3. No significant relief of inhibition was obtained with either nicotinic acid or tryptophane.

4. *Staphylococcus aureus* and *Mycobacterium tuberculosis* (607) were not inhibited by indoleacetic acid at the concentrations studied.

5. Fairly consistent stimulation at 0.1 mg/-ml levels of indoleacetic acid were obtained with *L. arabinosus* and *L. casei* in the presence of limiting concentrations of tryptophane.

6. The significance of these results in relation to possible metabolite-antagonist relationship between indoleacetic acid and tryptophane or nicotinic acid is discussed.

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Treatment of Experimental Intestinal Trichinosis with 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride (Hetrazan*).

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The drug 1-Diethylcarbamyl-4-methylpiperazine Hydrochloride (Hetrazan), when administered orally, causes the rapid disappearance of the microfilariae of *Wuchereria bancrofti* from the blood of infected individuals.[1] The marked effect of this drug on the circulating forms of *W. bancrofti* suggested its use in other parasitic infections in which treatment should be directed against such migrating forms. In view of the need for a drug in trichinosis which would destroy the migrating larvae as well as the intestinal forms, Hetrazan was tested on white rats infected with *Trichinella spiralis*. The effect of this drug on the intestinal trichinae is reported below.

Methods and Results. White rats weighing from 150 to 175 g were fed by stomach tube with 1,000 to 1,300 infective trichinae larvae. The larvae were obtained from rat muscle digested in a pepsin-hydrochloric acid mixture. Twenty-four hours after feeding the animals were started on Hetrazan. The drug was given on the basis of 200 mg per kg weight 3 times daily by stomach tube, for periods of 5 to 10 days. For the recovery of adult trichinae the treated animals and suitable controls were killed 24 hours after the last dose of the drug was administered. The small and large intestine were removed, slit open and cut into small pieces about 1 cm long. The sliced intestine was put in a Baermann apparatus with normal salt solution heated to 37°C. The adult worms settled rapidly to the tip of the funnel and were removed one hour after the apparatus was set up. The number of worms recovered from the intestines was determined directly by counting.

For the recovery of the muscle stages the rats were killed on or about the 30th day after feeding infective larvae. The rat muscles were ground and digested in a pepsin-hydrochloric acid mixture. The larvae were recovered from the mixture and their number estimated by counting aliquot portions of the total suspension.

The average number of adult worms recovered from the rats treated with Hetrazan was considerably less than the number recovered from the untreated animals (Table I). Thus the average number of worms

* The drug was supplied by the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y.

1 Santiago, D., Oliver-González, J., and Hewitt, R. I., in press.

TABLE I.
Effect of Hetrazan on Experimental Trichinosis as Determined by the Number of Adult and Larval Trichinæ Recovered from Rats. Six Rats Used in Each Experiment.

No. of infective larvæ fed per rat	Amt of drug given orally per rat (mg per kilo wt T.I.D.)	Length of treatment, days	Days after feeding infective larvæ when killed					
			5		10		30	
			Avg No. of worms recovered from intestine	Avg No. of larvæ recovered from muscle	Avg No. of worms recovered from intestine	Avg No. of larvæ recovered from muscle	Avg No. of worms recovered from intestine	Avg No. of larvæ recovered from muscle
1,000	200	5	91	0				
"	0		481	0				
"	200	10			312	0		
"	0				61	0		
1,300	200	5					0	320
"	0						0	31,200
"	200	10					0	112
"	0						0	26,100
"	200	20					0	2

recovered in 6 rats treated with Hetrazan for 5 days was 91, as compared with 481 which was the average number of worms recovered in the untreated animals.

Similarly the average numbers of larvae recovered from the muscles of the treated rats were much less than those recovered from the untreated animals.

Discussion and Summary. According to the results presented above, Hetrazan reduces the number of adult *Trichinella spiralis* when the drug is administered orally to rats infected with this parasite. That the number of adult worms is reduced is also shown by the fact that the larvae recovered from the musculature of the rats, treated early during infection, are less in number than those recovered from the untreated rats.

Hetrazan, when administered orally to man is relatively non-toxic.[1] The amount of drug required to kill the microfilariae of *W. bancrofti* is well under the lethal dose for rats (one mg per kg in man as compared with an LD_{50} of 285 mg per kg in rats). Hewitt *et al.*[2] have reported that the amount of drug necessary to kill the cotton rat filarid is from 10 to 25 mg per kg which has to be given constantly for a period of 2 to 4 weeks. However, the amount of drug necessary to act on the filarid worm of man is considerably less (one mg per kg 3 times daily for 5 days). Although the same species of *Trichinella* is involved in infection of man and rat it may be that, as in the case of the filarial infections, the amount of the drug necessary to overcome the infection in man is less than the amount needed for the treatment of rats.

Hetrazan acts on other intestinal nematodes particularly on *Ascaris* of man and dog.[3] It is suggestive that this drug may be useful mixed with the animal feed in order to treat infections with *Ascaris* and intestinal trichinae.

Work is in progress to determine the effect of Hetrazan on the migratory and muscle stages of *T. spiralis*.

[2] Hewitt, R., Kushner, S., Stewart, H., White, D. E., Wallace, W., and SubbaRow, Y., in press.

[3] Unpublished data.