

Effect of Estrone* on Lactogen Content in Pituitary and Blood of Male Rabbits.†‡

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Reece and Turner^{1, 2} were the first to demonstrate that the administration of estrone or estradiol will increase the lactogenic hormone in the pituitaries of male and female rats, and male guinea pigs. Later, testosterone propionate³ and diethylstilbestrol^{4, 5} were likewise shown capable of augmenting the lactogenic potency of pituitaries in female rats and male guinea pigs. The present authors have obtained a maximum rise with estrone and diethylstilbestrol of 410 and 438% respectively in the lactogen content of the pituitaries of immature male guinea pigs. In actual units of lactogenic hormone, the immature male guinea pigs (weighing an average of 334 g), contains 3.06 Reece-Turner units (R.-T.U.) per pituitary. Upon the administration of estrone or diethylstilbestrol the average lactogen content per pituitary rose to a maximum of 17.75 and 16.50 R.-T.U. respectively.⁵ This seems highly significant in view of the fact that the lactating guinea pig pituitary has been observed at no time during the lactation cycle to contain more than 18.38 R.-T.U.⁶

In addition to the increase in the lactogenic hormone of the pituitary which can be obtained with estrogen, lactation itself has been initiated by the administration of estrogens.^{2-4, 7-9} This seems to

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¹ Reece, R. P., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 402.

² Reece, R. P., and Turner, C. W., *Mo. Agr. Exp. Sta. Bul.* 266, 1937.

³ Reece, R. P., and Mixner, J. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 66.

⁴ Lewis, A. A., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **48**, 439.

⁵ Meites, J., and Turner, C. W., unpublished data.

⁶ Holst, S., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 479.

⁷ Folley, S. J., Scott Watson, H. M., and Bottomley, A. C., *J. Physiol.*, 1940, **98**, 15.

⁸ Lewis, A. A., and Turner, C. W., *Proc. Am. Soc. An. Prod.*, 1940, **33**, 63.

⁹ Walker, S. M., and Stanley, A. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **48**, 50.

indicate that estrogen causes the pituitary to release more lactogen into the blood stream. However, there has been some doubt expressed as to whether the increase in the lactogen content of the pituitary which follows upon estrogen treatment actually represents an increased release of lactogen into the blood stream or only a storage of lactogen in the pituitary.

Recently, it has been reported that lactogen can be detected in the blood stream of normal, pregnant and lactating rabbits.¹⁰ As little as 1 cc of whole untreated rabbit blood was found to give positive responses when injected intracutaneously over the crop sacs of common pigeons. It was of interest, therefore, to determine whether we could demonstrate a simultaneous increase of lactogen in the blood stream as well as in the pituitary of normal male rabbits upon the injection of estrone.

Methods. Male New Zealand white rabbits, weighing approximately 2500 g, were used in this experiment. Ten rabbits served as a control group and received no estrone, while 3 experimental groups were injected subcutaneously with 3 different levels of estrone. Approximately 10 cc of venous blood (from an ear vein) was obtained from each rabbit both before the injections of estrone were begun and after the last injection. Potassium oxalate was used to keep the blood from clotting. All the experimental rabbits were injected with estrone for a 10-day period and killed on the eleventh day.

The whole untreated blood from each rabbit group was assayed by injecting a total of 0.50 and 1.00 cc intradermally over the two crop glands of 10 pigeons for 4 days and then determining the number of positive responses in the crop glands on the fifth day. The pituitaries of each group were macerated separately in a small agate mortar, taken up in a little distilled water, and assayed by the Reece-Turner pigeon method.²

Results. All 3 dosage levels of estrone brought a considerable increase in the lactogen content of the male rabbit pituitary (Table I). It will be noted that 5000 I.U. estrone elicited a significantly smaller increase in lactogenic hormone than was secured with 500 and 1000 I.U. It was also observed that the mammary glands of the rabbits receiving the highest dosage of estrone were less extensively developed than in the animals receiving the smaller amounts of estrone. Similarly, it has been observed⁵ that large dosages of diethylstilbestrol will produce less increase in the lactogen content of the pituitaries of male guinea pigs than can be obtained with

¹⁰ Meites, J., and Turner, C. W., *J. Clin. Endocrinol.*, 1941, **1**, 918.

TABLE I.

Effect of Estrone on Lactogen Content of the Pituitary.								
No. of rabbits per group	Avg body wt, g	Amt of estrone inj. per animal		Pituitary wt, mg	Avg Reece-Turner lactogen units,* pituitary	Avg R.-T. units, mg pit. tissue	Avg R.-T. units, 1000 g body wt	Avg % inc. in lactogen, 1000 g body wt
		Daily I.U.	Total I.U.					
10	2545	Controls		26.43	2.24	.084	.88	
7	2761	50	500	24.37	8.25	.340	3.00	240
7	2589	100	1000	32.00	12.16	.380	4.69	433
9	2598	500	5000	29.10	6.06	.208	2.29	160

*One Reece-Turner lactogen unit = .045 International Units (Meites, J., Bergman, A. J., and Turner, C. W., *Endocrinol.*, 1941, **28**, 707.

smaller doses. However, even the highest amount of diethylstilbestrol used (100.0 mg) was found to produce some increase. In comparison to the high lactogen content of the pituitary which can be secured with estrogens in the immature male guinea pig, it is interesting to observe that the 3 levels of estrone injected failed to increase the lactogen content of the pituitaries of the experimental rabbits to levels at all comparable to that of the lactating rabbit (60.00 R.-T.U. at 5 days postpartum⁵). However, it is possible that dosages of estrone other than those used in this experiment might have increased the lactogenic potency of the male rabbit pituitary to a greater degree than was observed here.

The data in Table II reveal that a very definite increase was secured in the lactogen content of the blood stream following the administration of estrone. These results prove that the measured increase in the lactogen content of the pituitary which can be secured upon the administration of estrone occurs simultaneously with an increase in the release of lactogen into the blood stream. This explains why

TABLE II.
Effect of Estrone on Lactogen Content in Blood.

Total amt estrone inj. per rabbit, I.U.	Amt rabbit blood inj. per pigeon, ml	No. + responses in 10 pigeons before estrone admin.	No. + responses in 10 pigeons after estrone admin.
Controls	1.00	4	
	0.50	2	
500	1.00	5	10
	0.50	2	10
1000	1.00	4	9
	0.50	4	7
5000	1.00	6	8
	0.50	4	5

lactation can be initiated in some animals upon the administration of proper amounts of estrogens.

Summary. Three groups of male rabbits were injected with 3 different levels of estrone in order to determine whether estrogen could effect a simultaneous rise in the lactogenic hormone of the pituitary and blood stream. Assays of the pituitaries revealed that a considerable increase in lactogen was obtained, although the highest dosage of estrone (5000 I.U.) gave a smaller increase in lactogen than was secured with the two lower levels (500 and 1000 I.U.). Assays of the whole, untreated rabbit blood also showed that a definite increase in the release of lactogen into the blood stream was secured following the injection of estrone. These findings are believed to account for the initiation of lactation following suitable estrogen treatment.

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Lactogenic Content of Pituitaries of Pseudopregnant Rabbits.*†

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It has been suggested that copious lactation can be initiated only when (a) there is a well developed mammary gland present and (b) when there is a high lactogen content in the anterior pituitary.¹ After the middle of pregnancy one of these two factors is present, namely, a well developed mammary gland, but the production of lactogenic hormone by the pituitary remains at too low a level to initiate abundant lactation. Thus in the rat,^{2, 3} guinea pig,⁴ and rabbit,^{1, 4} the lactogen content of the pituitary remains as low during pregnancy as in the non-pregnant state. Almost immediately following parturition, however, there is a great increase in the lactogenic hormone of the pituitary (from 200 to over 400%), and full lactation is initiated.^{2, 3, 4} An increased lactogen content in the

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1 Turner, C. W., and Meites, J., *Endocrinol.*, 1941, **29**, 165.

2 Reece, R. P., and Turner, C. W., *Missouri Agr. Exp. Sta. Bull.* 266, 1937.

3 Reece, R. P., Hathaway, I. R., and Davis, H. P., *Dairy Science*, 1939, **22**, 1.

4 Holst, S., and Turner, C. W., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 479.