35.5±0.5 mg/100 ml at 30 min., ergotamine;
34.2±5.8 " " " " " , no ergotamine;
41.0±2.4 " " " 60 " , ergotamine;
38.5±6.5 " " " " " , no ergotamine;

The ergotamine-treated preparations differed from the nontreated in showing less variability in potassium levels. Survival, as judged both by time and number, seemed slightly better than expected for this class of animal receiving a dosage of histamine (10 mg) which previously was fatal to 60% of the nontreated within one hour.

Discussion. The data obtained indicated that fluctuations in serum K tended to be suppressed by ergotamine tartrate. In the dosage used the difference from the untreated controls was not significant. However, if maximum amounts of ergotamine had been employed a slight lowering of the potassium levels might have been established as found by Houssay for the dog.[2]

Symptomatically, the course of histamine shock following upon the administration of 10 mg intraperitoneally appeared unchanged both in the intact rat and the rat bearing adrenocortical grafts. There was no evidence of a potentiation or synergism between cortical hormones and epinephrine as might be surmised from the findings of Vogt that the latter prolongs cortin secretion.[3] The lack of such interaction therefore cannot account to any extent for the high susceptibility in rats possessing only adrenocortical tissue. The experiments serve to emphasize the inefficiency of regenerated cortical substance, the relation of the rise in extracellular potassium to level of cortical activity and the minor influence of the sympathico-adrenal mechanisms upon potassium release in histamine shock.

Summary. Ergotamine tartrate in the dosage used did not significantly modify serum potassium changes characteristic of histamine shock in the rat. It did not influence histamine tolerance in either the normal or the demedullated animal.

2 Houssay, B. A., and Gerschmann, R., *Rev. Soc. Argent. de Biol.*, 1939, **15**, 327.

3 Vogt, M. J., *J. Physiol.*, 1945, **103**, 319.

15832

Effect of Sex Hormones on Pituitary Lactogen and Crop Glands of Common Pigeons.*

JOSEPH MEITES AND C. W. TURNER.
From the Department of Dairy Husbandry, University of Missouri, Columbia, Mo.

Estrogens, testosterone propionate and progesterone can exert a dynamic stimulus to the secretion of lactogenic hormone by the anterior pituitary. This is particularly true of the estrogens which have been shown to increase the pituitary lactogen content of rats,[1-3] guinea pigs[3,4] and rabbits[5] from 200 to 500%. A 40% increase has been obtained with testosterone propionate in rats.[6] Progesterone apparently has no effect on the lactogen content of the A.P. when administered in small or moderate dosages, but amounts well above the physiological level in rats (15.0 mg per day for 10 days) have increased it about 74% on a body weight basis.[7] Selye

* Contribution from the Department of Dairy Husbandry, Missouri Agricultural Experiment Station, Journal Series No. 1040.

1 Reece, R. P., and Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bull.* No. 266, 1937.

2 Lewis, A. A., and Turner, C. W., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 439.

3 Meites, J., Trentin, J. J., and Turner, C. W., *Endocrinology*, 1942, **31**, 607.

4 Meites, J., and Turner, C. W., *Endocrinology*, 1942, **30**, 711.

5 Meites, J., and Turner, C. W., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 190.

6 Reece, R. P., and Mixner, J. P., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 66.

has shown that many steroid hormones can exhibit common "folliculoid" properties when administered in sufficient dosages,[8] and this may well account for the action of progesterone on hypophyseal lactogen. From a cytological point of view it is interesting to note that estrogens and testosterone propionate have been shown to increase the number and secretory activity of the eosinophilic cells of the anterior pituitary,[9-13] which are agreed to be the source of lactogenic hormone in both mammals[14-16] and pigeons.[17] The ability of sex hormones, particularly estrogens, to increase lactogen in the anterior pituitary is also reflected in the greater quantities of lactogenic hormone found in the blood of rabbits after estrone administration[5] and in the initiation of milk secretion in a number of mammals following estrogen administration.[4,18] The authors have advanced the theory that estrogen is the factor normally responsible for stimulating the secretion of pituitary lactogen and initiating milk secretion at the time of parturition.[4]

Crop secretion in pigeons is analagous to milk secretion in mammals and both processes furnish the means for supplying nutrition to the young during the critical period after birth. Would the sex hormones, therefore, stimulate pituitary lactogenic secretion in pigeons as in mammals? Furthermore, if these steroids could increase the lactogen content of the pigeon pituitary, would it also be reflected in the initiation of crop gland secretion?

Experimental. Groups of 16 to 20 mature pigeons of both sexes were injected subcutaneously over the pectoral muscles daily for a 10-day period. These birds were kept together in groups of 8 to 10 in a cage. All the sex hormones were dissolved in corn oil and injected in 0.1 cc volumes. On the day after the last injection the birds were killed, weighed, sexed, and the pituitaries and crop glands were removed. The crop glands were washed clean, freed from adhering fat tissue, blotted dry between towel papers and weighed. They were then examined under light for evidence of visual proliferation. In the case of the diethylstilbestrol group and its controls, which constitute a preliminary experiment performed in 1942, the crop glands were not weighed but only examined for visual proliferation.

The pituitaries of each group were macerated with a small mortar and pestle, suspended in a definite volume of distilled water and injected intradermally over the crop glands of 10 common pigeons in 0.1 cc volumes for 4 days. The equivalent of 6 male or 4 female pigeon pituitaries was given to 10 birds, and each group of pigeon pituitaries was directly compared with another by injecting over both sides of the crop gland. The crop glands were rated for lactogenic response by the Reece-Turner method.[1]

Results. It will be seen that in the preliminary experiment performed in 1942, 250 μg of diethylstilbestrol did not increase the lactogen content of the pituitary or initiate crop milk secretion in 13 female pigeons. In the 1946 series, total dosages of 1,000 I.U. estrone, 10 mg progesterone or 5 mg testosterone propionate† caused no significant

7 Reece, R. P., and Bivins, J. A., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 582.

8 Clarke, E., and Selye, H., *J. Pharm. and Exp. Therap.*, 1943, **78**, 187.

9 Foster, C. L., *J. Endocrinology*, 1942, **3**, 79.

10 Baker, B. L., and Everett, N. B., *Endocrinology*, 1944, **34**, 254.

11 Zeckwer, I. T., *Science*, 1944, **100**, 123.

12 Wolfe, J. M., *Endocrinology*, 1941, **29**, 969.

13 Wainman, P., Reese, J. D., and Koneff, A. A., *Endocrinology*, 1942, **31**, 303.

14 Azimov, G. I., and Altman, A. D., *Comptes Rendus de l'Acad. des Sciences de l'URSS*, 1938, **20**, 621.

15 Friedman, M. H., and Hall, S., *25th Annual Meeting and Scientific Session, Assn. for Study of Int. Secretions*, 1941, p. 10.

16 Smelser, G. K., *Endocrinology*, 1944, **34**, 39.

17 Schooley, J. P., and Riddle, O., *Am. J. Anat.*, 1938, **62**, 313.

18 Folley, S. J., and Malpress, F. H., *J. Endocrinology*, 1944, **4**, 1.

† We are indebted to Dr. D. F. Green of Merck & Co., Rahway, N.J., for the diethylstilbestrol; to Dr. D. W. MacCorquodale of The Abbott Research Labs., North Chicago, Ill., for the estrone; and to Dr. F. E. Houghton of Ciba Pharmaceutical Products, Inc., Summit, N.J., for the progesterone and testosterone propionate used in this study.

change in the lactogen content of the pituitary, and there was no evidence of visual proliferation or weight increase in the crop glands. The differences in the pituitary lactogen content between the 1942 and 1946 female control pigeons may be due to the fact that the former pigeon pituitaries were assayed in the early fall while the latter were assayed in mid-winter. As in a previous report on the lactogen content in the pituitaries of common pigeons,[19] it was found that the female pituitary contains considerably more lactogen than the male. None of the sex hormones increased the pituitary weight of the pigeons.

Discussion. There appears to be an inverse relationship between the secretion of gonadal hormones and the formation of crop milk in pigeons. Thus, it has been demonstrated that (1) the testes and ovaries decrease in size during incubation and brooding, when crop secretion normally occurs,[20–22] and (2) the administration of lactogenic hormone markedly reduces the size of the pigeon gonads.[23,24] With the exception of one report in which nonhormonal factors favorable to broodiness were introduced,[25] the injection of sex hormones has proven ineffective in stimulating crop secretion in pigeons.[26,27] The mechanism responsible for the secretion and release of lactogen from the pigeon hypophysis may depend chiefly on psychic and

TABLE I. Effect of Sex Hormones on Pituitary Prolactin and Crop Glands of Common Pigeons.

Treatment	Sex	Total No. of pigeons	Avg body wt, g	Avg pituitary wt, mg	Avg crop wt, g	Avg crop wt 100 g body wt	No. of visual crop responses	Avg No. lactogen units* per pit.	Avg No. lactogen units 100 g body wt	Avg No. lactogen units mg pit. tissue
1942										
Controls	F	8	276	4.32			0	2.00	.72	.46
250 Diethylstilbestrol	F	13	292	4.13			0	2.31	.79	.56
1946										
Controls	1F	8	311	3.71	2.20	.70	0	1.62	.52	.43
	3M	10	326	3.44	2.47	.76	0	.85	.26	.25
5 mg Testosterone propionate	2F	11	285	3.82	2.22	.77	0	1.75	.69	.46
	4M	6	311	3.20	2.23	.71	0	1.12	.36	.35
10 mg Progesterone	2F	9	284	3.32	2.11	.74	0	1.50	.53	.45
	3M	7	326	3.28	2.52	.77	0	.85	.26	.25
1000 I.U. Estrone	1F	10	295	3.61	1.79	.60	0	2.06	.69	.54
	4M	7	336	3.45	2.22	.66	0	1.21	.36	.35

* Reece-Turner lactogen units 22.2 R.T. units = 1 International Unit (Meites, J., Bergman, A. J., and Turner, C. W., *Endocrinology*, 1941, **28**, 707).
1.2.3.4 These groups were compared with each other for lactogenic hormone by injecting their pituitaries over both sides of the crop glands in the same 10 pigeons.

[19] Hurst, V., Meites, J., and Turner, C. W., PROC. SOC. EXP. BIOL. AND MED., 1943, **53**, 89.

[20] Champy, C., and Colle, P., *C. R. Soc. Biol.*, 1919, **82**, 227.

[21] Riddle, O., Smith, G. C., and Benedict, F. G., *Am. J. Physiol.*, 1933, **105**, 482.

[22] Schooley, J. P., and Riddle, O., *Anat. Rec.* (Suppl.), 1936, **67**, 51.

[23] Riddle, O., and Bates, R. W., *Endocrinology*, 1933, **17**, 689.

[24] Bates, R. W., Lahr, E. L., and Riddle, O., *Am. J. Physiol.*, 1935, **111**, 361.

[25] Riddle, O., and Lahr, E. L., *Endocrinology*, 1944, **35**, 255.

[26] Patel, M. D., *Physiol. Zool.*, 1936, **19**, 129.

[27] Riddle, O., Bates, R. W., Miller, R. A., Lahr, E. L., Smith, G. C., Dunham, H. H., and Opdyke, D. F., *Carnegie Inst. Washington Year Book* No. 39, 1940, p. 221.

environmental rather than hormonal stimuli.[26] It seems clear from our study that the injection of sex hormones alone are ineffective in augmenting lactogen output by the pituitary or initiating crop milk secretion in pigeons.

It appears remarkable that the pigeon pituitary should be refractory to the administration of sex hormones, particularly estrogens which are such powerful activators of lactogenic hormone secretion in the pituitaries of mammals. Neither do estrogens increase the weight of the pigeon pituitary as in mammals. It would be of interest to determine what effect the sex hormones have on the cytology of the pigeon hypophysis.

Summary. The effects of estrone, diethylstilbestrol, progesterone and testosterone-propionate were determined on the lactogen content and weight of the pituitary, and on the proliferation and weight of the crop glands of common pigeons of both sexes. The results were all negative. It is concluded that the pigeon pituitary, unlike the mammalian, is refractory to the administration of sex hormones and is not stimulated by them to increase the secretion of lactogenic hormone.

15833

Statistical Evaluation of Growth Curves.

CARROL S. WEIL. (Introduced by W. S. McEllroy.)

From the Multiple Fellowship on Chemical Hygiene, Mellon Institute, Pittsburgh, Penn.

A problem that frequently confronts research workers in the biological sciences is the comparison of growth curves of groups of experimental animals subjected to different treatments. The customary practice has been that of visual estimation of significant differences from a plot of weight against time (Fig. 1), or the application of the "t" test to the mean weights at a particular time. These conventional methods of evaluation often give an ambiguous or unconvincing analysis of the results.

The purpose of this paper is to demonstrate how time-weight data (growth curves) have been treated more critically in a comparative study of exposure of rats to vapors

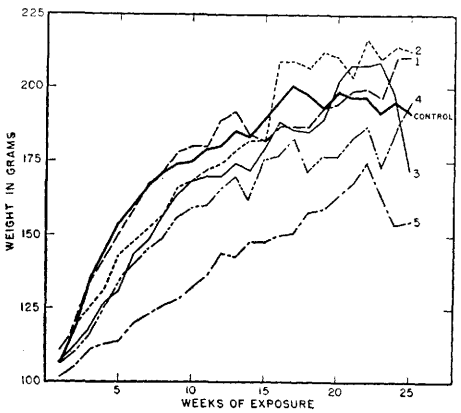

FIG. 1.
Combined growth curves of male and female rats.

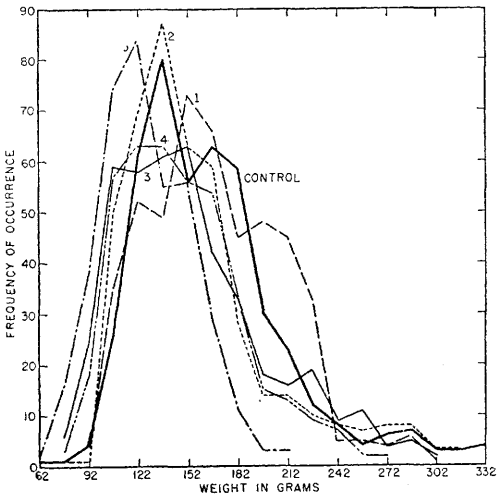

FIG. 2.
Curves showing the frequency of occurrence of individual weights for male and female rats, throughout the period of treatment.