vent the excessive intracellular hydration of the adrenalectomized animals, these extrarenal hormonal actions were not significantly established. Alterations in potassium metabolism were also briefly discussed.

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Cortisone and Action of Exogenous Thyrotrophin in Hypophysectomized Rats.* (19560)

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Several workers have reported a depression of thyroid function by cortisone in man and in the rat(1-8). A block of the thyrotrophic function of the pituitary was suggested as a possible explanation of this phenomenon (5,6). Perry(4), however, presented data which are not in agreement with this concept and we made observations(9) which appeared to indicate that pituitary thyrotrophin (TSH) output is enhanced rather than depressed by cortisone. Woodbury *et al.*(10), on the other hand, described a striking modification of the action of exogenous TSH in hypophysectomized rats by cortisone. They found that the TSH induced increase in the thyroid I^{131} uptake of their animals was partly prevented by simultaneously administered cortisone. Since these findings do not necessarily indicate an interference of cortisone with TSH action *per se,* the present study was undertaken to assess the influence of the steroid on the effectiveness of exogenous TSH in hypophysectomized rats, using the change in thyroid cell height as the index of thyrotrophic stimulation. This technic has been used previously by Griesbach and Purves(11) for assay of TSH and recent observations by Ghosh *et al.*(12) have also shown a roughly rectilinear relationship between thyroid cell height increment and log dose of TSH administered to hypophysectomized rats.

Method. Hypophysectomized male rats weighing between 130-145 g were purchased from the Hormone Assay Laboratories, Chicago. Twelve days after the operation they were divided into 4 groups. Group I (14 rats) received no treatment, group II (15 rats) was injected with 5 mg of cortisone† daily for 10 days, group III (14 rats) received daily injections of .3 mg TSH‡ for 10 days, while group IV (16 rats) was treated for the same length of time with both cortisone and TSH in the aforementioned dosages. The rats were fed Purina Laboratory Chow supplemented with horse meat and fresh oranges. All treated animals, as well as the controls, were sacrificed 24 hours after the last injection. The thyroids were weighed on a torsion balance, fixed in SUSA, imbedded in paraffin and cut at 5 μ. Sections running through the center of the gland were stained with Gomori's trichrome method. The slides were projected and the height of one cell per follicle was measured in 50 follicles picked at random from each gland.

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† Cortisone (Cortone acetate Merck) was generously supplied by Dr. Elmer Alpert of Merck and Co., Rahway, N. J.

‡ TSH (Parke Davis #50P4) was made available through the courtesy of Dr. D. A. McGinty and Mr. W. Donaldson of Parke, Davis & Co., Detroit, Mich.

TABLE I. Thyroid Weights and Average Follicular Cell Heights in Hypophysectomized Rats Given Cortisone, TSH or Cortisone + TSH for 10 Days.

	Thyroid wt, mg	Avg cell height ± stand. error, μ
Controls	6.9	4.1 ± .18
5 mg cortisone daily	7.7	4.3 ± .10
.3 mg TSH daily	8.8	8 ± .15
5 mg cortisone + .3 mg TSH daily	8.4	9.1 ± .22

Results. The thyroid weight response to TSH (Table I) was not marked and its statistical analysis was considered meaningless since a painstaking dissection of the glands was not undertaken in order to avoid histological artefacts due to prolonged handling. The average thyroid cell height (Table I) was almost doubled by TSH. Cortisone in itself had no morphological effects on the cells of the thyroid follicles. The effectiveness of TSH on thyroid cell height, far from being inhibited, actually appeared to be slightly but significantly ($P < .01$) enhanced by simultaneously given cortisone.

Discussion. The findings reported in this paper support the conclusion of Perry(4) that cortisone does not act as a thyroid depressant by inhibiting the action of TSH. They also suggest that the data of Woodbury *et al.*(10) regarding the interference of cortisone with the increase in thyroid I^{131} uptake, which exogenous TSH brings about in hypophysectomized rats, should not be interpreted as a blocking effect of the steroid on TSH action itself. Our studies on cortisone treated intact rats(9) pointed to an increased release of TSH consequent to cortisone administration and the possibility that cortisone might act as a mild goitrogen was considered. The observation that cortisone apparently may increase the morphological response of the thyroid cells of hypophysectomized rats to TSH is compatible with the idea of an antithyroid action of cortisone, since a pronounced potentiation of TSH action by thiouracil has been encountered previously in a histological study on hypophysectomized rats(13).

Summary. 1. Groups of hypophysectomized rats were given 5 mg of cortisone daily, .3 mg of TSH daily, and 5 mg of cortisone + .3 mg TSH daily for 10 days. Measurements of thyroid cell height were made. 2. The average thyroid cell height was 4.1 μ in the hypophysectomized controls, 4.3 μ in the cortisone treated rats, 8.0 μ in the rats treated with TSH, and 9.1 μ in the animals which received both TSH and cortisone. 3. It is concluded that cortisone, under the conditions of the experiment, did not block and probably even slightly enhanced the effect of TSH on the thyroid.

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