delayed initiation of lactation, there being no significant amount of milk until the 5th postpartum day. After this time, however, secretion was maintained at a normal level.

With the addition of inositol to the B-complex supplement there was a prompt initiation of lactation which was maintained at a level only slightly less than that of the controls. Further supplementation of this regime with p-aminobenzoic acid resulted in no significant improvement in milk secretion over that in the group which received the B-complex supplement and inositol alone.

These findings are in general supported by the infant mortality rates for the various experimental groups. From these data we may conclude that the B-complex supplement alone or with the addition of p-aminobenzoic acid will not support normal nutrition of young rats. Supplementation with inositol results in mortality rates only slightly greater than those observed in the control animals. Supplementation with both inositol and p-aminobenzoic acid results in mortality rates quite comparable to those of the controls.

Summary. The critical role of inositol in the maintenance of normal lactation in the albino rat has been confirmed. P-aminobenzoic acid does not seem to increase lactation directly but when given to animals also receiving inositol it slightly decreases mortality rates of the newborn.

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Action of Various Steroids on the Hypophysis of the Thyroidectomized Rat.

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The typical modification in the hypophysis of the thyroidectomized rat, namely the degranulation of the eosinophiles and the appearance of large basophilic vacuolated "thyroidectomy cells" are known to be prevented by treatment with thyroid extract,[1-3] but the effect of steroid hormones on the development of thyroidectomy changes has not been definitely established as yet. Zeckwer[2] reported that estrone does not prevent the occurrence of thyroidectomy cells, while Nelson and Hickman[4] claimed that it completely inhibits their development. Severinghaus[3] concluded—partly on the basis of similar experiments—that there is: "sufficient evidence not only to identify these thyroidectomy cells as basophiles, but also as modified basophiles similar in characteristics to castration cells"; it was pointed out, however, that the modifications of the acidophiles are not affected by folliculoid compounds. Subsequently Nelson[5] stated that the prevention of thyroidectomy cells requires three times more estradiol benzoate than the inhibition of castration cell formation.

More recently Clarke *et al.*[6] found that all hormonally active steroids (including folliculoids, testoids, luteoids and corticoids) inhibit the development of castration cells to some extent. In view of these observations it appeared of interest to establish whether the ability to prevent the formation of thyroidectomy cells is also a morphogenetic action common to all steroid hormones.

Table I summarizes our relevant experiments. It will be noted that male albino rats weighing 130-150 g were used throughout. These were thyroidectomized the day before the initiation of treatment and killed 22 days later. Each group consisted of 6 rats. All

1 Hohlweg, W., und Junkmann, K., *Arch. f. d. ges. Physiol.*, 1933, **232**, 148.

2 Zeckwer, I. T., *Am. J. Path.*, 1938, **14**, 773.

3 Severinghaus, A. E., *Sex and Internal Secretion*, Baltimore, 1939, 3rd Ed., p. 1045.

4 Nelson, W. O., and Hickman, J., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 828.

5 Nelson, W. O., *Federation Proc.*, 1942, **1**, 63.

6 Clarke, E., Albert, S., and Selye, H., *Anat. Record*, 1942, **83**, 449.

TABLE I.

No. of Group	Treatment	M.P. °C	Dosage in mg/day	Pituitary in mg	Thyroidectomy cells
1	*Peanut oil* (0.1 cc twice daily)	—	—	8.2 (7.3-8.9)	+
2	$\Delta^{1,3,5}$-estratriene-3,17(α)-diol *α-estradiol*	176 (176-177)	.05	18 (13-22)	0
3	17-ethinyl-$\Delta^{1,3,5}$-estratriene-3,17(α)-diol *Ethinyl estradiol*	138-139 (145-146)	.05	15 (15-16)	0
4	Δ^4-androstene-3-one-17(α)-ol *Testosterone*	154 (154-154.5)	10	7.8 (7.3-8.5)	+
5	Δ^5-androstene-3(β),17(α)-diol *Androstenediol*	182-183 (182-183)	10	8.3 (7.5-10.0)	+
6	Δ^5-androstene-3(β)-ol-17-one *Dehydro-iso-androsterone*	137 (144-146)	10	8.2 (6.5-9.4)	+
7	17-ethyl-etiocholane-3(α),20(α)-diol *Pregnanediol*	237 (237-239)	10	7.3 (4.1-9.0)	+
8	17-ethyl-etiocholane-3,20-dione *Pregnanedione*	118 (120)	10	7.6 (5.4-9.3)	+
9	17-ethyl-Δ^4-androstene-3,20-dione *Progesterone*	128 (128)	10	7.1 (5.1-9.0)	+
10	17-ethyl-Δ^4-androstene-3,20-dione-21-ol acetate *Desoxycorticosterone acetate*	152 (158-160)	10	7.5 (5.9-8.3)	+
11	17-ethyl-Δ^5-androstene-3(β)-ol-20-one *Pregnenolone*	186 (185-187)	10	6.9 (4.8-8.1)	+
12	17-ethinyl-Δ^4-androstene-3-one-17-ol *Ethinyl testosterone*	265-268 (270-272)	10	8.6 (7.9-9.3)	+

animals were injected twice daily, the controls with 0.1 cc of peanut oil and the other groups with various steroids administered as a fine crystalline suspension in the same amount of peanut oil. In addition to the common name (in italics), the descriptive systematic chemical name of each steroid is given as well as the melting point of our sample. This helps to avoid any doubt concerning the nature of the material used. The melting points of especially highly purified preparations as described in the literature, are mentioned in brackets underneath the melting point of our sample in order to facilitate the estimation of the latter's purity. The average pituitary weights (with the range in brackets) are recorded as well as the presence or absence of thyroidectomy cells.

Perusal of the table indicates that although 50 γ of estradiol or ethinyl estradiol sufficed to prevent the formation of thyroidectomy cells, none of the other steroids share this effect in doses of 10 mg per day. It is quite possible that even smaller doses of the 2 folliculoid substances would have sufficed to prevent the formation of castration cells, while still larger doses of the other steroids may have proved effective. It must be kept in mind, however, that a dose of 10 mg per day is a huge amount for a rat and that this—and even smaller doses—proved highly effective in counteracting the formation of castration cells in the gonadectomized male or female rats examined by Clarke *et al.*[6] It will be noted that the folliculoids caused a pronounced enlargement of the pituitary and upon histological examination the anterior lobe cells proved greatly enlarged and almost completely devoid of chromophil granules. Indeed, the action of thyroidectomy and the folliculoids appears to be additive in this respect since the loss of eosinophil granules was even greater in thyroidectomized than in intact male rats treated with the same amount of estradiol. Thus the loss of eosinophile granules, which is normally caused by thyroidectomy, was not prevented and it remains doubtful whether the absence of vacuolized thyroidectomy cells in groups 2 and 3 should be ascribed to a "cure" of the thyroidectomy changes by the folliculoid compounds such as is obtained, for instance, with thyroid extract. These steroids, which in the intact rat cause enlargement of anterior lobe cells and degranulation of the eosinophiles, appear to have exhibited this effect even in our thyroidec-

tomized animals and it is possible that the absence of thyroidectomy cells in the latter is merely due to the fact that the usual morphogenetic effect of folliculoid overdosage prevails over that of thyroidectomy.

Since all hormonally active steroids possess some degree of folliculoid potency[7] it may be surprising to note that they do not share the anti-thyroidectomy cell effect of estradiol. This is not unexpected, however, if we consider that the action of estradiol on the size and structure of the normal hypophysis is partly inhibited by simultaneous treatment with steroid hormones having testoid, luteoid or corticoid activity.[8] In view of this observation it appears understandable that the slight folliculoid activity of the hormonally active androstane and ethyl-androstane derivatives is masked and cannot evidence itself as far as the hypophysis is concerned. That is, such compounds cause no significant enlargement of the anterior lobe cells nor degranulation of the eosinophiles. It is quite possible that in the case of castration changes the various hormonally active steroids effect a physiological substitution therapy by virtue of their folliculoid activity even if the latter cannot manifest itself by morphological signs of overdosage (enlargement in size, degranulation of eosinophiles), while in the case of the thyroidectomy cells the folliculoids act merely by virtue of their pharmacological overdosage effects so that the formation of these cells cannot be inhibited unless overdosage changes are produced. It must be admitted, however, that if it were technically feasible to give even larger doses of the above androstane and ethyl-androstane derivatives, the thyroidectomy changes might be prevented by them since Nelson[5] showed that larger doses of folliculoids are required to achieve this latter result than to prevent castration changes.

Summary. Experiments on thyroidectomized rats indicate that the formation of vacuolized "thyroidectomy cells" in the pituitary is prevented by daily doses of 50 γ of estradiol or ethinyl estradiol but remains unmodified by as much as 10 mg a day of testosterone, androstenediol, dehydro-*iso*-androsterone, pregnanediol, pregnanedione, progesterone, desoxycorticosterone acetate, pregnenolone or ethinyl testosterone. Unlike the formation of "castration cells" the development of "thyroidectomy cells" is hence not inhibitable by all hormonally active steroids even if they are administered in these comparatively high dosages.

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[7] Selye, Hans, *Rev. Canad. de Biol.*, 1942, **6**, 577.

[8] Selye, Hans, *Canad. Med. Assn. J.*, 1940, **42**, 113.