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Anabolic-Androgenic Steroids and Athletes: What are the Issues?

ALAN D. ROGOL AND CHARLES E. YESALIS III

Departments of Pediatrics and Pharmacology (A.D.R.), Health Sciences Center and National Science Foundation Center for Biological Timing, The University of Virginia, Charlottesville, Virginia 22908; and Professor of Health Policy and Administration and Exercise and Sport Science (C.E.Y. III), College of Health and Human Development, The Pennsylvania State University, University Park, Pennsylvania 16802

LIKE health and other professionals most athletes are very pragmatic and success oriented. Training methods that include the use of chemical compounds and drugs are chosen if the athlete thinks the risk-to-benefit ratio is favorable. These agents may be needed merely for their placebo effect, or they may allow the athlete to train more diligently and/or more aggressively, or they may directly enhance athletic performance. One of the series of agents that is of current interest are the anabolic-androgenic steroids. All are derivatives of testosterone, which is responsible for the androgenic and anabolic effects noted during male adolescence and adulthood. Androgenic effects are those that relate to the growth of the male reproductive tract or to the development of secondary sexual characteristics in men. In the pubertal male organism, these are increases in the length and diameter of the penis, development of the prostate and scrotum, and the appearance of the pubic, axillary, and facial hair. Anabolic effects are the changes that occur in the somatic or nonreproductive tract tissues and include an acceleration of linear growth that appears before bony epiphyseal closure, enlargement of the larynx and thickening of the vocal cords, the development of libido and sexual potentia, and finally, an increase in muscle bulk and strength as well as a decrease in body fat. This androgen is also probably responsible for the increase in aggressive and sexual behavior, although its role in the psychological and behavioral aspects is controversial.

Scientific interest in drugs is usually focused on their therapeutic effects, prevention, diagnosis, or treatment of disease, or on their abuse potential. Little attention has been given to the use of drugs for the following

purported benefits: increase in physical strength, delay in the onset of fatigue, increase in exercise endurance, prevention of anxiety that could interfere with performance, enhanced attention and concentration, and development of a more satisfactory competitive attitude. The use of medicinal or chemical substances with the deliberate intention of altering athletic performance is generally considered unethical; for this reason drug use by athletes is usually covert.

Why are these agents taken?

The goals of the individuals who use anabolic steroids are dependent upon the activity in which they participate. Bodybuilders desire more lean mass and less body fat. Weight lifters, both power and Olympic, desire to lift the maximal amount of weight possible. Field athletes want to put the shot or throw the hammer, discus, or javelin farther than the competition; whether they be the ones at the event or holders of previous records. Swimmers, bicyclists, cross-country skiers, and runners hope to be able to perform their continuous, high intensity, long duration workouts without physical breakdown. Football players want to increase their lean body mass and strength so that they can be successful at the high school, college, or professional level. Another group of users of anabolic steroids simply want to look good, which currently means "big" and muscular (1).

How are these agents taken?

Anabolic steroids have traditionally been taken in "cycles," which are episodes of use of 6–12 weeks or more duration. However, there are athletes, such as some power lifters, who use the drugs on a relatively continuous basis and increase their dose at certain times of the year to, for example, prepare for a competition. Often athletes will take more than one steroid at a time and

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Address correspondence and requests for reprints to: Alan D. Rogol, M.D., Ph.D., Department of Pediatrics, The University of Virginia Health Sciences Center, Building MR-4, Room 3037, Charlottesville, Virginia 22908.

this is referred to as stacking. The purported rationale for stacking is that the user will activate more receptor sites than if only one steroid is used, and/or that a synergistic effect can be achieved with certain combinations of steroids. There is no scientific evidence to support this rationale. To avoid developing tolerance to a particular anabolic steroid (plateauing), some users stagger the timing of their drugs and will take the steroids in an overlapping pattern or stop taking one drug and start another. Often steroid users will pyramid their dosing patterns such that they incrementally move from low daily doses at the beginning of the cycle to higher doses and then taper their doses down toward the end of the cycle. In addition, the athlete may use a number of other drugs concurrently with anabolic steroids to further enhance physical capacities or to counteract the common side effects of steroids. These drugs include stimulants, diuretics, antiestrogens, hCG, hGH, anti-acneiform medications, as well as anti-inflammatories. This polypharmacy is termed an array (1).

Who takes these agents?

Because of the prohibition against anabolic-androgenic steroids use by the governing bodies of many sports, many athletes will not admit to their use. In fact, much of the activity surrounding their use is to find methods to avoid detection by sports officials. Thus, it is extraordinarily difficult to obtain accurate incidence and prevalence data. Use is certainly defined by sport, *e.g.* high in those sports (and positions) in which strength and explosive power are exploited and lower in those activities in which endurance is required. Perhaps the highest prevalence (virtually universal) is in male and female bodybuilders. Most data are from surveys of many types and it is difficult to compare individual studies since neither the scientific validity nor the extent to which the respondents in the surveys reviewed honestly reported their use of anabolic-androgenic steroids can be accurately measured. It is clearly possible that athletes intentionally underreported or even overreported their use of anabolic-androgenic steroids (1).

Recent studies have focused on high school students. As reviewed by Yesalis and co-workers (1), between 5% and 12% percent of boys and 0.5–2.5% of girls have (self) reported anabolic-androgenic steroids use. In a study of more than 3000 male students, more than one-third of the users did not intend to participate in interscholastic sports. Reasons for use in many of the nonathletes were “to look good” or to get “big.”

What agents are taken?

Drugs in each of three basic groups are used: 1) testosterone, 2) alkylated testosterone analogs, and 3) testos-

terone esters. Although many derivatives of testosterone have been prepared (to date, more than 1000) to attempt to dissociate the androgenic from the anabolic effects, this strategy may be doomed because both actions of these steroid derivatives are apparently mediated by the same intracellular receptor complex. It may very well be that the target tissues and thus the concentration of receptors and activity of the steroid-metabolizing enzymes, rather than the compounds themselves, determine the array of biological effects. Unmodified testosterone is rapidly cleared especially by the liver and might only be used in close proximity to announced drug tests or competitions in which drug testing is expected. The alkylated testosterone analogs can be administered orally because hepatic metabolism has been slowed, but are likely to be hepatotoxic. Esterification of testosterone in the 17- β hydroxyl position increases the lipophilic properties and presumably slows absorption. The longer the carbon chain of the ester function, the more lipid (and less aqueous) soluble the compounds are. The propionate ester has significant aqueous solubility and is much more rapidly cleared than the enanthate (7 carbons) or the cypionate (8 carbons). A far greater array of compounds (both veterinary and human) have been synthesized, and are the common agents taken. The chemical structures of the commonly used anabolic-androgenic steroids, and issues about their pharmacology have been reviewed recently (see Ref. 2, chapt. 4, especially Table 4-2). Although testosterone-equivalent doses for replacement therapy have been estimated, the amounts used by strength athletes often exceed these by 10- to 100-fold.

Endurance and sprint athletes use doses closer to those used medically for replacement levels. Clinically, these agents are prescribed as replacement therapy in men with central or peripheral hypogonadism and in some adolescents with marked delay of pubertal development. The quantities recommended either orally or parenterally are within severalfold of the normal male testosterone production rate, although they are not normally administered in the physiologically, pulsatile mode. At these levels normal pubertal progression without rapid epiphyseal closure and the maintenance of adult male strength, libido, and sexual function are common and the untoward effects minimal. Somewhat increased amounts are used to stimulate anabolism or positive metabolic effects in some patients with neoplastic diseases. Anabolic-androgenic steroids may also be prescribed for some patients with certain hormone-dependent tumors. Somewhat higher doses (*e.g.* 200 mg/week of testosterone enanthate) are being evaluated by the World Health Organization as a male contraceptive.

Do these compounds work, that is, do they enhance performance?

There is a rich (confusing and contradictory) literature concerning this issue. It is not my purpose to review

these data here and the interested reader may find summaries by Lamb, Wright, Wilson, and Haupt and Rovere (3–6). Despite the lack of consistent or conclusive scientific evidence as demonstrated by individual studies and/or by extensive meta analysis, an overwhelming number of athletes, trainers, and scientists believe that anabolic-androgenic steroids are performance enhancing. The contemporary stories of Canadian sprinters and (now formerly East) German athletes, who have held world records and won medals in international competitions while receiving anabolic-androgenic steroids, point to an ergogenic effect and a salutary effect on athletic performance of these agents. The most recent review of the extant literature (7) concludes following analysis of 16 evaluable studies that anabolic-androgenic steroids may slightly enhance muscle strength in previously trained athletes. No firm conclusion was possible concerning the efficacy of anabolic-androgenic steroids in enhancing overall athletic performance. The latter is clearly more complex than merely the acquisition of “extra” strength, for objectively measured size and strength of muscle are not the sole determinants of athletic performance. Other “variables,” for example attitude, diligence in training, agility, and the competitive spirit combine to affect athletic performance, to say nothing of the weather conditions and the psychological “state.”

What are the expected side-effects from the use of anabolic steroids in approximately replacement dosage and in supraphysiological amounts?

In adult men, the approximate physiological replacement dosage is usually followed by the effects just noted, increased strength; libido; and sexual potentia. Some men may experience acne and gynecomastia (7). In larger doses one can expect more profound changes in these categories, along with priapism (sustained penile erection) and edema secondary to the retention of sodium and chloride. This antidiuretic effect may in part explain the rapid weight gain and is probably why athletes taking these compounds can rapidly lose enormous quantities of weight immediately before certain competitions.

Replacement dosages in women can cause virilization, as indicated by enlargement of the clitoris and increased sexual and body hair. Menstrual dysfunction is common. In pre- and peripubertal children and adolescents, there may be disturbances in growth and sexual development, excessive androgens whether endogenous (*e.g.* congenital virilizing adrenal hyperplasia) or exogenous can advance the maturation of the skeletal system (and induce epiphyseal closure) out of proportion to their ability to increase length and inhibit children and adolescents from reaching their genetic height potential. In addition, the

adolescent age group is at the transition to adulthood in terms of their psychological makeup; therefore, this period may be particularly vulnerable to the psychological effects of heightened aggression, for example. There are profound and mainly irreversible effects for adolescent females and women. Clitoromegaly and amenorrhea are common although the latter may be partially reversible. Effects on the larynx lead to a permanently deepened voice.

Should adolescents (athletes and nonathletes) or women ever take anabolic-androgenic steroids? Leaving the issue of fairness aside (see below) the easiest recommendation to make is that no one should ever take these potent compounds for any nonmedically indicated reason. But as we have noted above, these supreme pragmatists (at least some of the athletes) will not heed that advice, especially when faced with immense quantities of anecdotal information from their colleagues and competitors. In addition, since many of the side-effects have not occurred in the athlete or her/his companions who take anabolic-androgenic steroids, there are only glowing stories of their efficacy. Many at this stage of life feel invincible with unrealistic views of many dangerous practices and thus the prudent course of effective education as a deterrent to the use of anabolic-androgenic steroids should occur at ages younger than the usual age of first experimentation (middle school). This seemingly innocuous course may be fraught with difficulty since there are some disquieting data to indicate that educational strategies may, in fact, promote use.

More profound effects are seen in men, and by implication, women and children who receive supraphysiologic amounts of anabolic steroids (8). Certainly not all effects occur in all persons, nor are the effects necessarily obvious. In addition to dosage, one must consider the duration of use to arrive at a total “exposure.” With some of the compounds, those containing a 17-methyl group, jaundice is regularly seen, although rarely detected in athletes. Jaundice may also occur as a secondary phenomenon to other induced liver diseases, including the pooling of blood within the sinusoids (peliosis hepatic) and very rarely hepatic carcinoma. However, it is difficult to determine the precise role of the androgen since many of these patients have received anabolic steroid therapy for underlying hematologic diseases that make them prone to other neoplastic diseases. Thus, these agents may lead to severe and fatal side-effects in persons with an underlying propensity to cancer that is unmasked by therapy.

More commonly in persons receiving large doses of anabolic steroids, however, is paradoxical impotence and lack of sperm production despite the heightened sexual drive. Although androgens are required for spermatogenesis, in high doses they feed back excessively upon the

hypothalamus and anterior pituitary gland to virtually abolish the circulating concentrations of LH and FSH. The latter is an absolute requirement for the maturation of spermatozoa within the seminiferous tubules of the testes.

In addition, it is important to note that some laboratory tests can be influenced by the level of androgenic hormones and that certain of these tests may show abnormal results in those persons taking these agents, for example lipid profiles, liver function tests, and concentrations of certain circulating hormone-binding proteins. It is assumed, but not proven, that these abnormal tests indicate organ involvement and a propensity toward atherosclerotic lesions in the arteries.

The significant untoward effects are most often quite separate in time from their use, whereas the desired effects are quite rapid, thus making the design of clinical studies to determine their efficacy very difficult, even before ethical issues are raised. It would be important, just as in any other clinical study, to follow athletes over a long period and to know precisely what agents were taken, and how much for how long. Such data are unavailable at present, and probably will remain so.

Are there psychological and/or behavioral effects of anabolic-androgenic steroids?

The psychological and behavioral aspects of maleness have been noted since antiquity and studied in uncontrolled fashion until the present century. In the 19th century the field of endocrinology was highlighted by Brown-Sequard who attempted (he was his own experimental subject) to show that aqueous extracts of dog and guinea pig testes contained substances that in addition to their androgenic effects, affected vitality, energy, and youthfulness. Effects on mood and mental disorders were explored in the mid-to-late 1900s and have recently been summarized by Bahrke and co-workers (9). Several investigators have suggested that some of the purported ergogenic benefits of anabolic-androgenic steroids may derive from their psychological effects; that is, they may lead to arousal, increased self-confidence and pain threshold and facilitate expression of the 'all-out' physical effort of training and competition. The majority of psychological/behavioral studies have been performed with small numbers of selected athletes. Some data indicate different mood changes after dynamic resistance exercise alone. These responses in mood could be enhanced by athletes taking anabolic-androgenic steroids. Reduction in fatigue after exercise in athletes receiving anabolic-androgenic steroids has been cited in several investigations (mainly self-report information); however, there may be a reasonable scientific basis for this finding since anabolic-androgenic steroids can block and even

reverse the catabolic effects of glucocorticoids (at the glucocorticoid receptor) that are released in abundance during and after significant physical exercise. At least in this case there is a reasonable hypothesis on which to design studies in animals *in vivo* and in isolated muscle and central and peripheral nervous system tissue *in vitro*. However, as Bahrke and co-workers (9) summarize: "Despite the suggestions and self-reports scientific data supporting the notion that psychological changes (enhanced arousal, confidence, aggression, motivation) play a primary role in mediating any ergogenic effects of anabolic-androgenic steroids is lacking" (9).

Are affective and psychotic symptoms associated with use of anabolic-androgenic steroids?

Anecdotes and even more formal studies have been reported for many years that indicate that some violent men may have higher than average circulating levels of testosterone and that exogenous anabolic-androgenic steroids may increase natural aggressive tendencies. None of these studies could be considered definitive based on design, numbers of subjects, inventories used, or variance in results. Although studies in lower animals appear more adequately controlled and do help explain naturally sexually dimorphic behavior, those in the human athlete to evaluate the effects of anabolic-androgenic steroids on affective and psychotic symptoms have not confirmed specific behavioral disturbances. In the main, these few studies lack statistical power and do not account for the "premorbid" condition of the athlete. Most do not account for the delivery of the pharmacologic agent in that type, dose, "stacking" regimen, and concurrent use of other hormones or drugs of abuse were not carefully controlled. No study has shown that symptoms and concurrent use are causally related. Thus, there is a great gulf between undoubted sexually dimorphic and aggressive behavior due to available androgenic steroids in lower animals and clinical studies in athletes. The absence of evidence is not the same as evidence of absence and more sophisticated longitudinal studies (probably placebo and training regimen controlled) to dissect the role of anabolic-androgenic steroids in behavioral disturbances are required.

Can anabolic-androgenic steroids produce a psychological dependence syndrome?

Preliminary data from several investigators [see Yesalis (1)] indicate psychological dependence upon anabolic-androgenic steroids: 1) preoccupation with drug use, 2) difficulty stopping despite psychological side effects, and 3) drug craving. Purported withdrawal effects include mood swings, violent behavior, rage, and depression possibly severe enough to lead to thoughts of suicide.

Such reports have led Kashkin and Kleber (10) to propose an anabolic-androgenic steroid addiction hypothesis that the psychoactive effects, withdrawal symptoms, and underlying biological mechanisms of steroid hormones appear similar to mechanisms and complications accompanying cocaine, alcohol, or opioid abuse. The data reviewed by these authors support the hypothesis that anabolic-androgenic steroid abuse can develop into a psychoactive substance dependence disorder with cognitive, behavioral, and physiological symptoms indicative of uncontrollable use of a psychoactive substance despite adverse consequences. If this hypothesis is confirmed, then specific treatment modalities, *e.g.* α -2 adrenergic agonist therapy as employed in abusers of alcohol or opioids, may be indicated.

Is it fair to take anabolic-androgenic steroids?

One of the arguments to ban anabolic-androgenic steroids is that it is unfair to the competition and makes a slanted playing field. Should all competitors be permitted to take these compounds as an aid to their training and let the chips fall where they may? We believe that it is unfair to force athletes to use these agents if they wish to compete on an equal basis and their use is thus an ethical or moral issue. At the very much higher doses, especially of the oral (17- α -alkyl) compounds, the risks are real, probably underestimated, and may be permanent. However, in the usual quantities (especially of the injectable esters), which often lie between replacement doses and those used in contraceptive studies (*e.g.* 200 mg/week), there are few objective, serious side-effects especially if the agents are taken intermittently. Thus the argument about fairness cannot be entirely based on the medical benefit-to-risk ratio (*i.e.* coercing other athletes to use these compounds if they wish to compete with athletes who "voluntarily" take them). We contend that the argument that anabolic-androgenic steroids "dehumanize" sport is the most persuasive despite the compelling issues of financial, material, and sexual rewards that can be attained with their use. The rewards often overshadow the physical and psychological consequences of anabolic steroids especially at the lower doses of injectable compounds cycled intermittently.

Summary, Conclusions, and Recommendations

We have reviewed contemporary aspects of the use of anabolic-androgenic steroids by athletes. Although no

specific study shows clear-cut results, there are too many "slightly" positive" studies (despite inadequate design) and anecdotal stories to deter us from stating that anabolic-androgenic steroids are efficacious. Many of the recognized side effects especially of the 17- α -alkylated agents are transient or uncommon and occur much later than the perceived salutary effects. However, issues of abnormalities in lipid metabolism, but especially the behavioral effects of heightened aggression, dependence, and addiction are understudied and may be the most prominent and difficult to attribute to the ingestion of the agents.

Even with the higher doses, there has been no epidemic of severe side-effects and deaths. The unknown quality of the increasing numbers of black market drugs should add an additional note of caution. Until the appropriate research studies have been completed no proper informed decision can be made of the benefit-to-risk ratio as can presently be made for tobacco, alcohol, and narcotic drugs. Our recommendation is that these agents should not be taken based on both ethical (fair play) considerations for competitive athletes and health (physical and psychological) for all nonathletes and athletes whether in competition or not.

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