(Neohetramine) to act as a stimulant in small doses and as an inhibitor in large doses. Similar effects have been observed(8) with prophenpyridamine (Inhiston).

The rats which received Thephorin in the dose of 0.16 mM failed to eat and seemed to show signs of toxicity after the last injection. However, the rats which received 0.04 mM of Thephorin showed an average *decrease* in time from ingestion of carmine to its defecation of 1.60 hours (40%; $P = <0.01$). This stimulation of motility is comparable to but somewhat greater than that seen after 0.04 mM of Benadryl.

Like the rats receiving 0.16 mM of Thephorin, the rats receiving Histadyl and Pyribenzamine in a dose of 0.12 mM, also failed to eat and were apparently poisoned by the drugs. Two of the 7 rats receiving 0.12 mM of Pyribenzamine died in less than 24 hours after the last injection. A dose of 0.04 mM of either Histadyl or Pyribenzamine failed to produce a significant effect.

Antistine when given in a dose of 0.12 mM produced an average *increase* in time of 1.05 hours (26%; $P = <0.01$). The Antistine, therefore, when given as 0.12 mM showed an inhibition of motility comparable to that seen when Benadryl was given in the larger dose of 0.16 mM. This comparison of Antistine and Benadryl is in agreement with the work of Erspamer and Paolini(9) who found Antistine to be a greater inhibitor of purgatives than Benadryl.

Inasmuch as the rat is relatively resistant to histamine(8) high doses of the antihistaminic drugs, approaching toxicity, were used in order to show the alterations in *in vivo* propulsive intestinal motilities as measured by observing the time from ingestion of carmine to its appearance in the feces. A comparable study in other species has not yet been made. However, both the data of this report and that of other work to which reference has been made, indicate that such a study should be made in order to see whether size of dose and chemical type of drug(13) should be taken into consideration when prescribing antihistaminic compounds.

Summary. 1. Antihistaminic drugs can affect the rate of *in vivo* propulsive intestinal motility as measured by observing the time between ingestion of carmine and its appearance in the feces. In comparable small doses Thephorin and Benadryl stimulate intestinal motility. 2. In larger doses, Antistine and Benadryl produce inhibition. This then shows a reversal in effect by Benadryl dependent on size of dose.

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Isolation of Coxsackie Viruses. Litter Differences Among Suckling Mice.* (18777)

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In planning a large scale study designed to throw light on the role of Coxsackie or C viruses in human disease by determining the frequency with which these agents may be demonstrated in specimens from various sources, an effort has been made to establish rigid technical criteria. It is common practice(1-4) to use one litter of suckling mice for each specimen being tested, although some investigators use two(5), and still others(6)

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select the mice at random, the animals being pooled and redistributed. Animals are usually observed for a period of 2 to 3 weeks. To limit the possibility of spontaneous or accidental infections of mice, it has been suggested that animal inoculations be limited to one "blind" passage in suckling mice(7). In this laboratory each specimen to be tested for C virus is inoculated into 12 to 20 2-day-old suckling white Swiss mice (CF No. 1) representing a minimum of 2 litters. Animals are observed frequently for a period of 2 weeks. Since, through cannibalism, a large number of animals are devoured, it was decided that at least 6 mice representing 2 litters must survive the observation period of 2 weeks, before a specimen is considered negative on first passage. When no symptoms are observed during the first week following the inoculation, 2 mice from each litter are sacrificed for a "blind" passage during which the above procedure is repeated. Since the possibility exists that adult female mice, although insusceptible to Coxsackie virus infection, might become immune as a result of laboratory exposure and transmit this immunity to their offspring, all normal stock mice are maintained in isolated quarters.

Using the procedure described above, 23 strains of Coxsackie virus have been isolated. Apparent litter differences in susceptibility of suckling mice to these agents on primary isolation were evident in a number of instances. The results with 3 strains recovered from stool specimens are summarized in Table I. Each of 8 litter mates inoculated with specimen No. 16 survived the observation period of 2 weeks, while each of 5 mice in a second litter developed symptoms consisting of tremors of the extremities, ataxia, weakness, cyanosis, and retardation of growth and were sacrificed on the fifth and sixth days after inoculation for further passage in suckling mice. Only 4 of 18 mice inoculated with specimen No. 186 developed signs and symptoms of Coxsackie virus infection. That these 4 mice were members of one of the 3 litters inoculated with this specimen may, of course, have been due to chance. Litter difference in susceptibility of suckling mice to C virus infection on primary isolation is also evident in the case of specimen No. 9. None of 8 litter mates showed signs and symptoms during the observation period, while 4 out of 7 mice in a second litter showed characteristic symptoms. Similar litter differences were observed with the viruses recovered from 5 additional specimens. On second passage in mice no litter difference was observed in susceptibility of animals to strains No. 9 and No. 186. Strain No. 16, on the other hand, was difficult to adapt to mice. This, of course, may be due to a virus strain difference rather than to variations in susceptibility of different litters to these agents.

TABLE I. Results of Inoculation of Suckling Mice with Stool Specimens Containing the Coxsackie Virus.

Stool specimen No.	Suckling mouse litter	Results	"C" virus infections
16	1	S, S, S, S, S, S, S, S	0/8†
	2	5,* 5, 5, 5, 6	5/5
186	1	S, S, S, S, S	0/5
	2	5, 5, 8, 8, S, S, S	4/7
	3	S, S, S, S, S, S	0/6
9	1	8, 8, 10, 10	4/7
	2	S, S, S, S, S, S, S, S	0/8

* Figure indicates day after inoculation symptoms observed. S animal showed no symptoms during observation period of 14 days.

† No. of mice which developed "C" virus infection/No. inoculated. (Animals missing, devoured or found dead within 48 hr after inoculation are excluded from analysis.)

Whether the observed differences are due to variability in litter susceptibility or to chance, it is obvious that some of these virus isolations might not have been successful if only one litter of suckling mice had been used. If the observed results are actually due to litter differences in susceptibility, it should be possible by selective breeding to develop a strain of mice of more uniform susceptibility as has been the case with other agents(8).

Summary. Data are presented which sug-

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gest differences in susceptibility of different litters of suckling mice used for the primary isolation of Coxsackie viruses. It is suggested that at least 2 litters including a total of 12 to 15 suckling mice be used for demonstrating Coxsackie viruses in clinical specimens.

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Augmentation by Pregnant Mares' Serum of Body Weight Response of Male Turkeys to Testosterone Propionate. (18778)

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In connection with experiments directed toward quite different ends, testosterone propionate has been observed to exert a greater effect on body growth of male turkeys when administered concurrently with pregnant mares' serum than in absence of this gonadotrophin. The capacity of androgens to stimulate somatic growth under certain conditions is well established(1-4), and testosterone propionate has been shown to act synergistically with pituitary growth hormone in this respect (5). Enhancement of the androgen-induced growth response by pregnant mares' serum, itself without effect on growth in these tests, seems however not previously to have been reported.

Materials and procedures. The experimental stocks consisted of 18 immature Broad Breasted Bronze and an equal number of mature Beltsville Small White male turkeys. The younger birds were 111 ± 7 days of age at the beginning of tests, close to 100 days from sexual maturity. The mature turkeys, 16 months old when placed under test, had entered the period of declining sexual activity some 3 months earlier, upon completion of their first breeding season. Seasonal quiescence in such males is associated with loss of body weight, and resurgent sexual activity with increasing weight(6). Insofar as latent capacity for increase in body weights is concerned, the immature and the mature males were thus much alike qualitatively.

The birds of all test groups were maintained under identical conditions; they were well housed, and had access to ample outside runs. Feed was available *ad libitum*. Treatment was carried out in 2 stages. During the first period of 22 days all the birds except uninjected controls received 7 injections of PMS, 200 rat units at each injection. At the termination of this period, testosterone propionate was administered to designated groups with and without continuing PMS injections; details are recorded in Table I. All birds were sacrificed at termination of secondary treatments, at which times their testes were removed and weighed. Body weights were taken at intervals from the beginning of tests until autopsy. The PMS* preparation, a solution containing 50 rat units per ml, was injected subcutaneously into the anterior cervical region. Testosterone propionate was dissolved in corn oil, 5 mg per ml, and was injected subcutaneously at alternate breast sites on successive days.

Results. The administration of PMS dur-

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