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INFLUENCE OF OESTROGEN ON THYROID FUNCTION AFTER ADRENALECTOMY

By

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The relationship between the thyroid, ovary and adrenal glands is very complicated. The activity of the adrenal cortex undergoes cyclic variation in female animals, with a maximal activity during the oestrous phase (*Anderson & Kennedy*, 1932; *Foster*, 1934, and *Zondek & Burstein*, 1952). The thyroid gland also undergoes cyclic variations, its activity being greatest during oestrus (*Soliman & Reineke*, 1954, and *Soliman & Badawi*, 1956). Oestrogen seems to be the common factor, as its administration to animals stimulates the functions of both the thyroid and the adrenal glands (*Soliman & Reineke*, 1955, and *Tepperman et al.*, 1943).

It is also evident that hyperthyroidism stimulates adrenal function as reported by *Wallach & Reineke* (1949), while adrenocortical extracts markedly diminish thyroid function (*Soffer et al.*, 1949). With these findings in mind, it was decided to investigate how the adrenal gland affects the response of the thyroid to oestrogen.

MATERIAL AND METHODS

Forty-eight adult female rats weighing 210 to 250 gm. were used. Twenty-four were ovariectomized and then divided into three groups of eight animals. The rest were ovariectomized and adrenalectomized and divided into three groups. Both operations were performed by the dorsal approach.

All groups of animals were fed an iodine deficient diet (*Remington*, 1937). The adrenalectomized rats were maintained on 1% NaCl in double distilled water, while the remaining animals were maintained on double distilled water. The animals were injected intraperitoneally daily with 5 μ g. of NaI in 0.2 ml. of double distilled water.

Oestradiol benzoate (Schering) was diluted so that either 1 or 50 μ g. was contained

in 0.1 ml. of corn oil. Groups I and IV, as indicated in Table 1, were kept as controls and injected intraperitoneally with 0.1 ml. corn oil. Groups II and V were injected with 1 μ g. of oestradiol benzoate 48 hours before the end of the experiment. The animals in groups III and VI were injected with 50 μ g. of oestradiol benzoate every other day for twenty days. The last injection was given 48 hours before the end of the experiment. All rats were then injected intraperitoneally with 0.5 microcuries of I^{131} six hours before autopsy. The animals were killed with ether, their thyroids dissected, weighed on a torsion balance and counted with a Geiger counter in a constant position relative to the counter. The pituitary glands and adrenals were also weighed. The data were analysed statistically using the «t» test.

RESULTS

I^{131} Uptake: As shown in Table 1 the I^{131} uptake by the thyroids of ovariectomized - adrenalectomized rats was less than that of the ovariectomized animals. It is also seen that the administration of a single dose of 1 μ g. oestra-

Table 1.
Influence of oestrogen on organ weights and I^{131} uptake by the thyroids of ovariectomized and ovariectomized-adrenalectomized rats.

Group	Treatment	Body weight		Thyroid wt. mg./100 gm.	Adrenal wt. mg./100 gm.	Pituitary wt. mg./100 gm.	I^{131} uptake % dose
		Initial	Final				
I	Spayed control	233.62 * \pm 9.73	269.62 \pm 3.91	5.85 \pm 0.21	15.82 \pm 1.70	4.77 \pm 0.40	15.03 \pm 0.66
II	Spayed - 1 μ g. oestradiol benz.	233.00 \pm 7.42	264.50 \pm 3.23	6.42 \pm 0.39	20.17 ² \pm 0.94	5.42 \pm 0.30	17.69 ¹ \pm 0.68
III	Spayed - 50 μ g. oestradiol benz.	217.75 \pm 6.49	233.00 \pm 6.15	7.37 ¹ \pm 0.16	24.45 ² \pm 2.09	5.83 \pm 0.10	15.97 \pm 0.75
IV	Spayed adrenalectomized control	216.00 \pm 4.80	226.50 \pm 2.90	7.17 \pm 0.50	-	4.37 \pm 0.33	11.26 ² \pm 0.61
V	Spayed adrenalectomized - 1 μ g. oestradiol benz.	226.50 \pm 7.14	237.25 \pm 2.47	8.05 ¹ \pm 0.45	-	5.16 \pm 0.20	20.48 ² \pm 0.96
VI	Spayed adrenalectomized - 50 μ g. oestradiol benz.	230.00 \pm 7.97	221.28 \pm 4.66	8.13 ¹ \pm 0.50	-	5.97 ¹ \pm 0.14	13.42 ¹ \pm 1.22

Each group contained 8 rats.

* Standard error.

¹ Significant at 5 per cent level when compared to its control.

² Significant at 1 per cent level when compared to its control.

diol benzoate increased the uptake of I^{131} . This increase was significantly greater in ovariectomized - adrenalectomized rats than in rats which were ovariectomized only.

The radioactive iodine uptake by the thyroids of ovariectomized - adrenalectomized rats treated with 10 doses of 50 μ g. of oestradiol benzoate injected every other day exceeded that of their controls. This same treatment did not influence the I^{131} uptake by the thyroids of the ovariectomized rats with their adrenals intact.

Organ Weights: The thyroid weights of rats treated with large doses of oestrogen had significantly heavier thyroids than their controls. The pituitary weights did not vary as a result of the different treatments. The adrenal weights of oestrogen treated animals were significantly heavier than those of the controls.

DISCUSSION

It is apparent from the present investigation that the I^{131} uptake by the thyroids of ovariectomized - adrenalectomized rats was much less than that of ovariectomized animals. *Flückiger & Verzár* (1955) found that thyroid function is slowed down after adrenalectomy as the thyroid hormone is then released more slowly by the thyroid. They believe that the most probable cause for this is that in adrenalectomized animals very little thyroxine is needed since certain metabolic processes are decreased. It is also possible that the adrenals are essential for the normal function of the thyroid.

The present data also show that the thyroid stimulating effect of oestrogen was more pronounced when the adrenals were removed. It is known that adrenocortical hormones have a depressant effect on thyroid function (*Soffer et al.*, 1949; *Williams et al.*, 1949, and *Gabrilove et al.*, 1950). It is also well established that oestrogen has a stimulating effect on the adrenal cortex (*Heskett & Hoffman*, 1943, and *Bourne & Zuckerman*, 1940). In the presence of the adrenal the oestrogen stimulating effect on the thyroid becomes weakened by the stimulated adrenal functions. These mechanisms could explain the non-responsiveness of the thyroid to prolonged administration of oestrogen in animals with intact adrenals, while the same treatment activates the thyroid when the adrenals are removed.

SUMMARY

Ovariectomized and ovariectomized - adrenalectomized rats were treated with either a single dose of 1 μ g. of oestradiol benzoate or with 10 doses of 50 μ g. of oestrogen given on alternate days. The six-hour radioactive iodine uptake

by the thyroids was determined. I¹³¹ uptake by the thyroid of ovariectomized - adrenalectomized rats was significantly lower than that of rats ovariectomized only. The I¹³¹ uptake by the thyroids of ovariectomized - adrenalectomized rats treated with 1 μ g. oestradiol was higher than that of rats with intact adrenals and given the same dose of oestrogen. The administration of 10 doses of 50 μ g. of oestradiol on alternative days did not change the I¹³¹ uptake by the thyroids of rats with intact adrenals as compared with their controls. The same treatment increased the I¹³¹ uptake by the thyroids of adrenalectomized rats as compared with their controls.

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