incubating for a short time prior to plating on nutrient agar. Since the protective effect was absent when cells were diluted in peptone broth alone, presumably the high osmotic pressure of the sucrose solution was preventing lysis and allowing the cells to return to normal form(6).

Summary and conclusions. A strain of *Salmonella typhimurium,* RIA, unable to grow in the presence of high concentrations of bile salts was less virulent for mice than 3 mutants which were not inhibited under the same conditions. Two of these were isolated on inhibitory medium, the third independently from a mouse which died following infection with avirulent strain RIA. A sensitive reversion from one of the resistant mutants exhibited a virulence pattern similar to that of the sensitive parent strain. Resistant bacteria produced greater damage to internal organs and were able to persist for longer periods of time in host animals although the incidence of fatal infection was only somewhat higher than in mice infected with bile sensitive organisms. Limited studies comparing bile sensitive and resistant strains of *Salmonella paratyphi* B yielded similar but less striking results(7). These observations indicated that salmonellae able to withstand the effect of bile salts were also better able to establish chronic infection in mice leaving relatively large numbers of survivors as carriers of the organisms.

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Estrogen Antagonisms: Effects of Gluco- and Mineralocorticoids on Estrone-Induced Uterine Growth.* (25493)

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The actions of estrogenic hormones are antagonized by a variety of other steroidal substances(1). We have attempted to compare the effects of various types of steroids as antagonists of estrogens. The effects of representatives of each of the 5 major classes of steroid hormones (estrogens, androgens, progestins, mineralo-, and glucocorticoids(2)), were studied in each available estrogen test. Recently we discussed the effects of progesterone, testosterone propionate and 17-ethyl-19-nortestosterone on uterine growth produced in mice by moderate dose of estrone(3). Similar studies also examined quantitative relationships among a long series of relatives of 19-nortestosterone(4). The present communication extends these observations to the effects of adrenal cortical hormones in our standard mouse uterine growth assay.

Materials and methods. The methods employed have been described(3,4,5,6). Briefly, test compound was mixed in solution with 0.3 μg of estrone; total doses were contained in 0.3 ml of corn oil. Mice received 0.1 ml of solution daily for 3 days, starting at 23 days of age, and were sacrificed on the 4th. Mean uterine wet weights from groups of 8-10 mice were used for analysis. The only deviations from these methods were in the separate administration of gluco-corticoids as microcrystalline suspensions and of the aldosterone as an alcohol-water solution.

Results and discussion. The glucocorticoids,

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TABLE I. Effects of Cortisol Acetate on Estrone-Induced Uterine Growth in Mice.

Dose (μg)			
Estrone	Cortisol	N	Mean uterine wt (mg)
.3	0	10	30.0
.3	100	9	32.8
.3	"	10	28.5
.3	300	10	33.6
.3	"	10	35.4
.3	1000	10	29.2

Estimated slope of fitted dose-response curve does not differ from zero: b = .32 ± 4.09.

cortisone acetate and cortisol acetate, appeared to have little effect upon uterine growth produced by 0.3 μg of estrone. Cortisol acetate was examined in a single test (Table I); at doses up to 1 mg it had no marked inhibitory effect upon the estrone-stimulated uterus. Cortisone acetate was studied in tests over a broad range of doses (Fig. 1). Although inspection of data suggested no interaction, a significance test seemed appropriate. Dose-response distribution was divided into 4 quadrats by a horizontal line through the mean response of 5 concurrent estrone-treated groups, and by a vertical line through the median dose. The number of points falling in each quadrat was determined and randomness of distribution was confirmed by a 4-fold contingency test ($\chi^2 = 0.287$, df = 1, $P > 0.59$). Thus cortisone acetate appeared to have no significant effect upon estrone-induced uterine growth.

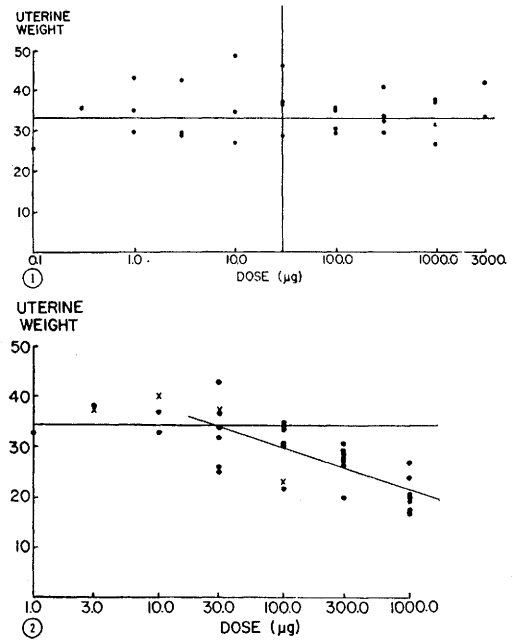

FIG. 1. Lack of effect of cortisone acetate on uterine response to .3 μg of estrone. Each point represents mean of 8-10 mice.

FIG. 2. Effects of desoxycorticosterone (●) and aldosterone (×) on uterine response to 0.3 μg of estrone. Aldosterone point at 100 μg is mean of 5 mice; all other points are mean of 8-10 animals. Fitted line for DCA: Uterine wt = 46.5 − 8.21 log dose. b = 8.21 ± 1.14.

In contradistinction to these findings Szego and Roberts(7) and Szego(8) showed that injected corticoids and stress counteracted water imbibition effects of estradiol-17β. Velardo(9) also found that glucocorticoids inhibited uterine growth produced by estradiol-17β. Rats were employed in each of these studies. Perhaps species differences are a partial explanation for contrasting results. Another difference from our procedure was the use of estradiol-17β as standard uterine growth stimulator.

Desoxycorticosterone also inhibited uterine water imbibition stimulated by estradiol-17β in rats(7), although Szego(8) pointed out later that results with this material were not consistent. Velardo(9) showed inhibition of estradiol-induced rat uterine growth with DCA. In our hands DCA was an inhibitor of estrone-stimulated uterine growth in intact, immature mice (Fig. 2). In comparison with our previous studies with relatives of 19-nortestosterone(4), DCA appears to be a weak estrone antagonist, only about 10% as active as progesterone. Qualitatively, there can be no doubt of the reality of this inhibition since the negative slope of dose response curve was highly significant ($t = 5.006$, df = 25, $P < 0.01$).

In addition to desoxycorticosterone, we had a small sample of aldosterone available for preliminary testing. The few data available for aldosterone suggest that this material is also an estrone antagonist, and that its potency is not remarkably different from that for DCA (Fig. 2). Since this particular sample of aldosterone assayed at about 50 times more potent than DCA in a rat salt-retaining test, it appears that little correlation exists between these 2 activities.

Summary. Uterine growth in intact, immature mice was stimulated by injection of 0.3

μg of estrone. When administered simultaneously, neither cortisone acetate nor cortisol acetate had any evident inhibitory effect. DCA, on the other hand, was a definite but weak estrone antagonist (10% as potent as progesterone). Aldosterone was active; its potency appeared to be about 10% progesterone.

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Lack of Relationship between Body Weight and Pharmacological Effect Exemplified by Histamine Toxicity in Mice.* (25494)

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The pharmacologic effects of many drugs and toxins appear to be proportional to their dose/unit body weight; for some drugs this may not be the case. The following study shows that toxicity of histamine in mice is not directly related to body weight.

Methods. Albino mice of Swiss strain weighing 15 to 25 g were used. Each group tested consisted of mice with a mean weight within $\pm$ 1 g of the desired mean body weight and with no individual mouse deviating by more than 1 g from the mean. Histamine diphosphate was dissolved in appropriate concentrations in 0.9% NaCl so that each animal received the desired dose in 0.2 ml of solution. Within each weight group all animals received the same dose of histamine diphosphate regardless of exact body weight of each animal. All injections were made intraperitoneally and mortality was recorded over a 24 hour period even though all animals that succumbed terminated within 6 hours after injection.

Results. A total of 360 mice were used in 18 groups of 20 mice each. The LD_{50} of histamine injected intraperitoneally was first determined in mice weighing 18 $\pm$ 1 g. Seven dose levels were utilized. Results and their statistical analysis are shown in Table I. Doses of 1.6 to 2.5 mg/g body weight produced submaximal responses. This dose range was then used to reevaluate the LD_{50} in 2 groups of mice, one of 18 $\pm$ 1 g and another of 25 $\pm$ 1 g. Both groups were tested simultaneously at 3 identical dose levels on a mg/g basis. Results are tabulated in Table II. When the doses are taken on a mg/g basis the smaller mice (18 $\pm$ 1 g) seem to have a larger LD_{50} than larger mice (25 $\pm$ 1 g). This difference is statistically significant and could have been interpreted as indicating that smaller animals are more resistant to histamine than larger. However the ratio of the two LD_{50}'s, *i.e.*, 1.29 with confidence limits of 1.15 to 1.44, is very close to the inverse ratio of weights of the 2 groups 25/18 = 1.39 suggesting that the difference between the 2 groups may be entirely due to the assignment of doses on body weight basis. In fact when the doses are expressed as mg/mouse, the results of the 2 groups fit a single dose-response probit regression indicating that they correpond to a single homogeneous population with an LD_{50} of 40 mg/mouse. This is further substantiated from the results of 3 different

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