uteri showed movements of the same type in spite of the different periods of pregnancy and why in 3 cases only the fall of blood pressure occurred.

We suggest that inside of the pregnant uterus (in the placenta) of the cat a rhythmic production of histamine occurs, which provokes the contractions of the uterus, and that a certain amount of histamine may escape the destruction by the histaminase, come into the general circulation and cause the short, but distinct fall of blood pressure. This hypothesis would agree with the hypothesis of Danforth mentioned above.

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Further Observations of Phenothiazine in Experimental Trichinosis.*

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A variety of therapeutic agents have been tried in experimental *Trichinella spiralis* infestations with but limited success.[1] A recent preliminary experiment indicated that 6 weeks' continuous use of a diet containing 0.25% phenothiazine reduced the severity of trichinous infection in rats 74%.[2] Further observations of the actions of this drug have been made and are herewith reported.

Methods. Adult white rats of the Wistar strain were used throughout. The general methods of drug administration, infection and muscle larvae counts were the same as before[2] except as noted in the individual experiments. Each experiment ran for 6 weeks. The results were evaluated by calculating the standard error of the mean for the larvae counts of the 4 animals in each group, and by calculating "t", according to Fisher's methods.[3] Variations with a chance

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1 van Someren, V. D., *Brit. Med. J.*, 1939, **1**, 376.

2 McNaught, J. B., Beard, R. R., and DeEds, F., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 17.

3 Fisher, R. A., *Statistical Methods for Research Workers*, 1934, 5th Ed., Oliver and Boyd, Edinburgh.

probability greater than 1 in 100, as indicated by the "t" table, were not considered significant.

Results. Notable, though incomplete, protection with phenothiazine had been previously reported[2] and it is here considered as Experiment 1 (Table I). *Experiment 2* was performed in order to ascertain the time when the administration of phenothiazine was most effective and whether a larger dose of the drug would further diminish the muscle-infestation.

Twenty-four female rats were segregated into 6 groups of 4 each. Each rat was infected with a quantity of rat meat containing 1535 encysted larvae. One group on the standard rat diet served as controls. The remaining 5 groups were placed, during consecutive weeks, on the same diet containing 0.5% phenothiazine. When these groups were not receiving medicated diet, they were on control diet. The results obtained and other pertinent details are presented in Table I. The total number of larvae recovered from each of the treated groups surpassed the number obtained from the control group. This result, namely that double the dose of phenothiazine given the first, second, third or fourth weeks, or continuously for 6 weeks, after infestation caused no reduction in muscle larvae seemed incompatible with our previous results.[2] However, the experiments differed in the following respects: (1) The concentration of phenothiazine in the diet of the animals of Experiment 2 was double that of Experiment 1; (2) The animals of Experiment 1 received the drug for 2 days prior to infection, while medication began after infection in Experiment 2; (3) The rats of Experiment 1 were infected by doses of 2350 encysted larvae while those of Experiment 2 received only 1535; (4) Older and heavier animals, showing a 20% gain in weight in 6 weeks, were used in Experiment 1, while the younger animals of Experiment 2 averaged a gain of 49%, except for those receiving continuous medication, which showed only a 20% gain; (5) Due to a temporary shortage of animals at the time of Experiment 1, male rats were used for the controls and female rats for phenothiazine administration. Only females were used in Experiment 2. Experiment 3 was designed to aid in clarifying the apparent discrepancy.

Experiment 3. Twenty-four rats of practically the same weight were segregated into 6 groups of 4 each. One group of males and one group of females served as controls and 4 groups of females received medication either before or after infection as shown in Table I. It is seen that, when female controls and female test animals were used, there was no protective action from phenothiazine, as in Experiment 2. The final yield of larvae in animals receiving pheno-

TABLE I.
Phenothiazine in Experimental Trichinosis of Rats.

Exp. No.	Group* No.	Sex	Initial Group wt, g	Gain in wt, %	Treatment with Phenothiazine	Total drug intake, g	No. of larvæ		Intake-Output Ratio
							Given	Recovered	
1	1 (C)	M	797	20			2350	762,400	1:81
	2	F	633	18	Prophylactic† and curative‡	3.78	2350	198,720	1:21
2	1 (C)	F	428	54			1535	804,100	1:131
	2	F	424	37	1st week only	1.03	1535	1,146,600	1:186
	3	F	440	52	2nd " "	.96	1535	900,900	1:146
	4	F	448	51	3rd " "	1.46	1535	842,100	1:137
	5	F	440	53	4th " "	1.17	1535	985,200	1:160
	6	F	424	21	6 weeks continuously	6.38	1535	1,105,200	1:180
3	1 (C)	F	743	2			1700	311,000	1:46
	2 (C)	M	739	20			1700	1,112,800	1:164
	3	F	735	4	Prophylactic	.42	1700	299,000	1:44
	4	F	733	0	"	1.27	1700	249,700	1:37
	5	F	746	—4	" and curative	3.86	1700	638,900	1:94
	6	F	736	—4	Curative	6.71	1700	553,120	1:81

* Four rats in each group.
† Drug was administered prior to infection.
‡ " " " after infection.
C—Controls.

thiazine prophylactically (previous to and concurrent with infection) in concentrations of 0.25% (Group 3) and 0.5% (Group 4) was not significantly lowered. Prophylaxis and continuous therapy with a phenothiazine concentration of 0.25% (Group 5), and continuous use of 0.5% phenothiazine in the diet after infection (Group 6), doubled the yield of larvae. The females were older and heavier than those used previously so that the gain in weight by the controls and those receiving light prophylaxis was only 2 to 4%, while the heavier medicated rats lost 4% in weight. That this mild weight loss probably was not due to the heavier infestation is indicated by the fact that the male controls containing twice the number of muscle larvae gained 20% during the same period. The males were not as old as the females but were comparable in weight. It has been shown previously[4] that the continuous administration of phenothiazine in the heavier dosage range caused some toxicity in rats as indicated by diminished rate of growth. It may well be that this toxicity lowered the resistance of the animals to the parasitic infestation.

In comparing the male controls of Group 2 with the female test animals, it was found that there was an apparent reduction in infestation of from 48 to 77%. These conditions also held in Experiment 1, where there was a reduction of 74%. Clearly, the apparent reduction in the 2 experiments was due to the fact that the females had much lighter infestations than the males fed the same number of larvae.

These results show conclusively that phenothiazine is ineffective in experimental trichinosis. The carefully controlled experiments made indicate a new field for study of the differences in yield of muscle larvae in male and female rats of various ages when infected with similar doses of *T. spiralis*. Campbell[5] recently reported that female rats infected by eggs of *Taenia taeniaformis* yielded only 67% as many liver cysts as did the males. Our observations indicate a similar situation in Trichinella infections.

Conclusions. Contrary to our previously published observations, no evidence was found that phenothiazine administered prior to, concurrent with, or after infestation, has any appreciable value in experimental trichinosis in rats. There is strong evidence of a sex variation in the susceptibility of rats to Trichinella infection, females having higher resistance as indicated by the number of encysted Trichinella found after feeding standard doses of larvae.

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[4] Eddy, C. W., Cox, A. J., and DeEds, F., *J. Ind. Hyg. and Toxic.*, 1937, **19**, 574.

[5] Campbell, D. H., *Science*, 1939, **89**, 415.