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Anabolic steroids in body builders: use, metabolic disposition and physiological effects*

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Introduction

Since early in the sixties anabolic steroids have been thought to have a positive effect on an athlete's ability to compete in certain sporting events. Highest among these were the strength and short term power events (weight-lifting, shot put, etc.). More recently American football programmes have used anabolic steroids both to increase body mass and strength. Scientific data needed to either deny or support anecdotal "locker room information" regarding anabolic effects has been very slow in developing [1].

One body of knowledge has come from the agricultural use of certain steroids for the increase of lean body mass and general weight gain in animals being prepared for slaughter. In these cases the doses used were high but most of the data focussed on water retention or lean body weight increases [2]. Human studies have been limited primarily to use of steroids in either replacement therapy or in the treatment of certain diseases (i.e. cancer) [1]. In these cases the doses used have been maintained at rather low levels when compared to those used by present day athletes. Excessive use of anabolics is particularly apparent when both the anabolic agents and dose information are obtained from unauthorized dealers.

The authors' laboratory became interested in this problem when approached by a group of body builders and asked to help evaluate the physiological effects of certain anabolic agents being routinely used. The doses that they were using were in the range of 20–100 mg day^{-1} and this offered a unique opportunity to study the metabolism, as well as some of the physiological effects of these agents in a healthy human population.

Methods

Patients

After obtaining informed consent and after an initial interview where the patients were told that the use of these agents was not recommended, a patient history was obtained.

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This included the length of time that they had used anabolic agents, the agents used, the doses and the dose schedule. A typical dose cycle is shown in Fig. 1. Many of the athletes were taking multiple steroids during their on-cycle (stacking) and urine samples were collected from those subjects, but these data are not included in this report. In order to avoid possible confusing effects of multiple steroids on physiological response, data reported here are from the use of a single anabolic agent during a cycle.

Samples

Urine samples (24 h) were obtained during both the on- and off-cycle periods. At least 3 weeks were allowed to elapse after each change to insure that the body had adjusted to the new drug levels (see arrows in Fig. 1). Urine volume was measured, the dose and agent used were noted and an aliquot was frozen at −70°C until analysis. All glassware used throughout the analytical procedure was acid washed and silanised. The specific method for steroid isolation from urine has been published elsewhere [3].

Results and Discussion

Using a technique that was developed by the authors for measuring adrenal suppression after use of superpotent topical steroids [4], both cortisol/cortisone and C-19 steroid metabolites were monitored in urine. Since longitudinal data were obtained on each patient, it was possible to monitor testicular and adrenal steroid output by using each subject as his own control. As shown in Fig. 2 there was a definite suppression in steroid excretion when the subject shifted from off-cycle to on-cycle. This suppression was seen with two different agents. The apparent rebound seen between the first and second cycle was unexpected and further studies are being carried out to see if this is dependent upon the agent being used or the dose. In the authors' laboratory the range of normal values for adult males is quite large. Therefore, rather than compare individuals to a population normal range, values for each individual are continuing to be accumulated on- and off-cycle to establish normal ranges for each individual.

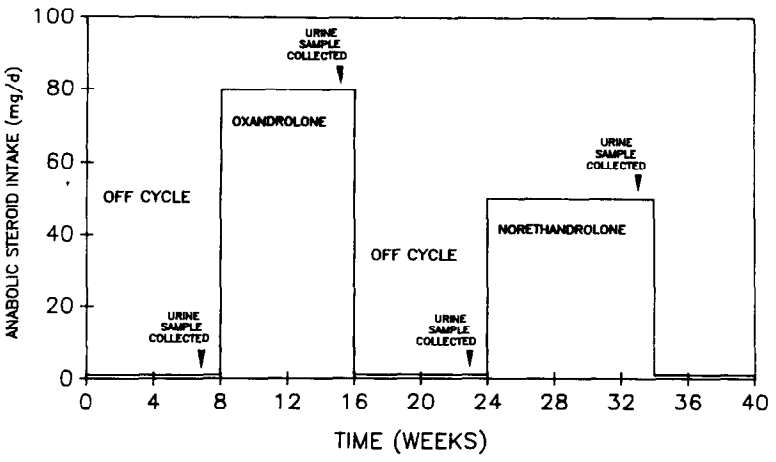


Figure 1
Typical anabolic steroid dose schedule followed by one of the subjects. Plot shows the anabolic drug, the amount used (mg day^{-1}), the length of time used and the points in time where 24 h urine samples were collected.

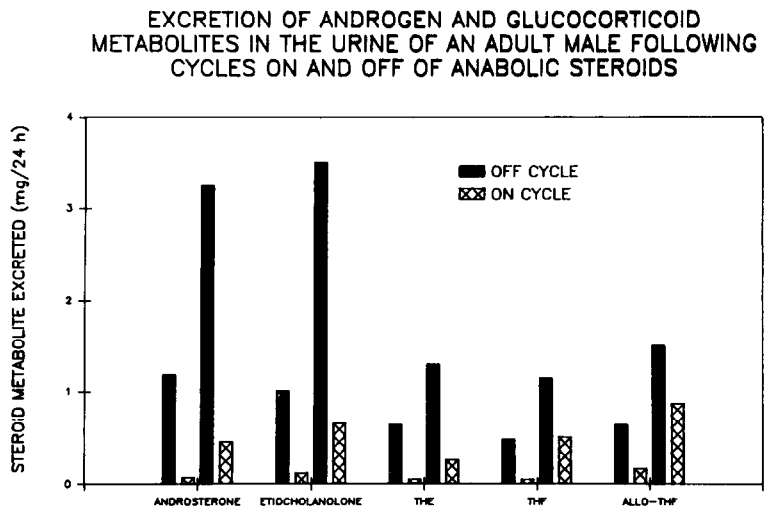


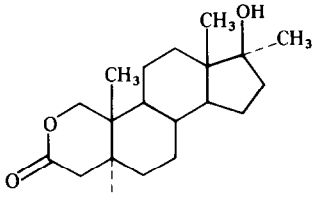
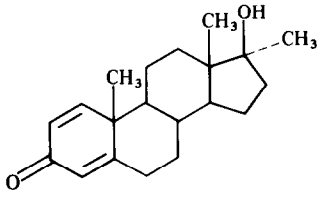
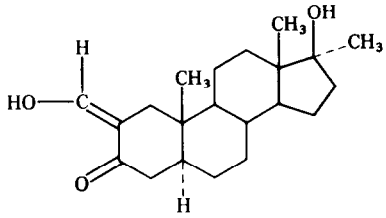
Figure 2
Profile of five normal urinary steroids showing the total excretion of each in mg 24 h^{-1}. Comparisons are made between times when subject was taking anabolic agents and when he was drug free. THE, tetrahydrocortisone; THF, tetrahydrocortisol; allo-THF, allotetrahydrocortisol.

A study of the metabolism of three of the anabolic agents led to a diverse set of results (see Table 1). For example, oxandrolone was found to be essentially unmetabolised. Analysis of the urinary steroids showed two major peaks. These were in addition to the normal urinary steroid metabolites of adrenal and other endocrine organ origin. The new peaks had methylene unit values (MUV; 27.25 and 28.42) and mass spectra that were identical to authentic starting material. A minor peak with a MUV of 29.47 was found in the urine of all subjects on oxandrolone. The mass spectrum of this peak had the characteristic ion of a 17-methyl, 17-hydroxy steroid TMS derivative (m/z 143) and an apparent M^+ of m/z 461. However, the structure of this compound is still unknown.

In contrast to the relatively unmetabolised oxandrolone was the urinary pattern found in subjects using oxymetholone. Here many of the metabolites appear to be end products of oxidation and decarboxylation of the carbon attached at C-2 of the steroid nucleus. Unmetabolised oxymetholone was not detected in any of the samples studied.

Methandrostenolone gave urinary peaks that represented both the isomerisation at C-17 of the starting anabolic agent and other products of metabolism. The authors were unable to obtain authentic standard for the 3,6-dihydroxy-3-oxo metabolite. Therefore the assignment of this structure must be considered tentative at this time. These results are in partial agreement with those of Durbeck and Buker [5], who also found 17-epi-methandrostenolone and 6-hydroxy methandrostenolone, but not the 3,17-dihydroxy-17-methyl-1-androstene metabolite detected in the present study. These same investigators reported detection of 17a-methyl-17B-hydroxy-1,4,6-androstatrien-3-one and 18-nor-17,17-dimethyl-1,4,13(14)-androstatrien-3-one not found in the present study. Differences between these studies may be due to the experimental procedures used; the present study utilised a number of urine samples from individuals who had been ingesting >20 mg of methandrostenolone per day for weeks whereas the study by Durbeck and Buker used a single urine sample collected 7 h after ingestion of a single dose of 10 mg of methandrostenolone.

Table 1

Anabolic agent	MUV	Chemical name of metabolite	Major mass spectral peaks
Oxandrolone 	29.47	Unknown	461, 446, 417, 143, 117
Oxymethalone 	26.39	3,17-dihydroxy, 17-methyl androstane	450, 435, 360, 345, 143
	27.47	2,17-dihydroxy, 17-methyl,3-oxo 2-androstene	462, 447, 372, 357, 267
	29.19	2,3,17-trihydroxy androstane	552, 537, 462, 143
Methandrostenolone 	26.45	3,17-dihydroxy 17-methyl 3-oxo 1-andostene	448, 358, 143
	28.58	6,17-dihydroxy, 17methyl 3-oxo 1,4-androstdiene	489, 458, 399, 368, 309 278, 237, 143

List of metabolites found in the urine of three subjects. For each derivatised metabolite (trimethylsilyl, MOX) the methylene unit value (MUV), chemical structure (if known) and significant mass spectral peaks are shown.

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