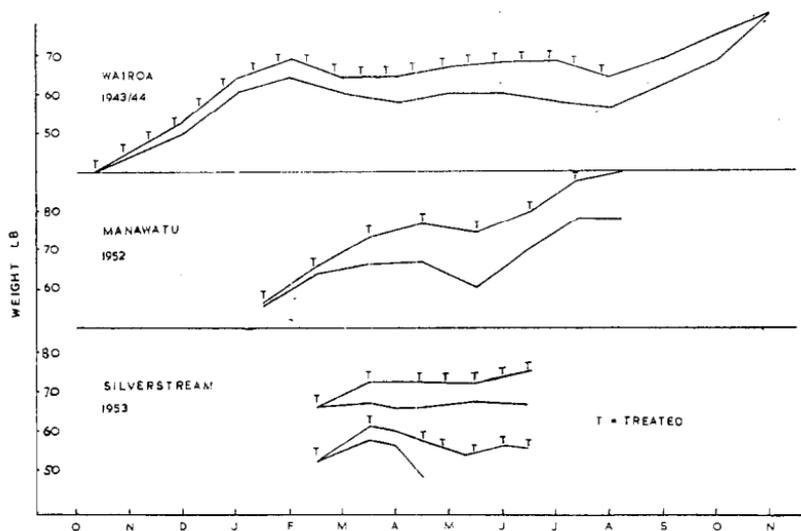
In a series of trials carried out in Great Britain, in which four research institutions co-operated, there were 6 flocks each of 28 animals running on pasture. Groups from each flock were dosed with 0, 5, 10, 20, 30, 40, and 50 g. of phenothiazine, both as tablets and as a drench. The pooled results showed that over 15 weeks the liveweight increased rather regularly with the dosage from 20 to 50 g. Doses of 5 and 10 g. gave no increase in weight though their effect in depressing egg count was the greatest relatively. A dose of 20 g. gave an increase of 3.6lb. and a dose of 50 g. an increase of 5.5lb. over the untreated controls.

PUBLISHED DATA FROM NEW ZEALAND.

Ewer and Sinclair (1951) (1952) at Kirwee showed that responses to drenching were small and seen mainly in those years when the late spring and summer months were wetter than normal. Comparisons were made between drenched and undrenched groups of unweaned lambs, lambs on fattening crops and wintering hoggets, under various conditions of nutrition and management. Unweaned lambs showed no response in any of the three years, when drenching with phenothiazine was done. Weaned lambs, fattening on crops for 2-3 months from January, showed a significant weight increase in 2 out of the 4 seasons when phenothiazine was used. The liveweight increases in those years were 6lb. in 1943 and 4lb. in 1945, over the controls. In the winter-fed hoggets over the 4 months, May to September, a significant response occurred only in 2 out of 5 seasons when the liveweight differences were 4lb. in 1942 and 6lb. in 1943. In 1946 a different drenching pro-

gramme was carried out which included single and repeated doses of 20 and 40 g. but that season the level of infestation was low and no differences could be detected. It is considered that the responses at Kirwee might be smaller than in some other districts of New Zealand because of the complete absence of *Haemonchus*, a parasite which is recognised as being one of the most pathogenic and the one which is most readily controlled by treatment. There was however a definite response in one season in a severe autumn outbreak of *Trichostrongylosis*. On this occasion animals drenched twice at 3 weekly intervals were, after 6 weeks, 5-6lb. heavier than the controls, a result that was duplicated on both high and low planes of nutrition.

Tetley in 1950 reported a trial in the Manawatu in which phenothiazine was given at monthly intervals from weaning in December until mid-April. At the end of the trial there was only a 3lb. liveweight difference between the treated and control animals. More recently Whitten and Macfarlane (1953) reported a field drenching trial that was carried out on improved hill country in the Manawatu under a system of rotational grazing. The paddocks were grazed for 7 days and rested for 3-4 weeks before being grazed again. In this instance, groups treated at monthly intervals with phenothiazine or with bluestone and nicotine sulphate were compared with untreated controls. In this trial the greatest differences occurred in May when the bluestone and nicotine sulphate group were 5.8lb. and the phenothiazine group were 11.6lb. heavier than the controls. In this experiment it was clear that fairly heavy infestations could build up under this system of rotational grazing but even the untreated group showed a spontaneous loss of infestation during the late autumn months. The curve of the egg counts suggested also that a similar response might have been obtained even if drenching had been confined to the months of March, April and May. (See Fig. 1).



UNPUBLISHED DATA FROM NEW ZEALAND.

At Wairoa in 1943, unthrifty hoggets were dosed at 3 weekly intervals from July to October and at the end of this time a 4lb. liveweight difference between treated and control groups was recorded. It was thought that the peak of the infestation was probably passed by the time the treatment was begun so the following year, in order to obtain a maximal response, a further trial was conducted. In 1943-44, lambs were given one and a half times the recommended dose every 14

days from the age of 6 weeks until they were 12 months old at the end of the following winter. The greatest bodyweight difference was 9lb. in May and thereafter the two curves converged until the difference disappeared entirely after the spring growth of feed had become established. (See Fig. 1).

Further trials were carried out at Manutuke comparing the response to drenching on short and long pasture. In 1947 the animals were dosed every 3 weeks from April until August. At this time the drenched group on the short feed was 14.5lb. heavier than the controls while on the long feed the difference was only 3.7lb. in favour of the drenched group.

In an experiment carried out at Five Rivers in Southland in the summer of 1946-47 by Mr. C. V. Dayus, there were 2 groups of 30 lambs. The drenched group were given 15 grammes of phenothiazine every 2 weeks from early December until the end of February. No significant differences could be detected in the weight gains over the experimental period.

A further experiment was carried out on some very unthrifty hoggets on the Arohena Block near Te Awamutu at the end of August, 1948. A 20% mortality had been experienced in this flock over the autumn and winter months. Three groups of 50 hoggets were used, one was given a single dose of 15 g. phenothiazine, one was given 30 g. phenothiazine, and one group was left as controls. The mean weight of the hoggets at the time of treatment was 50lb. and 5 weeks later when the final weighing was done, there was no significant difference between the groups. Subsequent investigation showed that the lambs on this property were suffering from a cobalt deficiency.

In 1948 Miss Quin of Elliott's Rural Laboratories, carried out a series of trials on 27 properties located in the Waikato, Manawatu, Hawkes Bay, Marlborough, and Canterbury. On each property a single dose of phenothiazine was used after weaning on a group of 40 lambs. The liveweight changes over the next 6 weeks were compared with those of similar groups of controls. On no property did the liveweight difference reach significant levels.

Following the results obtained in 1952 (Whitten and Macfarlane) a trial was conducted on unimproved hill country in the Shannon district where lambs set-grazed a hill paddock continuously. On this occasion there were 5 groups of 50 lambs, and liveweight gains (January to May) were as follows:—

1. Undrenched controls	0.8 lb.
2. Monthly bluestone & nicotine sulphate January to June	2.0 lb.
3. Monthly phenothiazine, March to May	4.8 lb.
4. Monthly phenothiazine, March to May	4.5 lb.
5. Monthly drenching January to June, alternating phenothiazine and bluestone/nicotine sulphate	4.6 lb.

In this trial differences were small but again they were greatest in May when the bluestone/nicotine group fell half-way between the controls and the other 3 groups which were all 4lb. heavier than the untreated sheep. The conclusion reached was that the parasite problem here was a relatively small one and that monthly drenching with phenothiazine was more than was necessary. This is supported by the fact that alternation with an inferior drug or restricting its use to March, April and May did not lessen the response.

Over the past season also, further data were obtained at Silverstream, near Wallaceville, on the effect of repeated drenching under rather severe outbreak conditions. Two groups of 34 lambs were selected at weaning, one group of backward lambs (mean body weight 52lb.) were set-grazed on a low plane of nutrition. The other group were rather better lambs (mean weight 64lb.) and were grazed on a rather higher plane of nutrition. Half of each group was drenched with phenothiazine at 2-3 weekly intervals from February until July.

Differences of 8-9lb. were recorded on both planes of nutrition

between drenched and undrenched animals. The significance of this result is reduced by the fairly heavy mortality that occurred especially in the low plane group and resulted in a serious reduction in group size. This mortality, though regrettable in some ways, did provide definite evidence of treatment differences. Phenothiazine reduced the mortality in both low plane and high plane groups (See Fig 1, Table 1).

TABLE I: Total Deaths (Silverstream). February-June.

	Drenched	Controls	Totals
High Plane	0/17	7/17	7/34
Low Plane	3/17	11/17	14/34
Totals	3/34	18/34	21/68

In another trial at Wallaceville run concurrently under similar conditions to the high plane group the body weight differences between 20 untreated controls and 20 lambs that were drenched every 3 weeks from January until July, were only 2.5lb., a difference which in this instance did not reach the 5% level of significance. The mortality in this experiment over the experimental period was 3 in the drenched group and 7 in the controls. The difference in mortality between the two groups was not significant.

In the present season, two trials have been carried out by the author in Canterbury, where groups of 30 lambs, with a mean initial weight of 54 and 38lb., were given a single dose of 15g. of phenothiazine as tablets in late November. There were no differences in their weight after 4 and 8 weeks respectively.

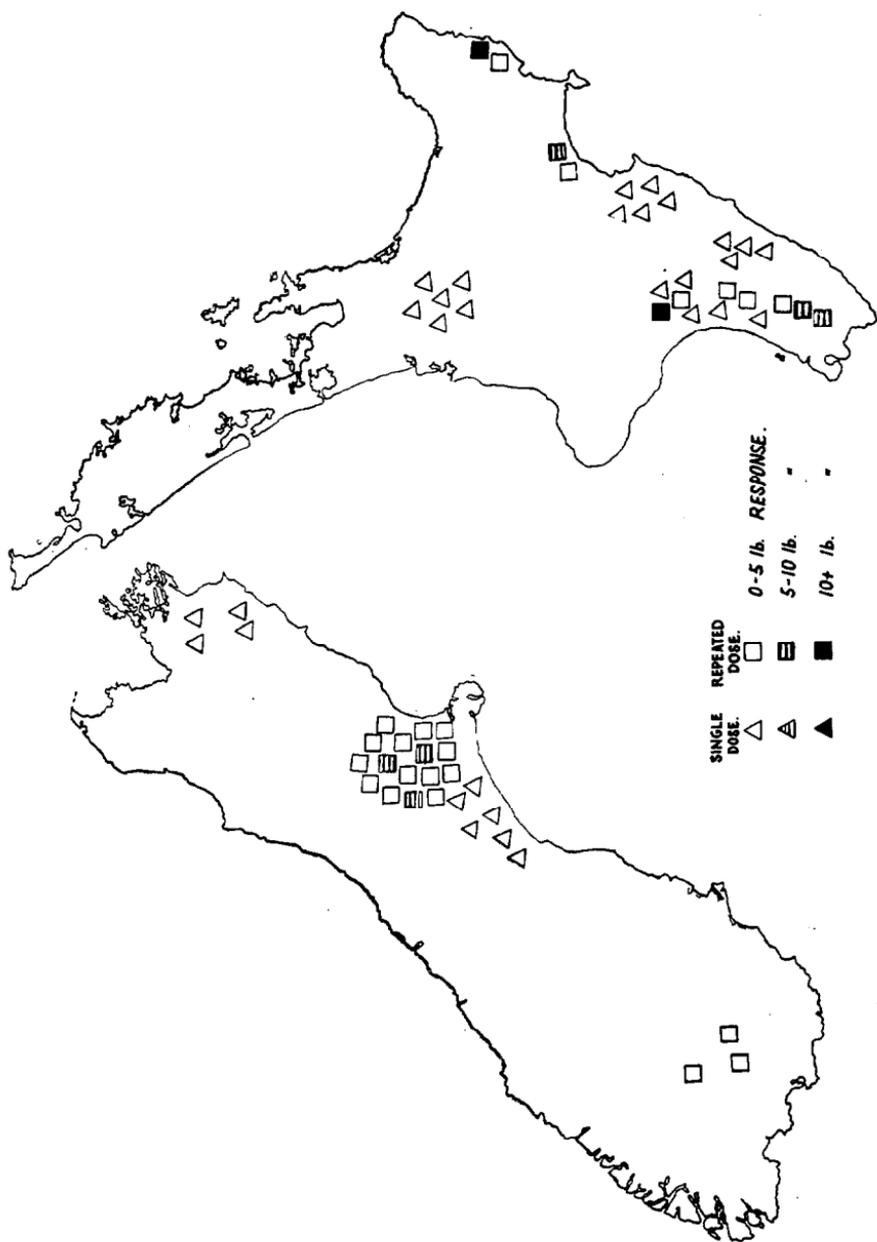
Similar trials were carried out on two properties in Southland, by Andrews and Anderson. In their trials groups of 26 and 22 animals with a mean initial weight of 43 and 48lb., were dosed at 14 day intervals with 20g. of liquid phenothiazine from mid-November until the end of December. No difference in weight between drenched and control animals was noted.

DISCUSSION

From the data presented it is clear that a spectacular body weight response to drenching phenothiazine to young sheep, is witnessed only infrequently. There are several possible explanations for this. It may be that parasites, at the levels commonly encountered in the field, are not quite as pathogenic as has been considered in the past, especially when the plane of nutrition is high. On the other hand, the damage done by the worm may require more than the simple removal of the parasite for rapid recovery to take place. Environmental factors can be responsible for fluctuations in the worm burden of sheep, that may equal or exceed those that can be produced by treatment. Little is known of the mechanism by which these occur but immunity and "self cure" play a part. It is at present difficult to predict such fluctuations and many drenching experiments are difficult to interpret when fluctuations of this kind are observed in the control groups. Finally, poor thrift in young sheep may be primarily parasitic in relatively few instances and the differential diagnosis of wasting diseases at present lacks the precision necessary for advice on the control to be satisfactory.

CONCLUSION.

It is well recognised that New Zealand is pre-eminent as a stock raising country because of the low production costs associated with grassland farming. If production costs are to be kept low, it is necessary to watch carefully for avoidable increases in such costs. The economic use of drugs is but one of the small things that must be debited against our primary industry. At the present time we are importing annually about £85,000 worth of phenothiazine and to this sum must be added the cost of processing and distribution and a margin of profit for those that handle it. Phenothiazine is a costly drug to use but it is only one of those on the market for use against sheep



parasites. There are those, of course, who consider drenching as an insurance against loss and are prepared to carry on knowing that in most seasons their effort will bear no fruit but that the cost might be recovered in the occasional bad season when drenching may result in avoiding more serious losses.

In past meetings of this society, we have heard of the difficulties of eliminating the lag period between the research worker and the application of his findings. Here is one instance, and I am sure there are many others, where wide-scale application has taken place before the real value of the measure has been assessed.

SUMMARY

The available published and unpublished data on the body weight responses of young sheep, to drenching with phenothiazine, have been brought together. The trials covered most of the main sheep raising districts of New Zealand and in all, over 5000 animals were involved. In some trials single doses and in others repeated doses were given.

Comparisons made in New Zealand with drenched and control animals grazing together, showed a response of 5-10lb. in seven and a response of over 10lb. in two out of sixty trials. Drenching in one experiment carried out under severe outbreak conditions, resulted in a marked reduction in mortality over the autumn and winter months.

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Discussion

Dr. FILMER: Only in the Wairoa trial was the trial continued into the following spring, and here the difference between groups disappeared. Is it likely that this would have occurred in the other trials?

Mr. WHITTEN: The difference at Wairoa was 9lb., one of the biggest, and as the gap closed up here it is almost certain to do so in the other trials.

Mr. SINCLAIR: At Kirwee, body weight differences from a variety of causes in the winter disappeared in the following spring.

Mr. ANDREWS: Is malnutrition a predisposing cause of parasitism? In one trial we appeared to get a marked weight response to phenothiazine in a group of lambs suffering from cobalt deficiency. We had no controls but the response was quite marked.

Mr. WHITTEN: Malnutrition has an effect both on susceptibility to infestation and on the subsequent development of resistance.