# EFFECT OF TESTOSTERONE AND ITS 5α-DERIVATIVES ON PLASMA THYROTROPHIC AND THYROID HORMONE LEVELS IN RATS

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Relations between the thyroid gland and gonads are complex and exhibit sex differences. For instance, whereas estrogens evidently potentiate hormone formation in the thyroid gland [3, 4], information on the effect of androgens on thyroid function is highly contradictory [1, 2, 6]. There are no data whatever on the effect of physiologically active products of testosterone metabolism on the thyroid gland.

The object of this investigation was to study the effect of testosterone and its 5α-reduced metabolites (dihydrotestosterone and 5α-androstane-3β, 17β-diol on the concentration of iodothyronines and thyrotrophin (TSH) in the blood plasma.

## EXPERIMENTAL METHOD

Experiments were carried out on 110 male Wistar albino rats weighing 180-200 g. The animals were divided into eight groups (from 8 to 12 rats in each group). Group 1 included control animals, receiving persic oil by subcutaneous injection in a dose of 0.2 ml daily for 14 days. The animals of groups 2, 3, and 4 received testosterone propionate, dihydrotestosterone, and androstanediol respectively in a dose of 1 mg in 0.2 ml persic oil, also by subcutaneous injection daily for 14 days. In some experiments a model of an excited thyroid gland was used, for which purpose the rats were subjected to partial thyroidectomy (three quarters of the thyroid parenchyma was removed). Seven days after the operation the animals were given injections of persic oil (control for this series, group 5), testosterone propionate (group 6), dihydrotestosterone (group 7), or androstanediol (group 8) by the scheme described above. At the end of the experiment the animals were autopsied and blood collected. The levels of TSH and tri-iodothyronine ($T_3$) in the blood plasma of all rats were determined by test kits from Cea-Ire-Sorin (France—Italy), the levels of total thyrozine ($T_4$) and the thyroxine-binding capacity of the plasmaproteins ($T_3$ test) using radioimmunologic kits from Byk-Mallinckrodt (West Germany), and the free thyroxine index (FTI) was calculated as the quotient by dividing the total thyrozine level by the value obtained for the $T_3$ test. The results were subjected to statistical analysis.

## EXPERIMENTAL RESULTS

Parameters of the state of thyroid function in rats treated with testosterone propionate and its metabolites are shown in Table 1. Administration of all these androgens caused no marked change in the blood TSH level compared with the control. Meanwhile the effect of the male sex hormone and its metabolites on the thyroid gland was exhibited quite clearly. Whereas in control animals receiving persic oil only the blood thyroxine level was 6.04 μg/100 ml, and the tri-iodothyronine level 1.8 ng/ml, in agreement with data in the literature [5, 6], administration of testosterone propionate led to an increase in the $T_4$ and $T_3$ levels, whereas dihydrotestosterone and androstanediol, on the other hand, led to a significant fall in these parameters. The FTI was increased in animals receiving testosterone

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TABLE 1. Effect of Testosterone and Its 5α-Reduced Metabolites on Parameters of Thyroid Function in Rats (M ± m)

| Substance injected | TSH, microunits/ml | $T_4$, μg/100 ml | FTI | $T_3$, ng/ml | $T_3$-test |
|---|---|---|---|---|---|
| Persic oil (control) | 41,0±0,7 | 6,04±0,81 | 7,06±1,20 | 1,86±0,32 | 0,78±0,01 |
| Dihydrotestosterone | 39,6±0,7 | 1,96±0,38* | 1,67±1,47 | 0,85±0,42* | 1,14±0,32 |
| Androstanediol | 41,0±0,7 | 4,64±0,75* | 5,01±0,50 | 1,12±0,25 | 1,12±0,26 |
| Testosterone propionate | 42,6±1,0 | 10,36±0,44* | 12,40±1,27* | 2,48±0,31 | 0,85±0,14 |

Legend. Here and in Table 2: * $pH \leqslant 0.05$ compared with control.

TABLE 2. Effect of Testosterone and Its 5α-Reduced Metabolites on Parameters of Thyroid Function in Rats After Partial Thyroidectomy (M ± m)

| Substance injected | TSH, microunits/ml | $T_4$, μg/100 ml | FTI | $T_3$, ng/ml | $T_3$-test |
|---|---|---|---|---|---|
| Persic oil (control) | 59,7±1,3 | 5,32±0,92 | 7,09±1,17 | 2,06±0,33 | 0,62±0,14 |
| Dihydrotestosterone | 51,8±0,9 | 3,0±0,7* | 3,33±0,72* | 0,88±0,21* | 1,18±0,10* |
| Androstanediol | 52,4±0,8 | 3,42±0,85 | 4,36±0,87 | 0,81±0,27* | 0,71±0,16 |
| Testosterone propionate | 50,9±0,9 | 5,10±0,89 | 6,63±0,86 | 2,16±0,28 | 0,84±0,01 |

propionate, but unchanged in rats receiving its 5α-derivatives. Changes in the $T_3$ test (characterizing thyrozine-binding ability of the plasma) were not observed (Table 1).

In rats subjected to partial thyroidectomy, as a result of blocking of the negative feedback mechanism the blood TSH level rose from 41 to 50 microunits/ml. Injection both of testosterone and of its 5α-derivatives into these animals caused no significant changes in the blood TSH level compared with that in the control rats receiving only persic oil after partial thyroidectomy (Table 2).

Consequently, an excess of androgens did not affect the thyrotrophic function of the pituitary. Determination of the levels of thyroid function in rats 21 days after partial thyroidectomy showed that the $T_3$ and $T_4$ levels were restored to their normal values, in agreement with data in the literature [8]. Injection of testosterone propionate into these animals did not affect blood levels of $T_3$ and $T_4$ of FTI. The thyrozine-binding capacity of the plasma also was unchanged. Dihydrotestosterone and androstanediol reduced the blood levels of iodithyronines in rats subjected beforehand to partial thyroidectomy compared with the corresponding values in control animals receiving only persic oil after partial thyroidectomy (Table 2). Androstanediol did not affect the thyrozine-binding capacity of the plasma, whereas dihydrotestosterone significantly reduced it.

Comparison of the results shows that, first, testosterone and its metabolites affect the thyroid gland not through adenohypophyseal TSH but, evidently, directly; second, effects caused by these androgens in the thyroid gland are not identical and they depend on the state of thyroid function. Whereas testosterone stimulates intrathyroid hormone production in the intact gland and does not change its state in the previously excited gland, its 5α-reduced metabolites, on the other hand, inhibit thyroid activity, lower the blood levels of thyrozine and tri-iodothyronine, and lower FTI, both in intact and in partially thyroidectomized animals.

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