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Anthelmintics for Dictyocaulus filaria in Sheep (*)

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SUMMARY. — Cyanacethydrazide, methyridine, diethylcarbamazine and tetramisole were compared in sheep naturally infested with *Dictyocaulus filaria* in four controlled experiments. Worm burdens were assessed by counts of *D. filaria* larvae recovered by a Baermann technique from 2-g. samples of faeces. Experimental groups comprised seven to 10 sheep, randomised on the mean of two counts before treatment, and on bodyweight. Results were assessed by reduction in counts of larvae done several times during 18 to 30 days after treatment. Dose rates recommended by the manufacturers were used. Methyridine, given once by mouth, and diethylcarbamazine, given by intramuscular injection on three successive days, were equally effective, and superior to cyanacethydrazide given once by subcutaneous injection. A single dose of diethylcarbamazine was much less effective than three doses, even when the amount injected at one time was increased to equal the total amount recommended for three days. Tetramisole, given once by mouth, was more effective against *D. filaria* than three daily doses of diethylcarbamazine, and was also highly effective against gastro-intestinal nematodes.

Introduction

In Iran, many mortolities in sheep and goats during the winter months are ascribed by field veterinarians to infestation with lungworms (Reports of the Veterinary Department, Ministry of Agriculture, Iran, 1961-62). In studies initiated by the Helminthology, Section of the Near East Animal Health Institute, it has been noted that *Dictyocaulus filaria* is the most prevalent of the lungworms commonly infesting sheep in Iran (Table I).

Dictyocaulus viviparus is widely recognised as the cause of serious losses in calves, but differing views are held on the importance of *Dictyocaulus filaria* in sheep. In several sheep-raising areas lungworms, although quite prevalent, are regarded to be of little importance, experience having shown that, if there is adequate control of gastro-intestinal nematodes and an adequate plane of nutrition, sheep develop sufficient acquired immunity to overcome *D. filaria* infestations without the need of specific treat-

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TABLE I

INCIDENCE OF LUNGWORMS IN SHEEP AND GOATS IN IRAN DETERMINED BY RANDOM EXAMINATION OF FAECES AND *Post-mortem* EXAMINATIONS

	Sheep		Goats	
	Faeces	*Post mortem*	Faeces	*Post mortem*
No. of animals	1,712	99	297	19
Per cent. positive for				
Dictyocaulus	41	56	21	42
Muellerius	16	9	22	5
Protostrongylus	26	6	16	16

ment. However, Goldberg (1952) and Michel (1954) have shown that infestations of *D. filaria* can depress growth and terminate in death of lambs. Infestations of *D. filaria* in sheep are regarded seriously in Iran. Lambs born in January to February do not often develop serious infestations of gastro-intestinal nematodes until the following winter, when they are neary one year old. Infestations with *D. filaria* may precede this in late autumn and early winter when nutritional levels are low, and specific treatment for lungworms may be needed to prevent losses.

The newly available anthelmintics that have proved to be effective against *D. filaria* in sheep include cynancethydrazide (Walley, 1957), diethylcarbamazine (Ozerskaya, 1955, 1959, cited by Gibson, 1962), methyridine (Walley, 1961) and tetramisole (Thienpont *et al.*, 1962), but direct comparisons of these anthelmintics under the same experimental conditions have not been reported.

This paper presents results of four controlled experiments in Iran, in which cyanacethydrazide, diethylcarbamazine, methyridine and tetramisole were compared for control of *D. filaria* in sheep.

Materials and Methods

The sheep used in each of four experiments were female lambs about 10 months old, naturally infested with *D. filaria*. Lungworm larval counts and gastrointestinal nematode egg counts were done, using 2-g. samples of fresh faeces, at least twice prior to randomisation into experimental groups. The sheep used in the first three experiments were very lightly infested with gastro-intestinal worms and were all treated with 50 mg. per kg. thiabendazole before starting the experiments. In the fourth experiment, the mean gastro-intestinal worm egg counts were about 1,000 eggs per g. of faeces, and larval culture and differentiation showed the infestations were chiefly *Trichostrongylus* spp. and *Ostertagia* spp. These sheep were not treated before the exepriment.

Experimental groups were randomised on the basis of lungworm larval counts

(D. filaria) and bodyweights, and, in the fourth experiment, on gastro-intestinal worm egg counts. The sheep were handfed in stables throughout each experiment.

The anthelmintics compared in these experiments were diethylcarbamazine,* cyanacethydrazide,† methyridine‡ and tetramisole.§ In each experiment the doses were calculated, at the dose rates shown under «Experiments,» according to the mean bodyweight of the experimental groups.

Diethylcarbamazine was administered by intramuscular injection, cyanacethydrazide by subcutaneous injection, methyridine by mouth and tetramisole by mouth.

The results were assessed by examination of faecal samples because the sheep used were not available for slaughter.

Experiments

Ideally, all of the anthelmintics should have been compared in one experiment, but lack of a sufficient numbre of suitably infested animals at one time prevented this, leading to a series of experiments as suitable sheep became available.

Experiment 1

Three groups, each of seven sheep, were used. Group treatments were:—

a. Diethylcarbamazine, three daily doses of 20 mg. per kg.
b. Cyanacethydraizde, single dose of 20 mg. per kg.
c. No treatment.

Results were assessed by counts of *D. flaria* larvae in faecal samples done 10 times in 30 days after treatment.

Experiment 2

Four groups each of 10 sheep were used. Group treatments were:—

a. Diethylcarbamazine, three daily doses of 20 mg. per kg.
b. Diethylcarbamazine, single dose of 20 mg. per kg.
c. Cyanacethydrazide, single dose of 20 mg. per kg.
d. No treatment.

Results were assessed by counts done eight times in 30 days after treatment.

Experiment 3

Four groups each of eight sheep were used. Group treatments were:—

a. Diethylcarbamazine, three daily doses of 20 mg. per kg.
b. Diethylcarbamazine, single dose of 60 mg. per kg.
c. Methyridine, single dose of 200 mg. per kg.
d. No treatment.

Results were assessed by five counts in 29 days after treatment.

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* "Franocid": Trade mark of Burroughs Wellcome and Co.

† "Dictycide"; ‡"Mintic"; §"Nilverm": Trade marks of Imperial Chemical Industries Limited.

Experiment 4

Three groups each of nine sheep were used. Group treatments were:-

a. Dietylcarbamazine, three daily doses of 20 mg. per kg.

b. Tetramisole, one dose of 15 mg. per kg.

c. No treatment.

Results were assessd by nine counts in 18 days after treatment. This experiment was terminated at 18 days when one of the controls died.

Results

The results of the four experiments are shown in Fig. 1 to 4 respectively.

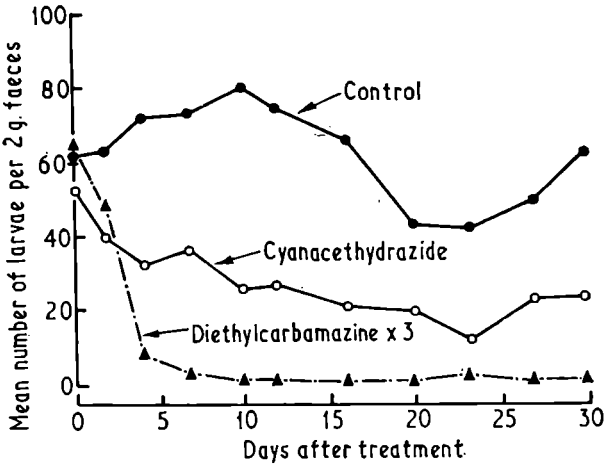


FIG. 1. The effect of 20 mg. per kg. cyanacethydrazide and three daily injections of 20 mg. per kg. diethylcarbamazine on *D. filaria* in sheep.

In *Experiment 1* counts of *D. filaria* larvae in the control group showed an initial rise, followed by a fall, and a return to near pre-treatment levels at 30 days. Cyanacethydrazide caused a decline during 23 days after treatment and therafter counts for this group rose, as in the control group. Treatment with three daily doses of diethylcarbamazine reduced counts to near zero within seven days and thereafter counts remained at or near zero.

In *Experiment 2* counts in the control group showed a general decline throughout the 30 days of the experiment. Cyanacethydrazide caused a reduction in the first eight days after treatment, but thereafter counts in this group tended to parallel counts in the control group. Three daily doses of diethylcarbamazine produced a much greater and sustained reduction in counts, similar to the result obtained in Experiment 1. A single dose of diethylcarbamazine gave a result comparable to cyanacethydrazide during the first three weeks, and thereafter counts declined, to give a better end-result than cyanacethydrazide.

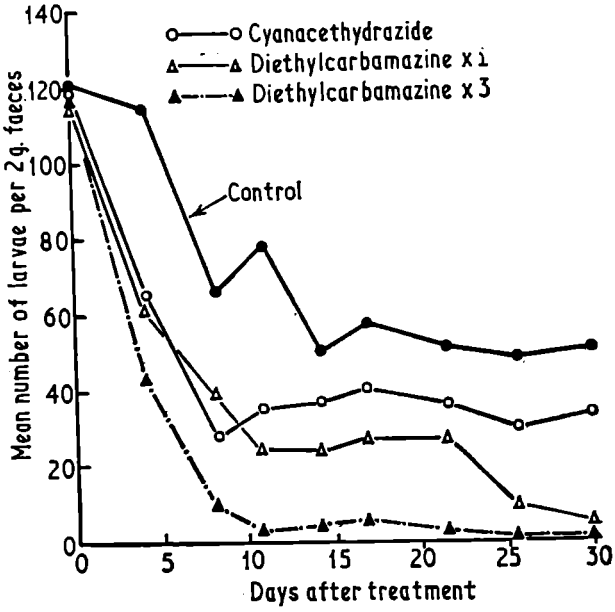


FIG. 2. — The effect of 20 m. per kg. cyanacethydrazide. one injection of 20 mg. per kg. diethylcarbamazine and three daily injections of 20 mg. per kg. diethylcarbamazine on *D. filaria* in sheep.

In *Experiment 3* counts in the control group declined during the experiment to about half the initial level, as in Experiment 2. Treatment with three daily doses of 20 mg. per kg. diethylcarbamazine again reduced counts to near zero within a week, followed by a temporary rise in counts between nine and 15 days after treatment. Increasing the single dose to 60 mg. per kg. diethylcarbamazine did not increase the efficiency shown by a single dose of 20 mg. per kg. in Experiment 2. A single dose of methyridine effected a reduction in counts comparable to that obtained with three daily doses of diethylcarbamazine.

In *Experiment 4* the counts of *D. filaria* larvae in the control group showed an overall rise throughout the 18 days of the experiment. Treatment with three daily doses of 20 mg. per kg. diethylcarbamazine caused a substantial reduction in counts during the first week, followed by a rise comparable to the rise in the control group. Treatment with tetramisole caused a rapid reduction of counts to near zero within two days and thereafter counts remained at or near zero.

The results of gastro-intestinal worm egg counts in this experiment are shown in Fig. 5. In the control group there was an overall rise in counts during the experiment. Treatment with diethylcarbamazine had no appreciable effect. Tetramisole caused a reduction of counts to zero within two days and thereafter the worm egg counts remained at or near zero.

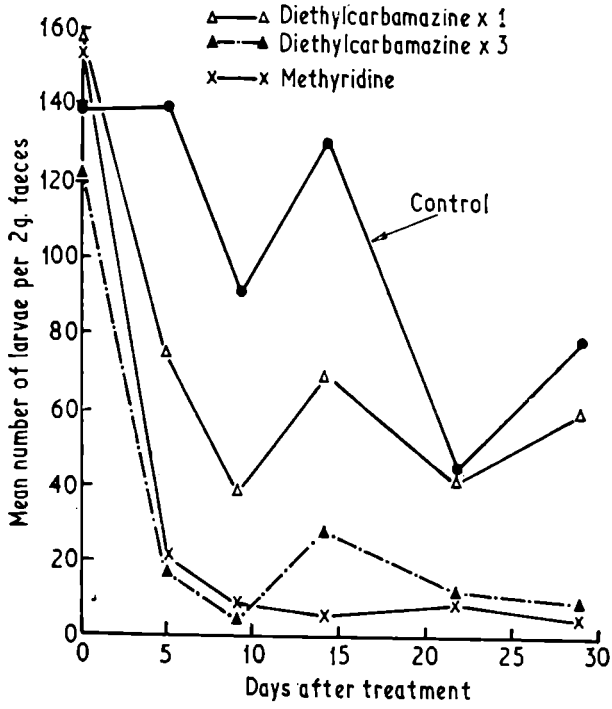


FIG. 3. — The effect of one injection of 60 mg. per kg. diethylcarbamazine, three daily injections of 20 mg. per kg. diethylcarbamazine and one dose of 200 mg. per kg. methyridine on *D. filaria* in sheep.

Discussion

Individual results in this series of experiments confirm previous reports of high efficiency against *D. filaria* in sheep in respect to diethylcarbamazine given by three daily injections, methyridine given once by mouth, and tetramisole given once by mouth. However, it is considered that in choosing between anthelmintics, conclusions based on results of direct comparisons made in the same experiment are more valid than conclusions drawn from results of different experiments.

From results of Experiments 1 and 2 (Figs. 1 and 2) it was concluded that three daily doses of diethylcarbamazine were more effective than a single dose of cyanacethydrazide.

From results of Experiments 2 and 3 (Fig. 2 and 3) it was concluded that a single dose of diethylcarbamazine was less effective than three daily doses, even when the total dose normally given over three days was given at once. The superiority of three daily doses of diethylcarbamazine over a single dose, and over cyanacethydrazide, was associated with a more uniform effect in individual animals within the experimental groups.

In Experiment 3 (Fig. 3) methyridine was as effective as three daily doses of diethylcarbamazine.

diethylcarbamazine.

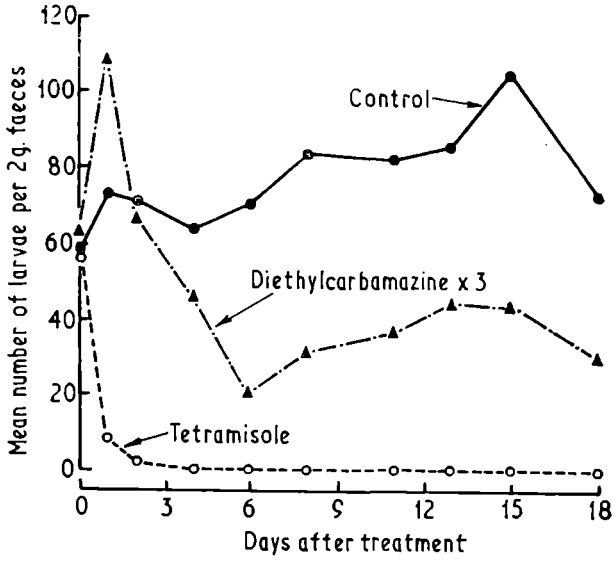


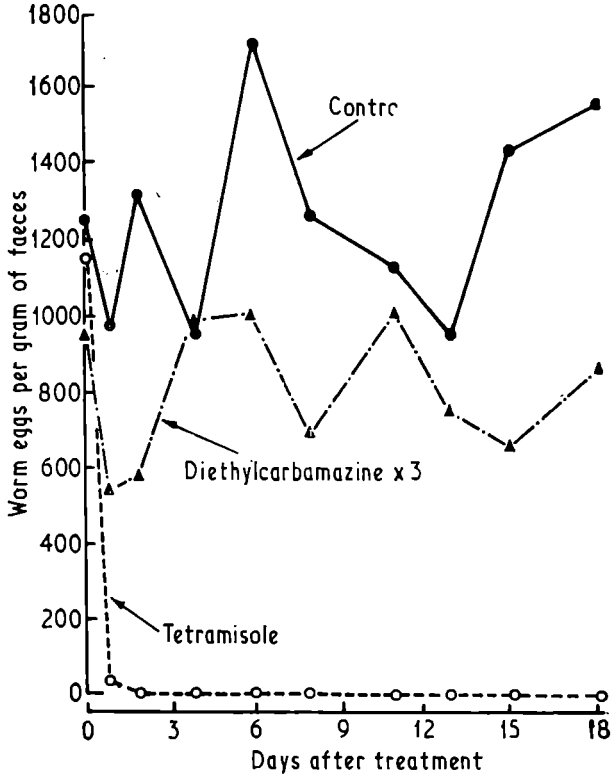
FIG. 4. — The effect of three daily injections of 20 mg. per kg. diethylcarbamazine and one dose of 15 mg. per kg. tetramisole on *D. filaria* in sheep.

Tetramisole did not become available until after Experiment 3 was completed. In Experiment 4 it was compared with diethylcarbamazine in preference to methyridine, because results for three daily doses of diethylcarbamazine had been very uniform in the three previous experiments. In Experiment 4 (Fig. 4), tetramisole was decidedly more efficient against *D. filaria* than three daily doses of diethylcarbamazine.

Tetramisole was highly efficient against *D. filaria* (Fig. 4) and against the gastro-intestinal worms (Fig. 5) thus confirming results previously published by Walley (1966) and Forsyth (1966).

No direct comparison was made between methyridine and tetramisole in the present experiments.

The relatively lower efficiency of three daily injections of diethylcarbamazine in Experiment 4, compared with results of the first three experiments, is difficult to explain. The relative «failure» was apparent throughout the group. It probably relates to the different conditions between experiments and might be regarded as a parallel to the relative failures sometimes experienced with anthelmintics in field use. There were major differences in conditions between experiments in the present series. In the first three experiments the counts of *D. filaria* larvae in the control groups showed an overall decline during the first 20 days of the experiments, indicating that the worm populations were mainly adult at the times of treatment. Also the sheep were virtually free of gastro-intestinal worms. In Experiment 4 the overall rise in counts in the control group indicated a high proportion of immature *D .filaria* in the sheep at the time of



mg. per kg. diethylcarbamazine and one dose of 15 mg. per kg. tetramisole on gastro-intestinal nematodes of sheep.

FIG. 5. — The effect of three daily injections of 20

treatment, and these sheep carried significant burdens of gastro-intestinal worms concurrently. These differences in experimental conditions may have adversely affected the action of diethylcarbamazine in Experiment 4. Nevertheless, tetramisole was highly effective against *D. filaria* and against the gastro-intestinal worms under the same conditions.

Diethylcarbamazine is known to be more effective against immature *D. viviparus* than against the adult worms in cattle. Results of the present series of experiments suggest that this may not apply to *D. filaria* in sheep.

Further work on direct comparison of the efficiency of anthelmintics available for use against *D. filaria* in sheep is needed before firm conclusions can be drawn. The eventual choice of anthelmintic will depend, not only on the comparative efficiency, but also on other factors including cost, ease of use, safety and presence of gastro-intestinal worms under the conditions of intended use.

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