using hemiscastrate female rats showed that hypothyroidism reduces weight but does not completely block the hypertrophy of the remaining ovary. The purpose of the present study was an effort to explain the effect of thyroidectomy upon weight of the remaining ovary in the hemicastrate rat through a histological examination of the ovary.

Adult female rats (160–180 g) were divided into 3 groups. The first group was left intact to serve as controls, while the second group was unilaterally ovariectomized. In the last group, both the right ovary and the thyroid were removed. Animals were killed 14 days after operation. At autopsy, the left ovary was removed, weighed and fixed in formalin for histological evaluation.

Hemicastration was followed by a significant increase (48%) in weight of the remaining ovaries over those of the intact controls (Table). Removal of the thyroid partially blocked the compensatory hyperthrophy; the mean ovarian weight of the hemicastrate-thyroidectomized rats (49.9 mg) was significantly greater than that of intact controls (39.9 mg) yet was significantly smaller than those of the himicastrate group (58.9 mg).

The lower body weight in the thyroidectomized group may reflect a reduced food intake and WILLIAMS[6] has stressed this effect on compensatory hyperplasia. However, when the ovarian weights in the present study were expressed as percentages of total body weight, the resulting proportionate weights of the hemicastrate-thyroidectomized group were significantly different from those of both the intact and hemicastrate groups. Preliminary results from our laboratory suggest that administration of thyroxine (10 µg/day) to unilaterally ovariectomized-thyroidectomized rats has no effect on ovarian weight (50.5 mg).

PETERSON, EDGREN and JONES[7] demonstrated that ovaries of hemicastrate rats have an increase number of corpora lutea which may account for the increased weight of the remaining ovary. In the present study, removal of the thyroid significantly decreased the number of corpora lutea in the ovary of the hemicastrate. This reduction of corpora lutea partially explains the reduction in ovarian weight and may be a reflection of reduced gonadotropin release from the pituitary.

Résumé. Le nombre de corps jaunes dans l'ovaire de rates intactes, hémicastrées, hémicastrées et thyroïprivées fut déterminé. Les corps jaunes de l'animal thyroïprivé et hémicastré furent sensiblement plus petits que ceux de l'animal hémicastré. Cette diminution des corps jaunes se traduit par une diminution concomitante du poids ovarien et pourrait expliquer le blocage partiel de l'hypertrophie compensatrice du reste de l'ovaire.

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Comparative Responsiveness of Euthyroid and Hypothyroid Rat Pituitary Tissue to Thyrotropin Releasing Hormone in vitro

The hypothalamic thyrotropin releasing hormone (TRH) has been shown to elicit a prompt release of thyrotropin (TSH) from pituitary glands of several species of euthyroid animals in vitro[1–5]. The present study compares the release of TSH from euthyroid and hypothyroid rat pituitary tissue with varying doses of synthetic TRH in vitro.

Materials and methods. Euthyroid and thyroidectomized female Sprague-Dawley rats weighing 150–200 g were obtained from Charles-River. The thyroidectomized rats were sacrificed 21 days after thyroidectomy; in all cases the rats were sacrificed by decapitation and the pituitary glands were immediately removed and placed in TC 199 medium (Difco). Each pituitary gland was then hemisected; one half was placed in a 'control' test tube containing 1.0 ml TC 199 medium while the corresponding half was placed in an 'experimental' test tube also containing 1.0 ml of TC 199. Preincubation proceeded for 30 min at 37 °C with the medium renewed 1 time. At the preincubation period, each hemi-pituitary was placed in 1.0 ml of freshly oxygenated (95% O 5% CO) and pH adjusted (7.4) TC 199 medium containing either no additions (control hemi-pituitary) or 0.1, 1.0, 10.0, 100.0 or 1000.0 ng/ml synthetic TRH (Calbiochem) (experimental hemipituitary). In all cases a corresponding hemipituitary served as the control for the experimental hemipituitary. 4 rats were used for each dose of TRH. Incubation was then allowed to proceed at 37 °C with gentle agitation every 5 min. 10 ml aliquots of the incubation medium were obtained at 15, 30 and 60 min and immediately placed in medium for radioimmunoassay of rat TSH (rat TSH kit was obtained through the courtesy of Dr. A. PARLOW and NIAMD, Bethesda, Maryland). After each experiment the wet weights of the hemipituitaries were obtained by weighing on a Mettler balance to the nearest 0.01 mg. Serum thyroxine by competitive protein binding was undetectable in thyroidectomized animals.

Results. With increasing doses of TRH there is an increase in release of TSH with the maximum effect seen at 10–100 ng/ml TRH with both euthyroid and hypothyroid pituitaries. There was no significant difference between the responsiveness of euthyroid vs. hypothyroid pituitary tissue when exposed to 1.0, 10.0, 100.0, or 1000.0 ng/ml TRH at 15, 30, or 60 min. However, at 30 min and 60 min the response of the euthyroid pituitary tissue to 0.1 ng/ml TRH was significantly greater than

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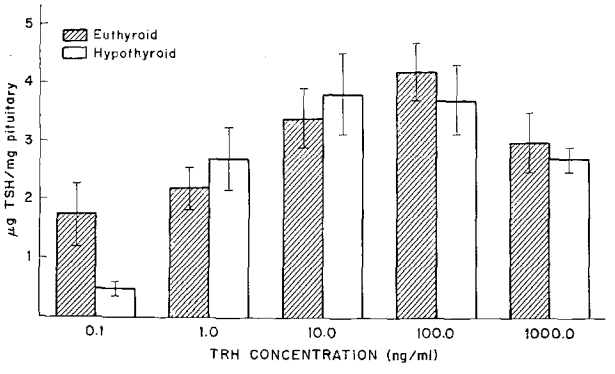
that of hypothyroid tissue ($p < 0.05$). With 1000 ng/ml TRH the mean increase in TSH was less than with 100 ng/ml; however, the difference was not statistically significant. These results are shown in the Figure.

Discussion. The results described above demonstrate that increasing doses of TRH elicit increasing release of TSH from pituitary tissue obtained from euthyroid and 21-day-thyroidectomized rats in vitro. The 0.1 ng/ml concentration of TRH was more effective in causing TSH release from euthyroid pituitaries than from hypothyroid pituitaries, the rate of release of both approaching maximum within 30 min.

Several alternatives might explain this finding of relative unresponsiveness of hypothyroid pituitary tissue to 0.1 ng/ml TRH. First, if it is true that the hypothalamic secretion of TRH increases in hypothyroidism, as has been suggested[6], then repeated exposure of the pituitary to increased concentration of TRH might result in a state of relative refractoriness to TRH. Progressive unresponsiveness to TRH following repeated infusions of TRH has been shown to occur by others[7]. Secondly, it is possible that the pituitary gland requires a minimal amount of thyroid hormone for its routine metabolic processes including the synthesis of TSH. If this is true, then the diminished responsiveness of the hypothyroid pituitary tissue to 0.1 ng/ml TRH might simply reflect a diminished metabolic activity that is overcome by larger concentrations of TRH. Lastly, it is possible that there are 2 'pools' of TSH, a 'labile' one responding to low doses of TRH present primarily in euthyroid pituitary tissue and a second form present in both euthyroid and hypothyroid pituitary tissue.

Euthyroid and hypothyroid pituitaries did not respond differently to the higher concentrations of TRH (1.0, 10.0, 100.0, 1000.0 ng/ml) and both euthyroid and hypothyroid pituitaries continued to release significant amounts of TSH at 60 min. If the pituitary concentration of biologically and immunologically active TSH is decreased in hypothyroidism, as has been shown by several investigators[8–13], and at the higher concentrations of TRH (1.0, 10.0, 100.0 and 1000.0 ng/ml) hypothyroid pituitary tissue is as capable of releasing TSH/mg pituitary as is euthyroid pituitary tissue, then it is possible that the pituitary gland of hypothyroidism possesses an enhanced potential to release TSH, a potential which becomes manifest at higher concentrations of TRH.

Zusammenfassung. Die Kapazität von Rattenhypophysen, auf eine TRH-Stimulation in vitro TSH auszuschütten, zeigt bei hohen TRH-Konzentrationen keine Differenz zwischen eu- und hypothyreoten Tieren, während eine niedrige TRH-Konzentration eine höhrere TSH-Ausschüttung bei Hypophysen euthyreoter Tiere verursacht.



Response of rat pituitary tissue to increasing concentrations of TRH after 60 min incubation in vitro. The results are expressed as mean increase of TSH in the experimental incubation medium minus the control medium per mg of pituitary tissue ± standard error of the mean.

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Loss of Sexual Activity in Rabbits Actively Immunized with Testosterone

Active immunization with testosterone or estrogens leads to hyperplasia and hyperfunction of the interstitial testicular tissue[1,2]. A decrease in the amount of free steroid available to hypothalamo-pituitary receptors caused by antibody binding and a subsequent increase in gonadotrophin secretion, despite high concentrations of total circulating testosterone or estrogen respectively[2], underlies these alterations. In general, it is assumed that steroids which have lost their ability to act on hypothalamo-pituitary receptors have also lost their biological activity. It was, however, recently observed that there is no obligatory correlation between peripheral androgenic effects of a given steroid and its ability to inhibit pituitary LH secretion[3]. A possible corollary to this evidence is that binding of testosterone to circulating antibodies might have different effects on androgen-sensitive receptors in different organ systems. Thus we were prompted to investigate the biological effects of testosterone in rabbits immunized against this androgen. Sexual activity, one of the most characteristic biological effects of testosterone, was chosen as a parameter for this study.

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