

# Androgenic-anabolic steroid effects on serum thyroid, pituitary and steroid hormones in athletes

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## ABSTRACT

Endocrine responses in seven power athletes were investigated during a 12 week strength training period, when the athletes were taking high doses of androgenic-anabolic steroids, and during the 13 weeks following drug withdrawal. During the use of steroids significant decreases ( $P < 0.05$  to  $0.001$ ) in the serum concentrations of thyroid stimulating hormone, thyroxine, triiodothyronine, free thyroxine, and thyroid hormone-binding globulin (TBG) were found, whereas the value of triiodothyronine uptake increased ( $P < 0.001$ ). In relation to the changes in the thyroid function parameters measured, we suggest that the primary target of androgen action was TBG biosynthesis. In five of the seven subjects, serum concentrations of growth hormone increased at some point of the study 5 to 60-fold. Because of the use of exogenous testosterone, serum testosterone concentration tended to increase. This increase was associated with a corresponding increase ( $P < 0.001$ ) in serum estradiol. Furthermore, there were major decreases in serum LH ( $P < 0.01$ ) and FSH ( $P < 0.01$ ) concentrations, and testicular testosterone production was therefore decreased. This was characterized by a very low serum testosterone concentration ( $5.1 \pm 1.8$  nmol/l) 4 weeks following drug withdrawal. Cessation of drug use resulted in return of all the variables measured to the initial values, except for serum testosterone, which was at a low level ( $14.6 \pm 8.8$  nmol/l) 9 weeks after drug withdrawal, indicating prolonged impairment of testicular endocrine function.

No consistent changes were found in the eight control athletes.

A recent trend in the use of anabolic hormones in power events seems to be the incorporation of testosterone conjugates among the anabolic steroids administered.<sup>2,10,23</sup> This form of drug self-administration may lead to simultaneous use of very high doses and of several compounds,<sup>3,12,13</sup> the obvious reason being the favorable effect on performance of power athletes.<sup>1,11</sup>

This use of high doses of androgenic-anabolic steroids leads to hypogonadotrophic hypogonadism.<sup>4,16</sup> The hypogonadal state is characterized by remarkably impaired spermatogenesis<sup>21</sup> and decreased circulating concentrations of LH, FSH, testosterone (T), and several of its precursors and metabolites.<sup>4,20</sup> In addition, the induced hyperandrogenic state is associated with greatly decreased concentrations of sex hormone-binding globulin, SHBG.<sup>20</sup>

It was anticipated that the use of high doses of androgenic-anabolic steroids might also influence the concentrations of circulating thyroid hormone-binding globulin (TBG), known to be affected by treatment with danazol in a way similar to the way that SHBG is affected.<sup>14</sup> This could be reflected in the parameters of thyroid function, such as thyroxine ( $T_4$ ), triiodothyronine ( $T_3$ ), thyroid stimulating hormone (TSH), free thyroxine ( $FT_4$ ), free thyroxine index ( $FT_4I$ ), and triiodothyronine uptake ( $T_3U$ ). On certain of these variables, data already exist showing that these serum concentrations can be modified by androgenic-anabolic steroids.<sup>7-9,22</sup> The purpose of the present investigation was to study the effects of self-administered testosterone and anabolic steroids in high doses on thyroid function parameters in association with strength training. In addition, the concentrations of

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circulating growth hormone, gonadotropins, testosterone, estradiol, and cortisol under these conditions were measured.

## METHODS

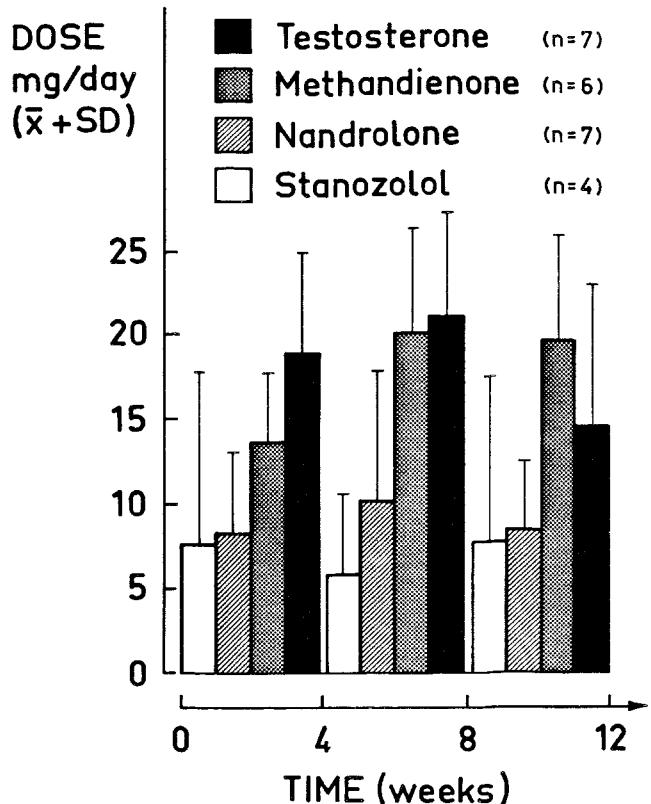
Seven competitive power athletes (mean age 29 years, range 24 to 34, mean weight 95 kg, range 80 to 103) who had previous experience in the use of androgenic steroids in their strength training, volunteered for this investigation and gave written informed consent to be studied. They were included in the study at the moment when they again decided to start the self-administration of testosterone and anabolic steroids. By this time all these athletes had been without any androgenic-anabolic steroids for a period of 10 to 12 weeks.

Because it is illegal in Finland for medical doctors to give a prescription for testosterone or anabolic steroids for other than medical reasons, the power athletes obtained their drugs on the black market and used them independently for the usual 3 months. Thus, for the purpose of this investigation,<sup>4</sup> power athletes who were selected had individual self-planned programs in strength training and in the use of testosterone and anabolic steroids. The athletes agreed to keep medication diaries, which made it possible to monitor the drug use. Reported mean daily doses of self-administered drugs are shown in Figure 1. Methandienone was taken orally by most of the subjects on a daily basis. Nandrolone and stanozolol (both 50 mg per injection) were usually self-injected once a week. Testosterone (250 mg per injection, consisting of 30 mg testosterone propionate, 60 mg testosterone phenylpropionate, 60 mg of testosterone isocaproate, and 100 mg testosterone decanoate) was self-administered one to two times per month.

Subjects trained for their specific power event (including high resistance strength training but no aerobic exercises) an average of six times per week and 1½ hours per training session. The athletes followed a high caloric diet with protein supplements.

After one day of reduced training and an overnight fast the subjects entered the laboratory at 7:00 a.m. for blood sampling and medical examinations. Venous blood samples were drawn from the antecubital vein at 7:00 to 8:00 a.m. in a recumbent position. After clotting, the serum was separated by centrifugation, and the sample was frozen and stored at -20°C for subsequent analyses. The height, weight, and subscapular, triceps, biceps, and iliac crest skinfold thicknesses of the subjects were measured. The amount of body fat was estimated according to the method of Durnin and Rahaman.<sup>6</sup> These procedures were performed at 0, 4, 8, 12, 16, and 25 weeks of strength training in the experimental subjects. The characteristics of the experimental subjects are given in Table 1. Eight men served as control subjects (mean age 31 years, range, 23 to 34; mean weight 75 kg, range, 56 to 86; mean body fat 13.5%, range, 9.5% to 19.0%). They all were training with weights two to three times a week without any competitive purposes. Blood samples were obtained from the control subjects at 0 and 25 weeks.

**Hormone determinations.** All hormone measurements



**Figure 1.** Reported mean daily doses (+SD) of self-administered testosterone and anabolic steroids (mg/day) of the experimental group. Trivial and systematic names: testosterone; 17 $\beta$ -hydroxy-4-androsten-3-one; methandienone: 17 $\alpha$ -methyl-17 $\beta$ -hydroxy-1, 4-androstadien-3-one, nandrolone; 17 $\beta$ -hydroxy-4-estren-3-one, stanozolol; 17 $\alpha$ -methyl-5 $\alpha$ -androstano 13, 2-d-pyrazol-17 $\beta$ -ol.

were performed by radioimmunoassays. Reagents for the determination of TSH, T<sub>4</sub>, T<sub>3</sub>, T<sub>3</sub>U, testosterone, estradiol (E<sub>2</sub>), cortisol, LH, FSH, and SHBG were purchased from Farnos Diagnostica, Turku, Finland; the reagents for FT<sub>4</sub> from Diagnostic Products Corporation, Los Angeles, USA; those for TBG from Behringwerke AG, Marburg, Germany; and the reagents for GH from Pharmacia Diagnostics AB, Uppsala, Sweden.

Serum albumin was measured spectrophotometrically using bromocresol green reagent, Albustrate (General Diagnostics, New York).

Means, standard deviations, and standard errors were calculated. The significance of intragroup differences was estimated using the two-tailed Student's *t*-test for paired means, and the significance between the experimental and control groups by using the *t*-test for unpaired means (SPSS program).<sup>17</sup> A *P* value of less than 0.05 was selected as the limit of statistical significance.

## RESULTS

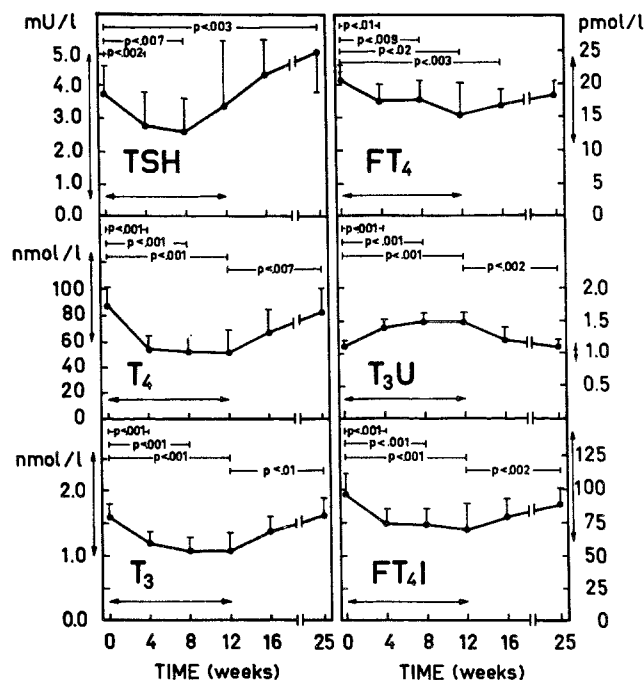
The changes in serum concentrations of TSH, T<sub>4</sub>, T<sub>3</sub>, FT<sub>4</sub>, T<sub>3</sub>U and FT<sub>4</sub>I are shown in Figure 2, and those of TBG and

TABLE 1  
Body weight and estimated body fat content of power athletes ( $N = 7$ ) self-administering androgenic/anabolic steroids during the weeks 0–12 ( $\leftarrow\rightarrow$ )<sup>a</sup>

Variable	Time (weeks)					
	0	4	8	12	16	25
Weight (kg)	90.0 $\pm$ 9.2	95.5 $\pm$ 10.0 <sup>b</sup>	96.9 $\pm$ 10.5 <sup>b</sup>	98.2 $\pm$ 11.6 <sup>b</sup>	97.1 $\pm$ 8.9 <sup>b</sup>	95.5 $\pm$ 8.0 <sup>b</sup>
Fat (%)	11.1 $\pm$ 2.7	11.6 $\pm$ 3.6	10.5 $\pm$ 2.2	10.4 $\pm$ 2.7	11.0 $\pm$ 3.2	11.3 $\pm$ 3.6

<sup>a</sup> Values indicate means  $\pm$  SD.

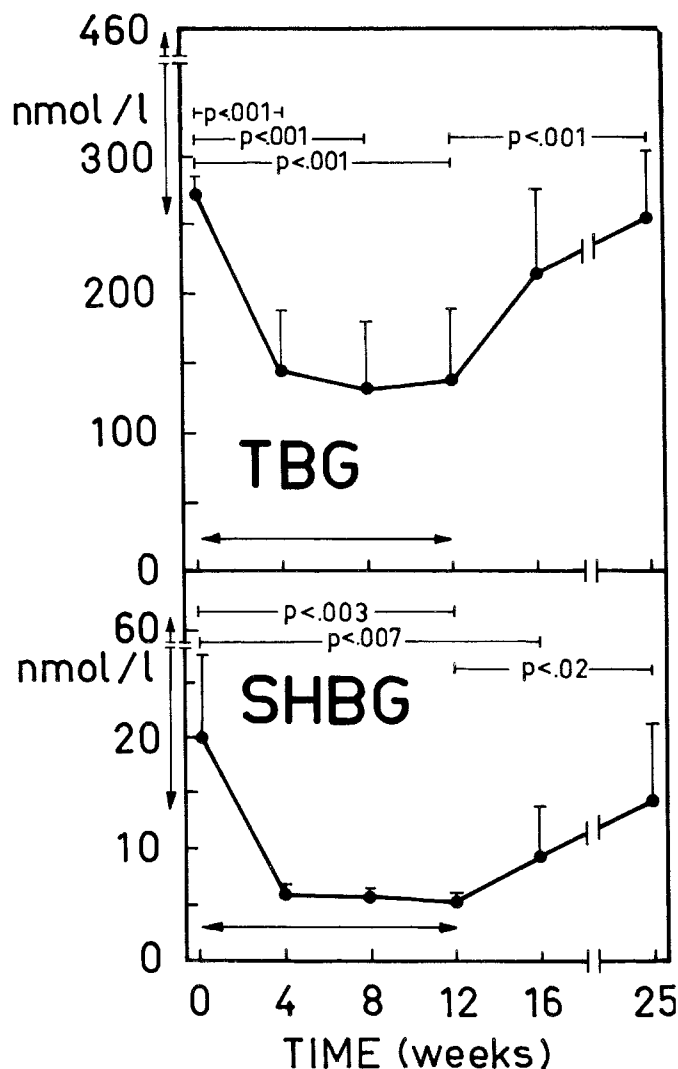
<sup>b</sup> Statistical significance for intragroup differences (two-tailed Student's *t*-test,  $P < 0.001$ ).



**Figure 2.** Serum concentrations of thyroid stimulating hormone (TSH), thyroxine ( $T_4$ ), triiodothyronine ( $T_3$ ), free thyroxine ( $FT_4$ ) and values of triiodothyronine uptake ( $T_3U$ ) and calculated free thyroxine index ( $FT_4I$ ) in the experimental group ( $N = 7$ ). Mean values, standard deviations, and statistical significances of intragroup differences are given (two-tailed Student's *t*-test). The use of androgens ( $\leftarrow\rightarrow$ ) and health-associated reference intervals ( $\dagger$ ) are indicated.

SHBG in Figure 3. The concentrations of serum albumin remained unchanged during the androgenic-anabolic steroid use (data not shown). There were no significant differences in the parameters measured between the experimental and control groups at the beginning of the investigation, and they did not change at all during the experiment in the control group, despite strength training (data not shown).

The use of large doses of androgenic-anabolic steroids led to significant decreases in the serum concentrations of TSH,  $T_4$ ,  $T_3$ ,  $FT_4$ , (Fig. 2), TBG and SHBG (Fig. 3), whereas the value of  $T_3U$  increased. The serum concentrations of the trophic hormones (LH, FSH), GH, and steroids ( $T$ ,  $E_2$ , cortisol) in the experimental group during the study are shown in Table 2. The use of synthetic androgens resulted



**Figure 3.** Serum concentrations of thyroxine-binding globulin (TBG) and sex hormone-binding globulin (SHBG) in the experimental group. For details see Figure 2.

in significant and expected decreases in serum concentrations of LH and FSH. In contrast to this, there was a significant increase in serum  $E_2$  concentrations, and a tendency to elevated  $T$  concentrations. The concentration of serum GH did not show consistent changes. In five of the subjects, at 8 and/or 12 weeks of the self-treatment, serum

TABLE 2

Serum concentrations of luteinizing hormone (LH) follicle stimulating hormone (FSH), growth hormone (GH), testosterone (T), estradiol ( $E_2$ ) and cortisol in the experimental group ( $N = 7$ ).<sup>a</sup>

Variable	Time (weeks)					
	0	4	8	12	16	25
LH (U/l)	6.8 ± 1.5	4.1 ± 1.0 <sup>b</sup>	4.1 ± 0.6 <sup>b</sup>	4.7 ± 0.3 <sup>b</sup>	5.2 ± 2.1 <sup>b</sup>	8.0 ± 2.5
FSH (U/l)	3.2 ± 1.6	1.0 ± 0.1 <sup>b</sup>	1.0 ± 0.1 <sup>b</sup>	0.9 ± 0.2 <sup>b</sup>	1.8 ± 2.3	3.6 ± 2.6
GH (μg/l)	0.37 ± 0.32	0.30 ± 0.08	3.1 ± 5.3	4.1 ± 5.3	0.24 ± 0.01	0.42 ± 0.29
T (nmol/l)	21.8 ± 9.3	17.5 ± 6.7	37.0 ± 18.3	25.4 ± 14.3	5.1 ± 1.8 <sup>b</sup>	14.6 ± 8.8
$E_2$ (nmol/l)	0.08 ± 0.04	0.15 ± 0.07 <sup>c</sup>	0.25 ± 0.11 <sup>d</sup>	0.12 ± 0.13	0.04 ± 0.03 <sup>c</sup>	0.05 ± 0.03
Cortisol (μmol/l)	0.57 ± 0.06	0.54 ± 0.11	0.53 ± 0.14	0.53 ± 0.16	0.56 ± 0.13	0.56 ± 0.15

<sup>a</sup> Mean values, SD, and statistical significances of intragroup differences are given. The experimental group self-administered androgens during the time indicated (0–12 weeks of strength training).

<sup>b</sup> Two-tailed Student's *t*-test,  $P < 0.01$ .

<sup>c</sup> Two-tailed Student's *t*-test,  $P < 0.05$ .

<sup>d</sup> Two-tailed Student's *t*-test,  $P < 0.001$ .

GH increased 5 to 60-fold (0.24 to 1.20; 1.1 to 13.60; 0.31 to 5.80; 0.24 to 8.30, and 0.24 to 14.90 μg/l in the five subjects, respectively), whereas in two subjects, no changes were observed. Cessation of drug use resulted in return of all the variables measured to the starting values (Figs. 2 and 3).

## DISCUSSION

The results of this study confirm the previous findings that androgenic-anabolic steroid use leads to gain in body weight<sup>4,13</sup> and to remarkable decreases in the serum concentrations of LH, FSH,<sup>4</sup> SHBG,<sup>20</sup> and TBG.<sup>22</sup> The inhibition of testicular endocrine function<sup>16,21</sup> also became obvious following the cessation of drug use. The serum testosterone concentrations were very low at 16 weeks of followup (Table 2), and a decrease in testicular testosterone production had been masked by exogenous testosterone prior to that time point. As observed previously,<sup>4</sup> serum estradiol concentrations increased during drug use due to aromatization<sup>5</sup> of some of the drugs used. Also in line with previous studies<sup>20</sup> is the observation that serum cortisol did not change in the course of androgen treatment (Table 2).

It is tempting to suggest that decreases in serum TBG led to decreased protein binding of the thyroid hormones,  $T_4$  and  $T_3$ , which is reflected in elevated  $T_3$ U-values. Increased availability of  $T_4$  and  $T_3$  would then lead to a compensatory decrease in serum TSH, and this, via decreased thyroid stimulation, would further decrease total concentrations of circulating  $T_4$  and  $T_3$  (Fig. 2). The measurements of thyroid function parameters performed support this reasoning. However, our data do not exclude the possibility of direct pituitary effects of the drugs used or their metabolites at the hypothalamic-pituitary level.

In general, our findings suggest that the availability of thyroid hormones at the cellular level was not disturbed in the athletes. However, in the individual athletes subjected to followup, some of the thyroid function tests performed during the drug use produced results outside of our health-associated reference interval. It is therefore possible that abnormal findings in thyroid function tests may be recorded in medical checkups of athletes using androgenic-anabolic

steroids. This may lead to erroneous medical decisions, especially because the athletes tend to be secretive about the use of these drugs, which are banned by national and international sport organizations.

The use of androgenic-anabolic steroids resulted in 5 to 60-fold increases in serum GH concentrations in five of the seven experimental subjects, whereas no changes were seen in the control subjects. Due to the inconsistent changes in the study subjects, the mean serum GH concentrations did not differ significantly at the different follow-up points. In earlier studies the possible direct regulation of GH secretion by steroid hormones has not been clarified in detail and in addition, the study subjects have not been adults. Both testosterone<sup>15,18</sup> and estrogens in a dose dependent fashion,<sup>19</sup> but not nonaromatizable androgens,<sup>15</sup> have been reported to increase GH secretion. The results of the present study suggest that GH secretion may be stimulated also in adults by androgenic-anabolic steroid administration, which might strengthen the anabolic effects of the steroids used.

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## COMMENTARY

**Herbert Haupt, MD, St. Louis, Missouri:** I feel that this paper is a valuable addition to the world's literature on the effects of anabolic steroids on athletes. Although the effects on thyroid function probably do not have any demonstrable effect on the athletes' performance, they can be disturbing when unsuspecting medical doctors evaluate athletes taking anabolic steroids and notice these abnormal thyroid profiles. As the medical profession becomes more involved in helping those athletes who have chosen on their own to use anabolic steroids, we need to be further informed as to the potential laboratory changes that can occur with the use of these drugs by athletes. However, we must be aware that this study simply supports the association of the use of anabolic steroids with abnormal thyroid profiles. Certainly there are other variables that may potentially influence the thyroid

profile, including the effect of intense training alone in this caliber athlete, the role of high protein diets, etc. The only way to clearly isolate the use of anabolic steroids as a cause for the thyroid profile changes would be to use a double blind crossover study using the same athletes. However, this has already been shown to be very difficult in the use of anabolic steroids because most athletes can see through the double blind protocol using the placebo, as it does not have the noticeable side effects of the anabolic steroid.

The finding of growth hormone changes in several of the athletes is quite interesting and sheds more light on the complex mechanism by which anabolic steroids have effects on athletes' strength.

My only criticism of this paper is that the control group used was not similar enough to the experimental group to be truly an effective control group. The eight control subjects were training with weights only two to three times a week compared to the intense training interval of the power athletes in the experimental group, who averaged six times a week, 1½ hours per training session. The experimental group was also composed of competitive athletes, whereas the control group was not competitive. For this reason I think it is difficult to make inferences that the changes in the parameters mentioned can be solely attributed to the anabolic steroids. Certainly, intense training alone may have caused some of these changes, and the control group does not adequately address this issue.

**Authors' Reply:** We would like to express our thanks to Dr. Haupt for his valuable comments on this paper. However, we cannot share his criticism of our study design in respect of the use of controls. We admit that the control group did not match precisely the experimental group in training intensity and frequency. The control group was important as a way of showing the presence/absence of seasonal or other variations/factors, but it was not crucial for monitoring the possible different or parallel effects of training versus steroid use.

This reasoning is plausible because the experimental group was also its own control group in the sense that the first measurement was taken before the drugs were used, and the last two measurements were taken after the drugs had ceased to be used (see Figs. 2 and 3) but with no break or essential change in the intensity or frequency of training. Further, no changes were observed in the athletes' diets throughout the study.

On this basis we are fully confident that our results reflect solely the effects of steroid use during strength training and not the strength training itself, as evidenced in Figures 2 and 3.