Effect of Graded Levels of Parathyroid Extract and Calciferol Upon Thyroid Hormone Secretion Rate (TSR) in Normal Female Rats[1] (34167)

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In a previous study in this laboratory, it was reported that a parathyroid extract (PTE) at a level of 30 USP units/100 g of body wt/day increased thyroid hormone secretion rate (TSR) a significant 21% associated with a slight increase in body weight (1). In the same experiment calciferol at a level of 0.2 μg/100 g of body wt increased TSR 48% but was accompanied by a dramatic decrease in body weight from 203 to 175 g. In order to further confirm the evidence of a stimulating effect of these two preparations upon TSR, graded levels were administered.

Materials and Methods. Eighty-eight female rats of the Sprague-Dawley Rolfsmeyer strain were maintained at a temperature of 78 ± 1°F with uniform lighting conditions and fed Purina lab chow *ad libitum*. The first 44 rats were divided into three random groups and their individual TSR's were determined at a weight of about 174 g. The second 44 rats were also divided into three random groups and their individual TSR's were determined at a weight of about 251 g. Thyroid hormone secretion rate (TSR) was determined by the method described previously by Grosvenor and Turner (2) for each group. The TSR, as estimated by this procedure, will be slightly higher than the actual TSR of the animals, because the final level of thyroxine which blocks the release of thyroidal ^{131}I must be in slight excess of the animal's own secretion of the thyroid hormone. Secondly, as the level of thyroxine is increased by 0.25 μg/100 g of body wt every 48 hr and the dose previous to the final one does not completely block the release of thyroidal ^{131}I, the error must be less than 0.25 μg/100 g of body wt. Carrier-free ^{131}I was obtained from Nuclear Consultant Corporation, St. Louis, Missouri, and was diluted in distilled water to contain 10 μCi/0.2 ml, and administered to rats intraperitioneally. Thyroxine (L-T_4) was administered daily; the first administration was 48 hr after that of ^{131}I in increments of 0.25 μg/100 g of body wt. The dose of L-T_4 which prevented further thyroidal ^{131}I output, that is 95–100% of the previous count, was estimated as the TSR of the animals. Correction was made for the radioactive decay and background. Twenty-one days after the TSR was determined, the groups (I, II, III) were treated with graded doses of parathyroid extract (PTE) *i.e.*, 20, 30, and 40 USP/100 g of body wt, respectively, and the other groups (IV, V, VI) were treated with graded doses of calciferol *i.e.*, 0.1, 0.15, and 0.2 mg/100 g of body wt, respectively. This treatment was started 2 weeks (14 days) before the start of TSR estimation and continued until the TSR of the animals was estimated. The difference between the TSR of the first and second determination in the same animal was used as an indication of the effects of these materials (PTE[2] and calciferol[3]) upon the functional activity of the thyroid gland. When TSR estimations were completed the rats of group IV and VI were then sacrificed and the following glands were removed and weighed: ovaries, uteri, adrenals, thymus, and thy-

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roids. The balance was sensitive to 0.01 mg.

Results. Administration of 20, 30, and 40 USP units of PTE/100 g of body wt/day for 14 days caused significant ($p<.025$) increases in TSR of 25.4, 35.6, and 54.1%, respectively, over their own controls (Table I). The body weights were increased. Administration of calciferol (Vit. D_2) in doses of 0.1, 0.15, and 0.2 mg/100 g of body wt caused a nonsignificant reduction in TSR in the first two groups but a significant ($p<.05$) 26.7% increase in TSR and 14.2% decrease in body weight from their own control in the VI group which was treated with 0.2 mg of calciferol/100 g of body wt. A nonsignificant increase in weight of the ovaries, uteri and decrease of thymus glands weight was noticed in the group treated with 0.2 mg of calciferol/100 g of body wt as compared to the 0.1 mg of calciferol/100 g of body wt-treated group (Table II). There was a significant increase in thyroid weights ($p<.001$) and adrenal weights ($p<.01$).

Discussion. A definite relationship between Vitamin D and the thyroid gland was reported by Lands and Stoland (3), Nitzesco and Bratiano (4) and Utiola (5). A prolonged and chronic stimulation of thyroid glands may produce a condition of hyperthyroxinogenesis. In this condition, food utilization and energy liberation are increased. A severe hyperthyroidism is generally characterized by nervousness, increased cardiac output and velocity of the blood flow. Hyperthyroidism can also be induced by administration of an excess dose of thyroxine (6). A relationship between vitamin D and thyroid gland function was reported in the 1930's. Histological studies showed that administration of vitamin D caused hyperplasia of the thyroid gland of the dog (7). Vitamin D and parathyroid hormone are known to have similar action on bone absorption and gasterointestinal transport of calcium (8, 9). Deutsch *et al.* (10) concluded that the calorigenic effect exhibited by the vitamin was via the thyroid gland. Administration of vitamin D to rachitic rat was reported to increase the basal metabolic rate (11). On the other hand, a calorigenic effect was observed when a parathyroid extract was given to dogs (12).

TABLE I. Effect of Graded Level of Parathyroid Extract and Calciferol upon TSR in Intact Female Rats.[a]

Treatment	Groups	No. of rats	Before treatment: Body wt (g)	Before treatment: Mean TSR[b] (μg/100 g of body wt)	After treatment: Body wt (g)	After treatment: Mean TSR[b] (μg/100 g of body wt)	After treatment: Change (%)	Probability[c]
PTE (USP units/100 g of body wt)								
20	I	21	178	0.67 ± 0.06	212	0.84 ± 0.05	25.4	<.025
30	II	14	169	0.59 ± 0.02	188	0.80 ± 0.08	35.6	<.025
40	III	9	174	0.61 ± 0.06	197	0.94 ± 0.12	54.1	<.025
Calcifero (mg/100 g of body wt)								
0.1	IV	15	244	1.03 ± 0.07	240	0.98 ± 0.02	—4.9	NS
0.15	V	15	247	1.05 ± 0.08	237	1.03 ± 0.09	—1.9	NS
0.2	VI	14	261	1.05 ± 0.07	224	1.33 ± 0.15	26.7	<.05

[a] PTE = parathyroid extract; TSR = thyroid secretion rate; NS = nonsignificant.
[b] Mean ± SE.
[c] Student's *t* test, level of significance of TSR before and after treatment of the same animals.

TABLE II. Effect of Calciferol on Endocrine Glands in Female Rats.

	Calciferol (mg/100 g of body wt)		
	0.1	0.2	Change (%)
No. of rats	15	14	
Mean body wt (g)	240	224	
Mean ovary wt (mg)	58.20 ± 5.90[a]	60.10 ± 6.3[a]	3.28
Mean ovary wt (mg/100 g of body wt)	24.20 ± 2.40	26.80 ± 2.8	10.60
Mean uterus wt (mg)	531.00 ± 53.20	687.50 ±150.0	29.50
Mean uterus wt (mg/100 g of body wt)	221.20 ± 22.20	306.90 ± 70.5	38.70
Mean adrenal wt (mg)	51.00 ± 1.50	56.30 ± 2.9	10.40
Mean adrenal wt (mg/100 g of body wt)	21.30 ± 0.56	25.10 ± 1.3	18.20
			$p < .01$[b]
Mean thymus wt (mg)	242.10 ± 31.90	211.70 ± 19.5	—13.60
Mean thymus wt (mg/100 g of body wt)	100.20 ± 18.90	93.90 ± 10.7	—6.20
Mean thyroid wt (mg)	7.91 ± 0.90	12.97 ± 0.9	64.00
			$p < .001$
Mean thyroid wt (mg/100 g of body wt)	3.29 ± 0.40	5.80 ± 0.4	75.60
			$p < .001$

[a] ± standard error.

[b] p = Student's t test, level of significance.

It was also reported that parathyroid given to rabbits increased the conversion of glucose and organic acids to CO_2 in bone slices (13). Although no functional relationship between the parathyroid and thyroid glands has been reported, the investigation cited suggest the possible participation of parathyroid extract in the regulation of certain metabolic pathways. When PTE was injected at levels of 20, 30, and 40 USP units/100 g of body wt for 14 days, it increased TSR of rats 25, 35, and 54% as compared to their own previous TSR before treatment. When calciferol was injected for 14 days at levels of 0.1, 0.15, and 0.2 mg, TSR was significantly ($p<.05$) increased only in the group which was injected with 0.2 mg of calciferol/100 g of body wt. However, decreases in body weight were observed. It is expected that the most likely mode of action would involve the increased secretion and discharge of the thyrotropic hormone. However, it is possible that these substances may act directly upon the thyroid gland to increase the responsiveness of the glands to a given level of thyrotropin.

Summary. The effect of graded doses of parathyroid extract and calciferol upon thyroxine secretion rate (TSR) of normal female rats was studied with the aid of radioactive iodine ^{131}I. Administration of 20, 30, and 40 USP units of PTE/100 g of body wt/day for 14 days induced a significant ($p<.025$) increase in TSR of 25.4, 35.6, and 54.1%, respectively, over their own controls associated with slight increase in body weight. Administration of calciferol (Vit. D_2) in doses of 0.1, 0.15, and 0.2 mg/100 g of body wt induced a nonsignificant reduction in TSR of the first two groups (groups IV and V) but a significant 26.7% ($p<.05$) increase in TSR above their own control in group VI associated with loss of body weight of 14.2% when 0.2 mg calciferol/100 g of body wt was given daily for the same period. A nonsignificant increase in weight of ovaries, uteri, and a decrease of thymus glands with significant increase in thyroid and adrenal weights was noticed in the group treated with 0.2 mg of calciferol/100 g of body wt as compared to 0.1 mg of calciferol/100 g of body wt.

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