

Anabolic-Androgenic Steroids: Use and Abuse in Pediatric Patients

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The “win at all costs” mentality fuels athletes to seek performance-enhancing substances, such as anabolic-androgenic steroids (AASs), to gain an advantage over their opponents. Nonathletes espouse this same attitude to “win” the battle of attractiveness. They view AASs as the means to achieving what they believe is a more desirable muscular physique. These beliefs have filtered from professional, Olympic, and collegiate levels into high schools, middle schools, and grade schools. An enhanced understanding of AASs and the motivations behind their abuse will arm the pediatrician with the ability to engage one's patients in a balanced discussion of the benefits and costly risks of AASs and successfully deter further use.

History

High levels of AAS abuse have been attributed to professional football players, bodybuilders, weight lifters, and track and field throwers since the 1960s. The exceptional athletic performance of the East German female swimmers in the 1976 Montreal Olympics brought further public attention to AAS athletic use. It was not until the 1980s, however, that the medical community admitted that these substances were effective [1]. Since that time, the pervasive use of AASs by professional athletes has garnered significant media attention, culminating most recently in the ongoing investigation of the use of illegal performance enhancing drugs by some of baseball's top players. *Juiced*, a book by Jose Canseco, details his steroid use and the widespread use of anabolic steroids in Major League Baseball.

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The fame achieved by such professional athletes may be what makes trying AASs so enticing to adolescents.

Physiology

Several studies have contributed to an enlarging body of evidence regarding the anabolic “tissue-building” effects of AASs on their primary target, skeletal muscle. The actions of AASs on the musculoskeletal system have been shown to influence lean body mass, muscle size and strength, protein metabolism, bone metabolism, and collagen synthesis [2–8]. Over a period of 10 to 20 weeks, a supraphysiologic dose of testosterone administered to healthy young men can increase lean body mass, as well as muscle size and strength with or without exercise [2,3,8]. These significant increases are dose dependent and only occur with doses of 300 mg per week and higher [3,8]. The most profound effects are noted when supraphysiologic doses accompany a training program and are used in conjunction with a diet adequate in protein and calories [2,9,10].

Testosterone-induced muscle hypertrophy and increases in muscle strength are the result of increases in the cross-sectional area of muscle fibers and myonuclear number [8]. Research suggests that these anabolic effects are mediated by testosterone-influenced increases in muscle protein synthesis, creating a positive nitrogen balance [5,7,11]. Androgen receptors in skeletal muscle regulate the transcription of the target genes that control the accumulation of DNA needed for muscle growth. Complementary effects include glucocorticoid antagonism, which minimizes the catabolic actions of corticosteroids released during the stress of athletic activity. Similarly, stimulation of the growth hormone insulin-like growth factor-1 axis [12] and enhanced collagen synthesis and bone mineral density [13] are additional anabolic effects.

AASs induce a state of euphoria and diminished fatigue that enables prolongation of training sessions by users. Recent data may explain how AASs exert these psychoactive effects on the brain. Henderson and colleagues [14] proposed that AAS-mediated acute and chronic changes in the gamma-aminobutyric acid (GABA) receptor system cause many of the known behavioral effects. For instance, the immediate effects of decreased anxiety and enhanced sense of well-being that are experienced by AAS users likely arise from enhancement of forebrain GABAergic circuits. In contrast, anxiety and aggression are the result of a down-regulation of GABA receptor expression secondary to chronic AAS exposure. Further study may reveal that expression of these behaviors is influenced by the age and gender of the AAS user and the particular chemical composition of the AAS administered.

Clinical uses

The anabolic properties of AASs have proven beneficial for some therapeutic applications. They have been used in clinical practice since the 1940s

for the treatment of trauma, burns, extensive surgery, radiation therapy, and chronic debilitating illnesses [15–18]. Before the advent of bone marrow transplantation and synthetic erythropoietin, AASs were used often in the treatment of various types of anemias. AASs have shown promise in treating short stature, as in Turner's syndrome, or constitutional growth and puberty delay. Since 1985, the clinical use of AASs has increased 400%, mostly due to the management of AIDS-associated wasting syndrome. AASs may enhance the effects of the increased caloric intake and exercise regimen [19]. A pilot study in malnourished HIV-infected children as young as 4 years old showed that oxandrolone treatment was well-tolerated and improved nutritional status. After 3 months of treatment, the study subjects experienced an accelerated rate of weight gain, increased body mass index, increased muscle mass, and decreased fat stores as compared with pretreatment values. The results were supported further by the improved serum albumin levels noted during the course of treatment. Future studies using a larger study population and longer- or higher-dose AAS administration would strengthen the current data [20]. In patients with severe burns, AASs may play an important role in reversing the catabolic state. A small prospective randomized study of patients who had burns showed that those receiving oxandrolone in addition to a high-protein diet experienced a significantly greater increase in weight and physical therapy index than did patients who were treated with diet alone [21]. AAS therapy seems to be promising in the treatment of malnutrition and muscle wasting seen in patients who have end-stage renal disease. In addition to the increase in lean body mass, these patients also benefit from a stimulated erythropoiesis resulting from the administration of AASs [22,23]. Such positive effects warrant further study [19].

Legal issues

The nonmedical use of AASs has been banned by the International Olympic Committee, the United States Olympic Committee, and the National Collegiate Athletic Association. Such use also is denounced by the American Medical Association, the American College Health Association, the American Academy of Pediatrics, the American College of Sports Medicine, and the National Strength and Conditioning Association [24]. Steroids are banned from use by all major sporting leagues, although each has its own testing and penalization policies [25]. The US Federal Government and most state governments have enacted laws regarding the distribution, possession, or prescription of AASs. The Federal Food, Drug, and Cosmetic Act was amended as part of the 1988 Anti-Drug Abuse act, such that distribution of AASs or possession with intent to distribute without a valid prescription became a felony. Such offenses are punishable by a prison term of up to 5 years or fines totaling \$250,000 [25]. In 1990, the

Anabolic Steroids Control Act was signed into law, thereby classifying AASs as Schedule III drugs within the Controlled Substances Act. The Drug Enforcement Agency now controls the manufacture, importation, exportation, distribution, and dispensing of AASs [26].

Sources

Despite the above-mentioned barriers, AASs are still making their way into the hands of adolescents and children. Most commonly, the sources are bodybuilding gyms that obtain the drugs by way of a multimillion dollar illicit black market: foreign mail order, Internet dealers, or Internet pharmacies [2]. Most concerning about such sources is that the purity and actual content of the product received cannot be guaranteed.

Prevalence of adolescent anabolic-androgenic steroid use

The first reported adolescent use of AASs was in 1959 by a high school football player [27]. Current estimates of high school steroid usage range from 4% to 11% in boys and up to 3.3% in girls [28,29]. The landmark study of prevalence that was performed by Buckley and colleagues [30] involved a nationwide survey of more than 3000 boys. They found that 6.6% of male high school seniors had tried steroids, with 67% initiating use by 16 years of age and 40% using multiple cycles. These results have been confirmed in later studies of Indiana high school football players documenting a 6% use rate [31] and a 2003 Centers for Disease Control and Prevention report finding a 6.4% use of steroids by 12th-grade boys. The largest nationwide cohort of nearly 50,000 students is being examined in the Monitoring the Future study [32]. As of 2004, results of this ongoing study indicated a 1.3%, 2.3%, and 3.3% annual prevalence of male AAS users in the eighth, 10th, and 12th grades, respectively. Girls in the 12th grade had a 1.7% use rate in this study, whereas the Centers for Disease Control and Prevention reported a 3.3% lifetime prevalence in 12th-grade girls.

Prevalence studies have extended to middle school populations as well. A 1993 study of Modesto, California seventh-grade students was the first to document the use of steroids in students aged 12 to 15 years [33]. The overall rate of use reported was 3.8%, with more male students (4.7% versus 3.2% in female students) admitting to using AASs. A later article published data from a study of Massachusetts students between 9 and 13 years of age [34]. AAS use was reported by 2.7% of all middle school students surveyed, with 2.6% of boys and 2.8% of girls reporting use. As in other studies, the prevalence of AAS use increased with increasing age. Both of these regional studies were consistent with data from Yesalis [35], who reviewed AAS prevalence rates among junior high school students in the United States (2% for sixth graders and 2.3 to 3% for eighth graders).

AAS use by adolescents is not limited to the United States. Three Canadian studies, two Swedish surveys, two South African investigations, one British study, and one Australian investigation reported an overall prevalence range between 1% and 3%. Although slightly lower, these rates approximate those reported in the United States, demonstrating that the impact of AASs on athletic performance and physical appearance reaches across cultures [36].

Risk factors for adolescent anabolic-androgenic steroid abuse

Many studies of adolescent AAS users and abusers have attempted to create a profile of the typical user. The following discussion reviews some of the data relating to demographics, school performance, athletic participation, and personality of AAS users.

Demographic factors

Generally, the relative risk of AAS use is at least two to three times greater for male adolescents. The review of numerous studies shows a wide variation in the age range of AAS users. Race and ethnicity of AAS users is equally unclear. Some studies reported greater use among minorities [30,33,37–40], whereas others revealed a higher rate among white adolescents [41–46]. One regional study reported a significantly higher rate in blacks [33]. Other studies reported no racial difference in adolescent AAS use. Likewise, no clear-cut relationship exists regarding geographic location, city size, or school size.

Academic factors

There may be some association between AAS use and poor academic performance. In a large national study, DuRant and colleagues [47] stated that students who reported below-average academic performance had a significantly higher prevalence of AAS use than did average or above-average students; however, two studies, reported no relationship between academic achievement and AAS use [48,49]. Future studies regarding this question are needed.

Athletic performance

Adolescents use AASs as a method to improve their athletic performance. AAS users are significantly more likely than are nonusers to participate in school-sponsored athletic programs [30,40,50–53]. Sports requiring muscular strength and power are those most closely associated with AAS use among their participants. Such sports include football, wrestling, and track and field [30,40,41,50,51,54–56]. Faigenbaum and colleagues [34] reported

greater AAS use in gymnastics and weight training in their study sample. Strength undoubtedly is an asset to gymnasts, and, thus, correlates well with the observed higher percentage; however, they were concerned with the suggestion that some young gymnasts may use AASs to stunt their growth because they believe that small stature confers an advantage in gymnastics. It is important to realize that approximately 30% to 40% of adolescent AAS users do not participate in a school-sponsored sport. These users likely participate in bodybuilding or weightlifting activities [30,40].

Personality and behavioral factors

A considerable percentage of adolescents turn to AAS use to help them achieve an attractive physique. This is the second most popular reason for using AASs. One study of bodybuilders suggests that the drive for a muscular physique sometimes reaches an unhealthy extreme and likens the use of AAS to the “unhealthy extremes” that are characteristic of anorexic and bulimic individuals. Just as eating disordered women see their bodies as larger than they actually are, some men perceive themselves as smaller than they actually are. Taylor [57] refers to this phenomenon as “bigamerexia” and suggests that this misperception may be a contributory factor in AAS use. This misperception is likely evident in many ninth-grade boys, who—in the early stages of puberty—are impatient with their muscular development. Perceiving themselves smaller than their peers, these boys may engage in AAS use as a shortcut to increasing muscle strength and size [39]. Exposure to the media may intensify this body dysmorphia. Field and colleagues [58] examined this possibility in a study of supplement use among adolescents. They found that girls and boys who reported thinking frequently about wanting more defined muscles and those who were trying to emulate the look of same-gender figures in the media were more than three times more likely to use agents to build muscle or improve appearance.

Adolescent AAS use has been associated with the use of other harmful drugs, including cigarettes, smokeless tobacco, marijuana, alcohol, cocaine, and injected drugs. These behaviors support a risk behavior framework hypothesized by Jessor [59] in his Problem Behavior Theory. He proposed that there are intraindividual similarities among adolescent problem behaviors such that they cluster to form a “risk behavior syndrome.” Thus, AAS use would be considered a part of this cluster rather than an isolated behavior. Middleman and colleagues [60] applied this theory to a study of Massachusetts high school AAS users. They noted that the frequency of AAS use was associated with driving after drinking alcohol, carrying a gun, sexual promiscuity, unprotected intercourse, injury in a fight requiring medical attention, history of a sexually transmitted disease, not wearing a helmet on a motorcycle, not wearing a passenger seatbelt, and a suicide attempt requiring medical attention. Another concerning health-compromising behavior is the sharing of needles and multidose vials by between 25% and 33% of

adolescent AAS users. This practice contributes to the risk for acquiring infections, such as HIV, hepatitis B, and hepatitis C [61,62].

Dosage and patterns of use

Anabolic steroids may be taken orally or injected intramuscularly [63] and are grouped into three main classes [14]. Testosterone esters, such as testosterone propionate, are injected compounds and constitute class I. Class II agents include the nortestosterone derivatives (eg, nandrolone decanoate and nandrolone phenpropionate). Class I and II AASs exert effects at androgen receptors as well as at estrogen receptors by way of aromatization to estradiol [17]. The third class of AASs are those alkylated at C-17 and are the orally administered compounds oxymetholone, methandrostenolone, and stanozolol. Alkylation of these compounds involves the addition of a methyl or ethyl group to the carbon at position 17 of the steroid backbone. The alkylation slows the hepatic metabolism of these agents [19]. These and other common oral and injectable preparations are listed in Table 1.

A typical pattern of use consists of a combination of injectable and oral steroids taken during 6- to 12-week cycles. Injectable forms tend to be favored by users because they are less hepatotoxic than the oral forms [1]. Because oral

Table 1
More commonly abused anabolic steroids

Generic name	How supplied	Recommended dosage	Abused dosage ^a
Oxymetholone (O)	50 mg	1–5 mg/kg/d	50–100 mg/d
Oxandrolone (O)	2.5 mg	5–10 mg/d	15 mg/d
Nandrolone decanoate (I)	25 mg/mL, 5 mL	100–200 mg/wk	200–400 mg/wk
Methandrostenolone (O & I)	5 mg, 10 mg/mL	—	15–30 mg/d, 50–100 mg/wk
Boldenone undecyclenatate (I)	50 mg/mL	—	5 mL/wk
Methenolone (O & I)	50 mg/ml; 50, 100 mg/mL	—	50–100 mg/d, 200 mg/wk
Testosterone propionate, phenyl propionate, isocaproate, decanoate (I)	250 mg/mL	—	250 mg/wk
Testosterone cypionate (I)	200 mg/mL	25–200 mg/wk	1–3 mL/wk
Testosterone enanthate (I)	200 mg/mL	25–200 mg/wk	1–3 mL/wk
Testosterone propionate (I)	100 mg/10 mL	50–150 mg/wk	200–400 mg/wk
Testosterone suspension (I)	100 mg/10 mL	—	50 mg/d
Stanozolol (O & I)	2 mg, 50 mg/mL	6 mg/d,	16–30 mg/d, 3–5 mL/wk

Abbreviations: O, oral; I, injectable.

^a Abused dosages may vary greatly by gender, personal experience, availability of specific steroids, performance and appearance goals, and the simultaneous use of several steroids.

Data from Bahrke MS, Yesalis CE, Brower KJ. Anabolic-androgenic steroid abuse and performance-enhancing drugs among adolescents. *Child Adolesc Psychiatr Clin N Am* 1998;7(4):826.

preparations are cleared from the system more quickly, they are the preferred form of steroids when drug testing is anticipated. The simultaneous use of multiple steroids is referred to as “stacking.” A pattern of increasing a dose through a cycle is called “pyramiding.” Pyramiding can lead to doses 10 to 40 times greater than the dose recommended for medical indications. By stacking and pyramiding doses, the user hopes to maximize steroid receptor binding, thereby reducing toxic side effects. These patterns have remained popular, despite the lack of scientific evidence of a benefit [29]. Some users take other drugs concurrently in an effort to minimize side effects. These “accessory” medications include clomiphene and human chorionic gonadotropin and are administered to reverse the endogenous testosterone production. Additionally, tamoxifen and antiaromatase drugs can prevent or decrease gynecostasia by limiting estrogenic effects and the metabolism of excess testosterone derivatives to estradiol [63]. It is not uncommon for users to take other legal performance-enhancing substances and dietary supplements, such as creatine, glutamine, and protein, while using AASs [64].

Adverse effects

For years, scientists have attempted to dissociate the anabolic properties from the androgenic characteristics of AASs, to no avail. Therefore, both components exert adverse effects on various tissues and body systems.

Hepatic

Various studies have shown transient elevations in liver function tests in conjunction with AAS use [10,65,66]. The C-17 alkylated oral preparations are associated most often with liver toxicity [67]. Elevations in aspartate transaminase, alanine transaminase, lactate dehydrogenase, and alkaline phosphatase have been reported [10]. Values measured can be two to three times the normal range, peaking within 2 to 3 weeks of consumption. Usually, a return to baseline is seen within several weeks of discontinuation [68]. Many AAS users also abuse alcohol, thus compounding the hepatic adverse effects.

Anabolic-related cholestasis has been reported to occur in varying frequency from a few cases to up to 17.3% in some studies [69,70]. The transient jaundice that results is secondary to biliary stasis rather than structural hepatic injury. Structural lesions have been studied in case reports of the blood-filled cysts of peliosis hepatis [71]. Internal hemorrhage or hepatic failure can occur secondary to such lesions.

Hepatocellular adenomas have been associated with high-dose AAS, long periods of administration of AAS, or in AAS users with a predisposing medical condition [10,67]. It is particularly difficult to differentiate adenomas from hepatocellular carcinoma by ultrasound. Prompt identification of these lesions is critical because the potential for malignant transformation may increase if a late diagnosis is made [72].

Cardiovascular

Altered lipid profiles in AAS users are reflected in increased low-density lipoprotein and decreased high-density lipoprotein [66,71,73]. The oral C-17 alkylated steroids seem to exert the greatest effects on the lipid profile [68,74,75]. Thrombus formation has been postulated by way of these adverse lipid changes and is supported further by findings of AAS-induced increased platelet aggregation, enhanced coagulation enzyme activity, and coronary vasospasm [76].

Hypertension in AAS users has been reported and is likely the result of blood volume increases and fluid retention [71,76]. This effect, as well as the finding of increased septal thickness and left ventricular mass reported in AAS users [77,78], can lead to significant detrimental cardiac remodeling.

Reproductive/endocrine

Exogenous steroid administration provides feedback inhibition of luteinizing and follicle-stimulating hormones, which leads to testicular atrophy and decreased spermatogenesis. This testicular impairment is reversed upon cessation of AAS use. Excess steroids undergo peripheral aromatization to estrogens, which results in feminizing changes of high voice pitch and male gynecomastia [71]. In long-term AAS abuse, this gynecomastia is irreversible, leaving surgical correction as the only solution [79]. In addition to the female side effects of decreased menstruation and breast tissue atrophy, virilizing effects also occur and include deepened voice, clitoromegaly, and hirsutism. Sometimes these effects are irreversible, even after discontinuation of AAS use [80].

Musculoskeletal

Experimental evidence exists that the use of AASs combined with intense exercise can cause structural and biomechanical alterations of tendons resulting in rupture. Structurally, the collagen fibril alignment is highly disorganized. From a biomechanical perspective, when muscle strength is increased with AAS use, the tendon becomes stiffer, absorbs less energy, and is more likely to fail during physical activity [81].

Premature growth cessation due to physal closure in younger users has not been studied systematically. Such case reports of the resultant permanent short stature have been described for several decades [82].

Dermatologic

Severe cases of acne, especially on the face and back of AAS users, are common dermatologic findings. Premature baldness is noted as well. Dickinson and colleagues [83] reported multiple cases of serious muscular abscesses resulting from the common practice of shared needles and shared

steroid vials among adolescent AAS users. A limited knowledge of sterile injection technique, as well as limited access to sterile needles and syringes are likely additional causative factors in these infections.

Psychiatric

AAS use has been associated with self-reported changes in mood and behavior. A study by Pope and Katz [84] identified psychiatric syndromes in weightlifters using AASs. Twenty-three percent of AAS users experienced major mood changes of mania, hypomania, or major depression. Also common in AAS users was aggressive behavior resulting in fights, domestic disturbances, assaults, and arrests. Data from the National Household Survey on Drug Abuse have demonstrated a strong association between AAS use and self-acknowledged acts of violence against people and crimes against property [85]. In general, the behavioral effects of AASs are variable, short-lived on discontinuation, and seem to be related to the type and dosage of AAS.

The potential for physical dependence upon AASs does exist. In one study of AAS users, 50% of them met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for dependence or abuse of steroids [86]. Physical symptoms of withdrawal are similar to those seen during alcohol and opioid withdrawal, including diaphoresis, myalgias, nausea, and increases in blood pressure and heart rate [87]. Withdrawal may also be characterized by depressive symptoms [88]. Deeply entrenched body dissatisfaction and body dysmorphic disorder may underlie a psychologic dependence. Clearly, the addictive potential of AASs cannot be discounted [89].

Prevention efforts

The implementation of drug-testing policies has been considered as a possible preventive strategy. Data from the National Federation of State High School Associations indicate, however, that only 13% of schools test athletes and, of those schools, only 29% test for AASs. The reasons for the low number of testing programs include financial constraints (~\$120 per test) and the fact that testing often can be circumvented by the user. Dose titration with newer transdermal delivery systems of testosterone or discontinuation of use before a scheduled test can maintain levels below a testing threshold [90]. Testing only athletes also will miss a significant percentage of nonathlete users.

Educational programs have been suggested as a more effective means of deterring AAS use. Goldberg and colleagues [91] tested a team-based educational intervention designed to reduce Portland, Oregon high school football players' intent to use AASs. The Adolescents Training and Learning to Avoid Steroids Program consisted of 50-minute class sessions that were delivered over a 7-week period by coaches and athlete team leaders. The

sessions combined drug education with attainment of personal skills to assist athletes in resisting the social influences that fuel an athlete's desire to use AASs. Athletes in this intervention group gained a greater knowledge of the consequences of AAS use, were more skeptical about the media's promotion of AASs, and had improved drug-refusal skills. These results are certainly encouraging and follow-up data are eagerly anticipated.

The pediatrician's office can be a valuable educational setting as well. Using "scare tactics" as a prevention effort to dissuade adolescents from becoming AAS users has been proven to weaken physician credibility and may even encourage use [92]. Rather, Metz [93] offers the concept of "thoughtful discouragement" as the key to effective prevention. He recommends that the clinician first recognize that a patient may be using AASs. The sports preparticipation physical examination offers an ideal opportunity to note any physical changes suggestive of AAS use and to ask whether the patient is using a performance-enhancing substance. Education is the next step and should be a balanced discussion focusing on the current research, the physiologic effects, and the adverse events. A concerning trend in 12th graders showed a steadily decreasing perceived risk for steroid use yearly since 1993. Only 55% of seniors now consider steroid use as a great risk [32]. Finally, healthy alternatives to AAS use must be presented. A supervised strength-training program among children as young as 8 years of age is a safe and effective means of increasing strength and improving athletic performance [94]. By emphasizing repetitions rather than maximum weight lifting, baseline strength can be increased by 30% to 40% [95].

Summary

Our society equates success with winning. The drive to win athletic competitions or the obsession with achieving the perfect physique has made adolescents and children increasingly vulnerable to the lure of AASs. The increases in muscular size and strength that are characteristic of AASs occur with attendant short-term adverse effects and the potential for long-term health consequences. A mindset of invincibility that is typical of many adolescents allows them to be willing to pay the price of these negative events for the chance to gain a competitive edge.

Educational programs addressing the social, media, and peer influences that perpetuate adolescent use of AASs have shown promise in decreasing the intent to use. Such educational programs need to be directed toward middle school classrooms to decrease the rate of first use in this age group. Physician dissemination of accurate information to parents, coaches, and school administrators is vital to the creation of intervention programs. By demonstrating a knowledge base that earns adolescent respect, the pediatrician will be able to effectively discourage AAS use and convince the patient that there is no substitute for sound nutrition and a sensible strength-training program.

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