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Adrenotrophic Action of ACTH in Thyroidectomized Rats

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Normal rats were thyroidectomized at an early age and kept on low iodine diet with two group controls (age and weight). After the experimental period the adrenal weight was recorded and significant differences were found between age control and thyroidectomized rats, and between the late group and weight control rats when injected with ACTH. This could be interpreted as a permissive effect of the thyroid hormones on the action of ACTH on the adrenal gland.

The effect that thyroidectomy has on the suprarrenal gland is not clear. Different authors (1, 3, 4, 5) working in thyroid adrenal inte-relationship, obtained contradictory results.

On a different line of work, EVANS *et al.* (2), showed deffinitively that in thyroidectomized rats iodide restores the capacity for growth, metabolic and heart rates, and reproductive function. The same group of authors suggest that this is due to the extrathyroidal synthesis of thyroid hormone in the rats, when they are fed on diet with a high iodine content (10). These findings induce to reconsidere some of the works on thyroid physiology. It could be that the disagreement on the alterations in suprarrenal gland in the thyroidectomized rats is due to a lack of control of the iodide content in the diet of the experimental animals used by different workers (6, 8, 9).

In the present work we have tried to study the changes on adrenal weight in thyroidectomized rats kept on low iodine diet, and the effect of treatment with iodine, triiodo-thyronine (T_3) and adrenocorticotrophic hormone (ACTH) as compared with controls.

Materials and Methods

Male Nestle rats were used. They were weaned at 21 days of age and fed on a comercial diet containing less than 1 μg of iodide/g. When they reached the weight of 80 g (40 days of age), they were surgically thyroidectomized and 4 days latter were injected with 500 μC carrier free 131-I. The rats were exposed to 12 hr of constant illumination daily at $22 \pm 1°$ C, and weighed weekly. Two months after thyroidectomy we began the treatment with KI, T_3 and ACTH. Two types of

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control animals were used: rats with the same weight (weight controls of 50 days of age) and rats the same age (age controls).

Potassium iodide (KI from B.D.H.) was dissolved in sterilized 0.9 % NaCl. ACTH, was a commercial preparation from Alter Lab. T_3 (Light and Cie.) was dissolved in NaOH saline solution *p*H 8. All three solutions were prepared fresh weekly and kept in dark bottles under refrigeration. They were injected subcutaneously once daily for four days in a volume of 0.25 ml. The controls were injected with the same volumen of saline solution.

Table I. *Effect of ACTH on the body weight and adrenal weight in thyroidectomized rats.*

The data correspond of media values. Number of rats in all groups: 8. All groups were injected for 3 days, except those with T_3, wich were injected for 4 days.

The administration of T_3 was at doses of 0.01 µg/day; ACTH, 1 I.U./day and KI, 1 mg/day.

The mean of age control is significantly different from corresponding values for weight control and thyroidectomized ($P < 0.05$).

The mean of thyroidectomized + ACTH is significantly different from corresponding value for weight control + ACTH ($P < 0.05$).

The mean of thyroidectomized + T_3 is significantly different from corresponding values for age control and weight control + ACTH ($P < 0.05$).

Groups	Body weight g	Adrenal weight (mg) fiducial limits (95 %)
Weight control	146.10	15.88 (14.96-16.96)
Age control	247.00	23.15 (21.62-24.31)
Weight control + + ACTH	155.00	30.13 (26.63-31.25)
Thyroidectomized	159.37	13.75 (12.67-14.83)
Thyroidectomized + + ACTH	140.00	17.00 (16.08-18.08)
Thyroidectomized + + T_3	140.00	17.13 (16.24-18.21)
Thyroidectomized + + T_3 + ACTH	144.12	27.75 (26.85-28.83)
Thyroidectomized + + KI + ACTH	155.00	20.56 (19.55-21.57)

At the end of the experiments the rats were killed by decapitation and the adrenals cleaned from fat and weighed immediately.

Results

The growth rate of the experimental animals are shown in figure 1. Results with fiducial limits (95 %) for adrenal weight and average body weights, in different situations, are shown in table I.

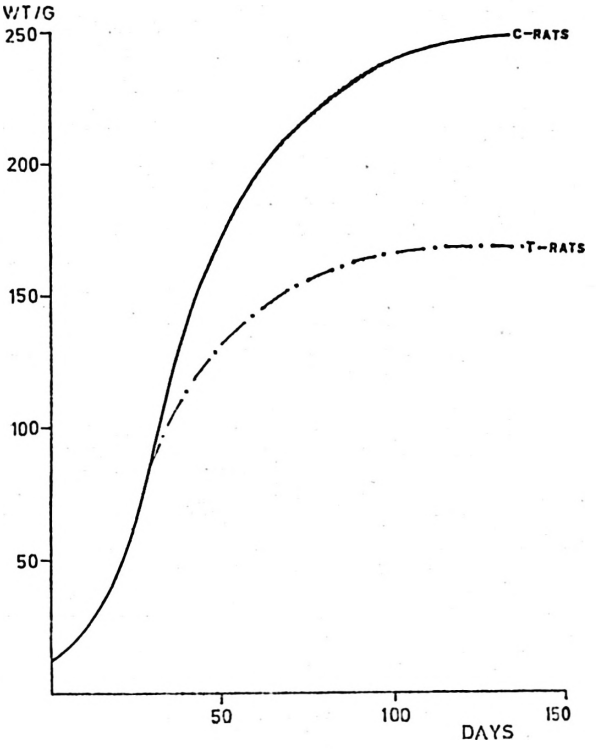

Fig. 1. *Comparison of the body weight evolution in thyroidectomized (T) and control (C) rats.*

Discussion

The rat has a large reserve of thyroid hormone circulating in blood bound to de plasma proteins, and this may be the reason why they go on growing for a month after thyroidectomy, until this store is emptyed. It was important for our study to work with animals absolutely free of thyroid hormone. To ensure this, we

waited one more month after the wheight plateau was reached, before starting the treatments (8, 9).

The changes in adrenal weight seem to show that under the conditions that our rats are kept, there is significant differences between our age controls and the thyroidectomized rats and there is no difference between the thyroidectomized and the weight controls. This may be interpreted as showing that thyroid hormone is needed for growth of the adrenal gland as it is needed for the growth of any organ in the rat, but does not show any specific action of thyroid hormone on the adrenal gland.

The differences in adrenal weight between thyroidectomized rats and weight controls are highly significant in the groups of rats treated with ACTH. These results point to the possibility that ACTH has no corticotrophic effect in thyroidectomized rats kept on low iodine diet. The corticotrophic effect of exogeneous ACTH is restored if the thyroidectomized rats are injected with a daily dose of 0.01 gamma of T_3 for four days. T_3 was used instead of thyroxine because the former does not accumulate in the rats blood (8).

The same dose of T_3 alone for the same period of time does not produce an increase in suprarrenal weight in these animals. The results obtained in the rats treated with KI confirme EVANS and TAUROG (2, 10) hypothesis that the administration of iodide may correct some of the signs of thyroide hormone defficiency in the thyroidectomized rat.

The fact that the doses of T_3, which fully restores the corticotrophic effect of ACTH has practically no effect on body growth (2, 10) plasma cholesterol or metabolic rate of thyroidectomized rats, makes it worth to considere the possibility that the thyroid hormone has cualitative different actions according to its concentrations in blood: at a very low concentration it could develope this type of «permissive action» on the effect of other hormones; at higher levels would induce the known physiological effects of thyroid hormone (allow body growth, increase metabolic, rate and heart rate), and at great levels will produce its pharmacological effects by uncoupling oxidative phosphorylation or by modifying the structure of mitochondria (7).

References

1. ELMER, A. W., GIEDOSZ, B. and SCHEPS, M.: *C. R. Soc. Biol.*, **133**, 309, 1940.
2. EVANS, E. S., ROBERT, A., SCHOOLEY, A. B., EVANS, C. A., JENKINS, T. R. and TAUROG, A.: *Endocrinol.*, **78**, 983, 1966.
3. HALMI, N. S. and BARKER, S. B.: *Endocrinol.*, **51**, 127, 1952.
4. HARRINGTON, C. H.: «Thyroid gland: its chemistry and physiology». Oxford Univ. Press, London, 1933.
5. HUM, R. F., GODHERG, R. C. and CHAICOFF, J. L.: *Endocrinol.*, **49**, 21, 1951.
6. LEVINE, H. and REMINGTON, R. E.: *J. Nutr.*, **6**, 325, 1933.
7. LOOMIS, W. R. and LIPMANN, F.: *J. Biol. Chem.*, **173**, 807, 1948.
8. MORELL, M., RODRÍGUEZ, E. and OSORIO, C.: *6th FEBS Abstract.* 600, Madrid, 1969.
9. MORELL, M., OSORIO, C. and RODRÍGUEZ, E.: *Actas 2.° Col. Intern. Gonadotrofinas humanas*, **1**, 283, 1969.
10. TAUROG, A. and EVANS, E. S.: *Endocrinol.*, **80**, 915, 1967.