THE TREATMENT OF ASCARIASIS IN DOGS WITH 1-DIETHYLCARBAMYL-4-METHYLPIPERAZINE HYDROCHLORIDE*

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It has been shown recently that 1-diethylcarbamyl-4-methylpiperazine hydrochloride produces marked effects against *Litomosoides carinii* in cotton rats (Hewitt, White, Wallace, Stewart, Kushner, and SubbaRow, 1947) and (Hewitt, Kushner, Stewart, White, Wallace, and SubbaRow, 1947), *Dirofilaria immitis* in dogs (Hewitt, Kushner, Stewart, White, Wallace, and SubbaRow, 1947), adult *Trichinella spiralis* in white rats (Oliver-Gonzalez and Hewitt, 1947), and *Wuchereria bancrofti* in man (Santiago-Stevenson, Oliver-Gonzalez, and Hewitt, 1947). The wide range of anti-helminthic activity exhibited by this compound has led to tests against other parasitic nematodes in animals and man. Data from fifty-one dogs infected with ascarids and treated with 1-diethylcarbamyl-4-methylpiperazine form the subject of this report.

MATERALS AND METHODS

Dogs from eight weeks to three or more years of age were used. No attempt was made to estimate quantitatively the number of ascarid eggs present before treatment. The compound was administered in capsules, in the various doses indicated in Table 1. Fasting prior to treatment or purgation following treatment were not

TABLE 1.—*Summary data from 51 dogs treated with 1-diethylcarbamyl-4-methylpiperazine hydrochloride for ascariasis*

Dose (mg. per kg.)	No. of dogs used	Total no. of ascarids passed	Ascarids found at autopsy (intestine)	Efficiency of treatment (per cent)
12.5 Oral 2 doses	6	52	7	88.2
25 Oral 1 dose	7	25	13	65.7
25 Oral 2 doses	7	62	None	100.0
30 Oral 1 dose	6	11	1	91.7
40 Oral 1 dose	7	56	18	75.7
50 Oral 1 dose	10	72	1	98.7
50 Oral 2 doses	4	33	None	100.0
50 I.P. 2 doses	4	9 (plus)	None	100.0

Total No. of dogs treated—51.
Total No. of ascarids passed—320 (plus).
Total No. of ascarids recovered from intestine (all dosages)—40.

practiced. Following dosage, the dogs were isolated in individual cages, and whenever possible all stool passages were examined for the presence of worms for at least two or three consecutive days. Examinations for eggs were made within two to thirteen days after treatment, and necropsies were performed within the same period. The entire intestine was examined for the presence of worms.

RESULTS OF TREATMENT

Ascarids were passed in the feces or vomitus within a few hours to four days after the capsules had been given. The most effective oral doses were 25 mg per kg given twice, or 50 mg per kg administered once (Table 1). When two doses were

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administered, the first capsule was given in the morning and another at late afternoon or the first capsule was given in the afternoon and the second on the following morning. A single dose of 30 or 40 mg per kg was nearly as effective as 50 mg per kg, although one dog in the 40 mg per kg group (No. 370) retained twelve worms. It is possible that this animal regurgitated the capsule.

Treatment was 100 per cent effective in the group given 50 mg per kg intraperitoneally for two doses. A summary of the results obtained is given in Table 1.

TOXICITY

Approximately one-half of the dogs vomited after the first or second dose, but no further symptoms occurred which could be attributed to the drug. One dog which received 12.5 mg per kg for two doses orally (No. 909) died from an unknown cause on the third day. When vomiting occurred after treatment, worms were frequently expelled in the vomitus.

Previous studies with this compound in dogs infected with heartworm (Hewitt, Kushner, Stewart, White, Wallace, and SubbaRow, 1947) demonstrate that it is well tolerated for long periods of time without demonstrable toxicity of serious nature. Dogs treated with 25 mg per kg three times daily for from two weeks to two months, gained in weight, behaved normally, and showed few signs of discomfort with the exception of occasional and transient nausea and vomiting. Tissues from two dogs treated with this dosage for two months revealed nothing remarkable at autopsy. Further studies in various other laboratory animals (Harned, Cunningham, Halliday, Vessey, Yuda, Clark, Hine, Cosgrove, and SubbaRow, 1948) demonstrate that the drug is practically non-toxic in the therapeutic doses used, and that mice, rats and dogs will tolerate doses many times in excess of the amount which has been shown to be effective for removing ascarids from dogs.

REMARKS

1-diethylcarbamyl-4-methylpiperazine hydrochloride is relatively non-toxic, and the danger of using too large a dose in dogs is slight. The compound is excreted rapidly and is apparently not irritating to the intestinal mucosa. Of singular interest is the fact that the intraperitoneal method of administration is also effective in removing the worms.

Many of the dogs used for the present tests also harbored hookworms, whipworms, and tapeworms. No measurable effect has been produced against any of these other worms.

The possible value of this compound for treating ascariasis in human patients is not known as yet, although preliminary data from six patients indicate that it does produce an effect against *Ascaris lumbricoides* (Oliver-Gonzalez and Hewitt, In press).

SUMMARY

Data are given from fifty-one dogs infected with ascarids and treated with 1-diethylcarbamyl-4-methylpiperazine hydrochloride, Single oral doses of 50 mg per kg were 98.7 per cent effective, and two oral doses of 25 mg per kg within a 24-hour period were 100 per cent effective. Two intraperitoneal doses of 50 mg per kg were 100 per cent effective. The compound is relatively non-toxic to dogs. Fasting preceding treatment and purgation following treatment were not performed.

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