From The Endocrine Society's Research Affairs Committee
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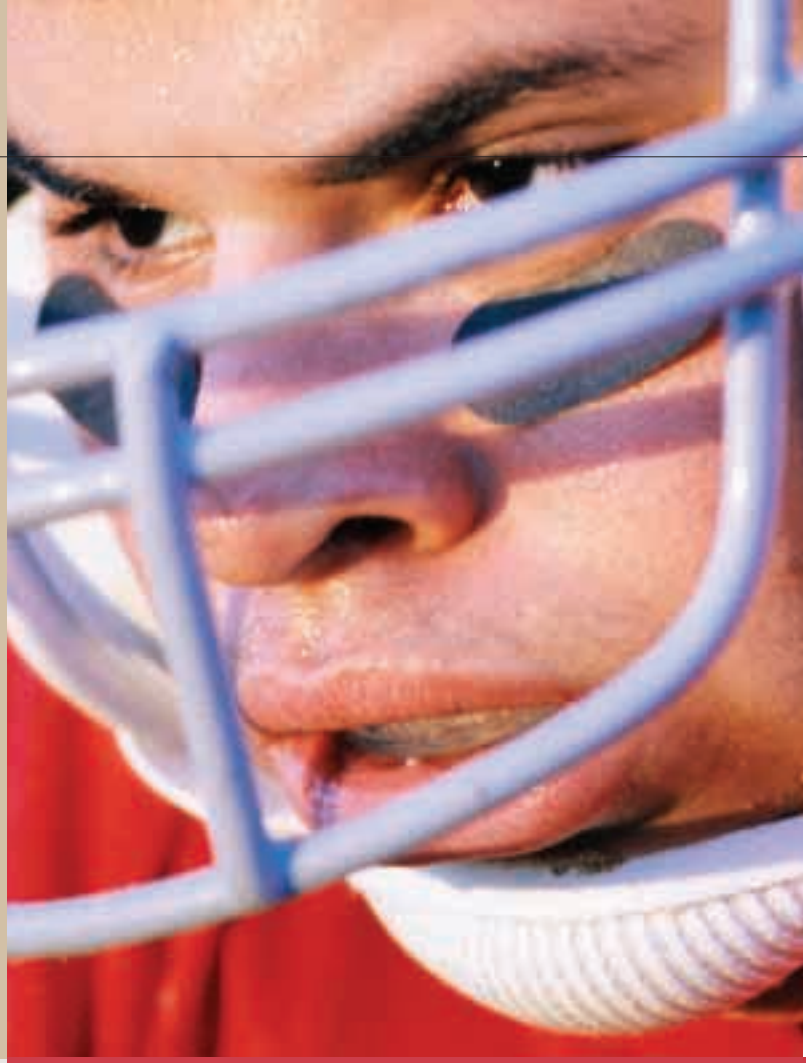
Is Adolescent STEROID Abuse/Misuse RAMPANT?

3 Perspectives on the Consequences of Use and Implications for Federal Oversight



Steroid misuse/abuse has become common in the past decade or two. Prominent among the reasons for abuse are athletic performance and to "look good." Abuse in girls is rising and is correlated with other risky behaviors. New regulations at the national level have been developed to curb this abuse and legislation to educate youth has become law.

Giving the endocrinology perspective is Alan D. Rogol, M.D., Ph.D., professor of clinical pediatrics at the University of Virginia.

Giving the public policy perspective is Gary I. Wadler, M.D., F.A.C.P., F.A.C.S.M., clinical associate professor of medicine at New York University School of Medicine and member of the World Anti-Doping Agency's Prohibited List and Methods Committee.

Giving the sports medicine perspective is Linn Goldberg, M.D., professor of medicine and head of the Division of Health Promotion and Sports Medicine Department at Oregon Health & Science University.

Hormonal Effects

The diverse biological actions of androgens, whether in the reproductive or non-reproductive tissues, are mediated by a single androgen receptor.[1] Androgens are required throughout a male's lifetime, from sexual differentiation in utero to adolescent sexual development to adult sexual function and fertility. Many tissues are affected by androgen action whether by testosterone itself, its 5-α reduced product dihydrotestosterone, or—relevant to abuse in adolescents—its aromatization product, estradiol. The androgens are mainly responsible for the sexually dimorphic body composition and adolescent behaviors, whereas the estrogens are responsible for augmented function of the hypothalamic-pituitary-GH-IGF-I axis,[2] bone mineral accrual, and epiphyseal maturation and eventual closure. Against this backdrop of adolescent physiological development, with its wide range in both *timing* and *tempo,* one must decipher the effects of AAS abuse/misuse.

Female adolescents take AAS often in the context of other risk-taking activities, for example, dangerous dieting, increased sexual activity, and riding with a driver who has been drinking. The most common adverse events in these females are altered menstrual cycles (note: menstrual cycles in adolescents are commonly irregular for the first 2 years beyond menarche), hirsutism, acne, and clitoral enlargement. Body composition alterations—especially greater muscularity—can occur quite early and with low doses of AAS, because young women naturally produce very little ovarian or adrenal androgen.

For males the key issue is the dose and perhaps type. Very small doses might produce no effect other than to suppress endogenous production of the gonadotropins and testosterone—the normal negative feedback from testosterone (or estradiol). Increased doses produce both estrogenic and androgenic effects. The former effects result from testosterone acting as a substrate for the aromatase enzyme. These prominently include gynecomastia, premature closure of the epiphyses with resultant adult short stature, and diminished gonadotropin production with resultant smaller testicle size. High-density lipoprotein cholesterol can be very significantly decreased. Severe acne and notable behavioral alterations, for example, "roid rage," depression (and suicide), and addiction are quite prominent in some who abuse larger doses.[3] Longer-term cardiovascular and hepatic toxicities are rare in adolescents.

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There is a steep and linear dose-response relationship for both the virilizing and anabolic actions of testosterone.[4] One might imagine that the androgen receptor would become saturated at doses far below those (ab)used by some athletes—likely several orders of magnitude greater than physiologic. Some tissues perhaps require high levels of the 5-α–reduced or -aromatized products, or even an anti-catabolic effect at the glucocorticoid receptor,[5] for the full spectrum of AAS action.

Thus, AAS abuse/misuse in adolescents is likely difficult to detect, given the adolescent endocrine system maturation and very significant alterations in body composition and the regional distribution of body fat. The emergent adverse events can leave lifetime changes to the cardiovascular and reproductive systems as well as diminished adult height.

From the Endocrinologist

- Androgen action plays an important role at puberty.
- Androgen abuse in female adolescents can present as irregular menses and increased muscularity.
- Androgen abuse in male adolescents can present as estrogenic manifestations such as gynecomastia.
- Behavioral aspects of androgen abuse might be prominent in adolescents.
- Androgen abuse might be difficult to detect given the large changes at puberty.

Legislative History of Anabolic Steroids

Although the history of anabolic steroids dates back to the 1930s, it wasn't until the 1970s and 1980s that they came under the Food and Drug Administration's jurisdiction. The Food, Drug and Cosmetic Act required anabolic steroids to be prescribed and dispensed by licensed physicians. However, it wasn't until this Act was amended by the Anti-Drug Abuse Act that anabolic steroids could be prescribed legally only to treat a legitimate disease and only within the context of a bona fide doctor-patient relationship. The Act enabled effective enforcement against black market dealers and individuals illegally dispensing steroids.

Anabolic Steroid Enforcement Act of 1990 and the DSHEA

Influenced by media reports of increasing anabolic steroid use in professional sports and in the nation's high schools, Congress in 1990 elected to schedule anabolic steroids as Schedule III controlled substances under Title 21 of the U.S. Code that regulates food and drugs. The Anabolic Steroids Control Act of 1990 applies in every U. S. federal court and places anabolic steroids in the same legal class as amphetamines, opium, and morphine. Critical to this Act was the requirement that for a substance to be categorized as an anabolic steroid it had to be defined as "any drug or hormonal substance, chemically and pharmacologically related to testosterone that promotes muscle growth…" However, it was the phrase "promotes muscle growth" that provided a loophole enabling androstenedione and its congeners to avoid the label "anabolic steroids," because there was a paucity of literature showing that androstenedione promotes muscle growth. In contrast, the language of the 1994 federal Dietary Supplement and Health Education Act (DSHEA) provided a legal framework to classify androstenedione and its congeners as dietary supplements, making them more akin to a foodstuff than to drugs requiring no prescription. DSHEA emancipated manufacturers of androstenedione and its congeners from needing to demonstrate pre-market purity, safety, and efficacy, provided there were no claims that these substances prevented, treated, cured, or ameliorated a disease.

Simply stated, DSHEA provided a means for anabolic steroids to circumvent the intent of the Controlled Substances Act of 1990. Following the 1998 home run exploits of baseball star Mark McGwire, there was an immediate, substantial rise in sales of the so-called "steroid precursors"—androstenedione and its congeners—substances neither prevented by DSHEA nor by the 1990 Act. Furthermore, it became evident that the burgeoning epidemic of anabolic steroid abuse was not limited to elite sports, where they were used as performance enhancers; abuse was also manifest among the teenage population, in great measure for their effects on physical appearance.

> **"Abuse was also manifest among the teenage population, in great measure for their effects on physical appearance."**

Anabolic Steroid Control Act of 2004

In response to these observations and intensive lobbying, the Controlled Substance Act was amended in 2004. The amendments clarified the definition of anabolic steroids and provided for research and education activities relating to steroids and steroid precursors. Specifically, the amendment eliminated the requirement that a substance had to promote muscle growth to be categorized as an anabolic steroid. This change in the law provided the basis for the re-categorization of androstenedione and its congeners as anabolic steroids, leading to their classification as controlled substances. Very importantly, the Act also provides for a review of the federal sentencing guidelines to increase penalties for offenses involving anabolic steroids in a manner that reflects the seriousness of such offenses and the need to deter anabolic steroid trafficking and use. State laws, which differ from federal laws in their anabolic steroid classification, list a wide range of penalties for violations. Unfortunately, black market trafficking in these substances remains a large problem, especially via countries such as Mexico, and through global Internet promotions.

It is especially noteworthy that the Anabolic Steroid Control Act of 2004 provides for grants to public and non-profit private entities and elementary and secondary schools to carry out science-based steroid prevention and education programs. In awarding such grants, the Secretary of Health and Human Services gives preference to applicants intending to use grant funds to carry out programs based on the Athletes Training and Learning to Avoid Steroids program (ATLAS), the Athletes Targeting Healthy Exercise and Nutrition Alternatives program (ATHENA), and other programs determined to be effective by the National Institute on Drug Abuse.

From the Public Policy Advisor

- Anabolic steroids are "controlled substances," both federally and by individual states.
- Androstenedione and its congeners are now categorized as Schedule III controlled substances under federal law.
- The Dietary Supplement and Health Education Act no longer applies to androstenedione and its congeners.
- Illicit availability of anabolic steroids remains a significant public health problem.
- Federal grants might become available for elementary, middle, and high schools for steroid prevention and education programs.

Adolescent Anabolic Androgenic Steroid Use

More than 7 million U.S. high school students participate in school sports programs,[1] and these youth are more likely to take anabolic steroids than students not participating in school athletics.[2] The use and abuse of anabolic steroids among youth has become a national problem.[3] The most recent Youth Risk Behavior Surveillance Study (YRBSS 2003) found that 6.1% of high school students used or are using anabolic steroid pills or shots without a prescription. Based on this self-report data, more than 850,000 high school students have tried, or currently use, anabolic steroids. In 1993, 1 of every 45 high school students admitted to anabolic steroid use. By 1999, the figure was up to 1 in 27 and by 2003, self-reported lifetime use was 1 in 16 high school students.[4]

Steroid Use Influences

There are many factors that influence adolescents' steroid use, some of which are sex specific. A Kaiser Foundation study found that more than 70% of youth desire to be like high-profile athletes and more than half (52%) believe these athletes use performance-enhancing drugs.[5] Durant et al.[6] found that adolescent steroid users are more likely to be male, inject drugs, use a variety of illicit drugs, drink alcohol, and be engaged in weight training. Although studies of young women's steroid use are limited, current findings suggest that users are more likely to have disordered eating and other compulsive behaviors, concerns about their body image, and adverse psychological effects caused by their steroid use.[7]

Public Policy Response to Steroid Use

Currently, the legislative approach to the problem of steroid use, in addition to previous laws placing them in the category of Schedule III controlled substances, has been addressed by the Anabolic Steroid Control Act of 2004[8] and a legislative initiative known as the "Clean Sports Act of 2005." The Anabolic Steroid Control Act amended the Controlled Substances Act and reduced the availability of over-the-counter precursor steroid supplements. The bill also called for grant awards to carry out science-based education programs in elementary and secondary schools to highlight the harmful effects of anabolic steroids—at a level of $15 million for each of 6 years. However, Congress failed to appropriate any funds for these efforts, although existing science-based programs, ATLAS[9] and ATHENA,[10] were authorized in the bill. The other response, as yet not placed into law, is the Clean Sports Act of 2005. This would strengthen the testing procedures and increase penalties for performance-enhancing drug use in professional American male sports. Congressman Henry Waxman, (D-CA), a sponsor of the bill, stated, "There is an absolute correlation between the culture of steroids in the major league clubhouse and the culture of steroids in high school gyms. If we can remove steroids from the clubhouse, we will fix the problems in school locker rooms."

It is doubtful that these legislative approaches will have much impact without funding. The perceived benefit of steroid use is widely recognized among youth. The perception of steroid effects on athletic enhancement will not lessen with testing of professional male athletes. Also, it is possible that the policy might have an unintended effect. Focusing on these drugs' athletic enhancement effects rather than on health consequences, the test and sanction approach favored by Congress—without accompanying adolescent education—could bolster an adolescent's awareness that steroids might make a significant difference in his or her athletic career. Drug testing has been integral to the Olympic Games for 30 years and, despite testing and public punishment, has not cut use among adolescents; in fact, to the contrary. Correlations between professional and adolescent athletes' use do not constitute cause-and-effect relationships. There appears to have been a general trend over the past 20 years toward ever more use by professional and Olympic athletes and adolescents, without general recognition that many professional athletes have been users. In fact, adolescent use was present before national surveillance demonstrated it.[11] In addition, the testing and sanction of only male professional athletes might not influence anabolic steroid use by young women or individuals seeking a more "attractive" body image rather than more athleticism. Most important, there are many factors responsible for substance use other than emulating professional or Olympian athletes. Among them are peer, family, community, and media influences. Without responses to these factors or funding evidence-based programs, the current and planned

From the Sports Medicine Specialist

- 6.1% of high school students admit to anabolic steroid use.
- Young women and men use steroids for different reasons.
- Male use tends more toward risk taking and striving to be bigger and more athletic, whereas females use steroids more for body shaping and disordered eating practices.
- Legislation has curbed precursor supplements available over-the-counter.
- Congress has signed—but not funded—legislation to educate youth.

legislative response fails to address factors spurring future adolescent use.

States have initiated discussions and recommendations to combat steroid use. The New Jersey Governor's Commission and subsequent order has recommended drug testing and education, using science-based programs.[13] ■

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Read more about this topic in an article, "Hormone Abuse in Adolescents and Adults: A Review of Current Knowledge." It was written by Endocrine Society members Linn Goldberg, M.D., Diane Elliot, M.D., Daniel Spratt, M.D., Alan D. Rogol, M.D., Ph.D., and Lisa H. Fish, M.D., and Barry Dickinson, Ph.D., of the Council on Scientific Affairs of the American Medical Association, and was published *The Endocrinologist* in 2005. To obtain free copies, contact The Hormone Foundation at 1-800-HORMONE or *hormone@endo-society.org*.

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This is the eighth appearance of the tri-point perspective articles in ***Endocrine News***. Past topics have been:

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