

# Popular Ergogenic Drugs and Supplements in Young Athletes

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## ABSTRACT

Ergogenic drugs are substances that are used to enhance athletic performance. These drugs include illicit substances as well as compounds that are marketed as nutritional supplements. Many such drugs have been used widely by professional and elite athletes for several decades. However, in recent years, research indicates that younger athletes are increasingly experimenting with these drugs to improve both appearance and athletic abilities. Ergogenic drugs that are commonly used by youths today include anabolic-androgenic steroids, steroid precursors (androstenedione and dehydroepiandrosterone), growth hormone, creatine, and ephedra alkaloids. Reviewing the literature to date, it is clear that children are exposed to these substances at younger ages than in years past, with use starting as early as middle school. Anabolic steroids and creatine do offer potential gains in body mass and strength but risk adverse effects to multiple organ systems. Steroid precursors, growth hormone, and ephedra alkaloids have not been proven to enhance any athletic measures, whereas they do impart many risks to their users. To combat this drug abuse, there have been recent changes in the legal status of several substances, changes in the rules of youth athletics including drug testing of high school students, and educational initiatives designed for the young athlete. This article summarizes the current literature regarding these ergogenic substances and details their use, effects, risks, and legal standing.

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### Key Words

adolescent health, athletes, drug abuse/use, nutritional supplements, steroids

### Abbreviations

NCAA—National Collegiate Athletic Association

DHEA—dehydroepiandrosterone

FDA—Food and Drug Administration

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**B**ECAUSE 57% OF all high school students play on formal sports teams, the use of both illicit and legal ergogenic drugs to enhance performance in amateur athletics is of significant concern today (Table 1).<sup>1</sup> Furthermore, up to one third of high school students who use anabolic steroids are in the population of nonathletes who use steroids to improve their appearance.<sup>2</sup> Drug and supplement use is not uncommon today. It is estimated today that 1 to 3 million US athletes are taking steroids, and 2500 metric tons of creatine were consumed in 1999.<sup>3,4</sup> Many substances are being used by today's youths, commonly without recognizing any risks of such drugs.<sup>5</sup> Even as this problem increases, there are concerns that pediatric residents are receiving minimal education in the field of sports medicine during both medical school and residency.<sup>6</sup> Although the focus of pediatric sports medicine is typically proper training and managing common injuries, an emerging issue is learning about the drugs that are chosen by young athletes to improve athletic performance. This article is intended to educate pediatricians, the most common medical contact for young athletes, about several drugs that commonly are used, with particular attention to their physiology, effects, adverse effects, legal and sporting implications, and the incidence of each drug's use. This article also discusses the history of ergogenic substances in sports, factors in society today that are encouraging the problem, and measures to protect this population of young people.

### **HISTORY OF DRUGS IN SPORTS**

Drug use by athletes to improve performance is not a new practice. As early as BC 776, the Greek Olympians were reported to use substances such as dried figs, mushrooms, and strychnine to perform better.<sup>7</sup> However, medical advances now have produced substances that are much more effective toward this end. A landmark discovery was made in 1889 when Dr Brown-Sequard announced at a scientific meeting in Paris that he had found a substance that reversed his 72-year-old body's ailments. He reported having injected himself with the extract of dog and guinea pig testicles under the assumption that these organs had "internal secretions that acted as physiologic regulators."<sup>8</sup> This bold statement was confirmed with the discovery of hormones in 1905 and the isolation of testosterone in 1935. Soon thereafter in the 1950s, Russian weightlifters began to outpace American Olympians through performance-enhancing injections. Attempting to make up lost ground, the then US Olympic physician teamed with chemists to produce an anabolic steroid for the Americans, now known as Dianabol.<sup>9</sup> In the decades that followed, steroids and stimulants spread throughout sports, and in 1959, the first reported case of a high school football player's taking steroids surfaced.<sup>10</sup> In the 1960s, the International Olympic Committee banned steroid use and began for-

mal drug testing in the ensuing decade.<sup>11</sup> During the 1980s, the reported positive test results ranged from 2% to 50%, depending on whether the tests were announced or conducted at random.<sup>12,13</sup> At the 1988 Seoul Olympics, the first gold medal in track and field was stripped when the Canadian sprinter Ben Johnson lost his 100-m victory after failing drug tests. Then, in 1994, an often-referenced survey was conducted by Goldman when aspiring Olympians were asked 2 simple questions. The first was, "If you were offered a banned performance-enhancing substance that guaranteed that you would win an Olympic medal and you could not be caught, would you take it?" Remarkably, 195 of 198 athletes said yes. The second was, "Would you take a banned performance-enhancing drug with a guarantee that you will not be caught, you will win every competition for the next 5 years, but will then die from adverse effects of the substance?" Still, >50% of the athletes said yes.<sup>14</sup> This survey made it clear that modern athletes often approach their sports with a "win at all costs" mentality. In 2005, information surfaced to suggest that this mentality is becoming more prevalent even in high school athletics, with several highly publicized deaths in teenagers who were on steroids and a recent scandal with 9 students on 1 high school football team admitting to steroid abuse.<sup>15,16</sup>

### **FACTORS IN SOCIETY TODAY**

Several factors that are unique to our current society may contribute to young people's using drugs to succeed in sports. First is the message that is being sent by many sports idols today. The recent steroid investigations in baseball and books by former players make it clear that steroids and other drugs have played a part in many record-breaking performances. However, the fame and the respect that still is garnered by these athletes sends the message that ergogenic drugs are accepted, if not necessary, to reach such success. As young athletes begin to model themselves after sport icons, heartbreaking stories are beginning to unfold. One young athlete in a tear-filled confrontation with his father only months before committing a now highly publicized suicide linked to his steroid use confessed, "I'm on steroids, what do you think? Who do you think I am? I'm a baseball player, baseball players take steroids. How do you think Bonds hits all his home runs? How do you think all these guys do all this stuff? You think they do it from just working out normal?"<sup>17</sup>

Second, society today places a huge emphasis on sports with collegiate football stadiums seating nearly 100 000 people and countless events featured on national television. From high school basketball all-star games to the Little League World Series, our youths are placed under the national spotlight at exceedingly young ages. With professional scouts now following high school sports and collegiate coaches eyeing even

**TABLE 1** Ergogenic Drugs

Ergogenic Drug	Category	Goals of Use	Athletic Effect	Adverse Effects
Anabolic-androgenic steroids	Controlled substance	Gain muscle mass, strength	Increase muscle mass, strength	Multiple organ systems: infertility, gynecomastia, female virilization, hypertension, atherosclerosis, physeal closure, aggression, depression
Androstenedione	Controlled substance	Increase testosterone to gain muscle mass, strength	No measurable effect	Increase estrogens in men; overlaps systemic risks with steroids
DHEA	Nutritional supplement	Increase testosterone to gain muscle mass, strength	No measurable effect	Increase estrogens in men; impurities in preparation
Growth hormone	Controlled substance	Increase muscle mass, strength, and definition	Decreases subcutaneous fat; no performance effect	Acromegaly effects: increased lipids, myopathy, glucose intolerance, physeal closure
Creatine	Nutritional supplement	Gain muscle mass, strength	Increase muscle strength gains; performance benefit in short, anaerobic tasks	Dehydration, muscle cramps, gastrointestinal distress, compromised renal function
Ephedra alkaloids	Possibly returning as nutritional supplement	Increase weight loss, delay fatigue	Increases metabolism; no clear performance benefit	Cerebral vascular accident, arrhythmia, myocardial infarction, seizure, psychosis, hypertension, death

younger talent, the pressure to succeed is placed now on younger, more impressionable shoulders than ever before.

Finally, several economic factors encourage drug use to gain an edge in sports. One is the resultant money and social stature that accompany athletic success when worthy of garnering professional contracts. Another more subtle but increasingly wide-reaching monetary influence is the rising cost of collegiate education. This has been shown to be a self-reported factor for high school girls to use performance-enhancing drugs while competing for prestigious and now very valuable athletic scholarships to college.<sup>18,19</sup> Whether they turn to ergogenic drugs for the competitive edge or as a means of keeping up with fellow students who are already using these substances, it is clear that the pressure to do so is significant today.

## ANABOLIC-ANDROGENIC STEROIDS

### Physiology

Anabolic steroids are synthetic derivatives of the hormone testosterone. The chemical structure has been modified by manufacturers to maximize anabolic effects by delaying metabolism via alkylation of the 17- $\alpha$  position or carboxylation of 19- $\beta$  hydroxyl group on the sterol D ring.<sup>20</sup> Steroids bind to androgen receptors within the cell cytoplasm. They then are transported into the nucleus before binding DNA and increasing mRNA transcription, which enhances contractile and structural protein synthesis.<sup>9,21</sup>

Steroids have 3 general effects that benefit the athlete. Binding androgen receptors promotes a positive nitrogen balance in muscle, which produces an anabolic state.<sup>22</sup> However, in the normal physiologic male individual, endogenous testosterone nearly saturates the available androgen receptors, making this effect of questionable importance. Therefore, it becomes critical that steroids are also anticatabolic. In the overtrained individual, glucocorticoids are increasingly released, which promote the breakdown of muscle glycogen for energy.<sup>23</sup> Once available androgen receptors are saturated, exogenous steroids competitively inhibit the binding of catabolic glucocorticoids, thereby preserving muscle mass being gained.<sup>24</sup> Finally, anabolic steroids have significant emotional effects. This is often manifest in increased aggression, which can push athletes to train more intensely, more often, or longer.<sup>25</sup>

### Dosing

Oral, injectable, and newer transdermal steroid preparations are available. Oral forms are short-acting and eliminated over days, whereas injectable steroids have longer lasting effects but risk positive drug testing up to months after use.<sup>4</sup> Steroids are usually used in the off-season, when athletes are strength training and when use is least

likely to be detected. Steroids are generally taken in 4- to 12-week cycles. Athletes often “stack” multiple steroids at the same time and “pyramid” the dosing schedule, taking highest amounts in the middle of cycles. Although attempting to maximize results, athletes may consume doses 50 to 100 times the amount that would replace physiologic steroid levels.<sup>9</sup> Between dosing cycles, it is typical for users to have a period of abstinence, known as a “drug holiday,” of varying duration. The most recent so-called “designer steroids” are steroids that are made with simple chemical modifications to preserve anabolic activity while being undetected during drug testing.<sup>20</sup> Common steroid preparations are listed in Table 2.

### Effects

Although not every study agrees, the consensus today is that these drugs do increase athletic measures with objective gains in strength and fat-free mass.<sup>26–28</sup> This fact was conceded in the 1980s by the American College of Sports Medicine.<sup>29</sup> Haupt and Rovere<sup>23</sup> reviewed the literature in the 1980s and concluded that athletes could not expect aerobic gains but that strength gains were substantial. Effects were most evident in those with previous weight-training experience and when single repetition maximal efforts were measured. A recent double-blinded study over a 12-week training cycle confirmed significant gains over placebo in ultrasound-measured muscle pennation and overall strength on a bench press test.<sup>30</sup> These drugs increase isokinetic and isometric strength, as well as muscle mass both via muscle hypertrophy and the formation of new muscle fibers.<sup>31</sup> It is important to note that because of ethical concerns, these studies on the effects of anabolic-androgenic steroids as well as those subsequently discussed concerning other ergogenic drugs were performed on adults, although they offer our best controlled evidence and are presumed to represent effects equally in adolescents.

### Adverse Effects

Nearly 30% of steroid users experience mild subjective adverse effects.<sup>23</sup> Steroid supplementation has potential adverse effects in multiple organ systems. From an endocrine perspective, exogenous steroids provide feedback inhibition of luteinizing and follicle-stimulating hormones, which produces testicular atrophy and possible infertility. The additional steroids also undergo pe-

ripheral aromatization to estrogens, which can lead to irreversible male gynecomastia. It is also common to see premature balding, acne, and precocious puberty.<sup>22</sup> Steroids have an impact on the cardiovascular system by adversely affecting lipid profiles, raising blood pressure, and causing left ventricular hypertrophy.<sup>32–34</sup> The oral preparations pose the greatest risk to the hepatic system, with common transient disturbances including cholestasis and nonspecific increases in liver enzymes. There are also rare cases of peliosis hepatitis with blood-filled liver cysts and anecdotal reports of hepatocellular carcinoma with proposed links to steroid abuse.<sup>35</sup> The musculoskeletal system, although with grossly increased strength, exhibits dysplastic collagen fibrils that can predispose to muscle strains and ligament sprains.<sup>36</sup> The immature athlete after initial acceleration of bony growth may have premature physal closure, permanently shortening their final adult height.<sup>36</sup> Infections such as HIV, hepatitis B, and hepatitis C remain a concern associated with injectable preparations as several studies confirm that between 25% and 33% of adolescents who are taking steroids share needles.<sup>37,38</sup> Specific to female users are adverse effects such as deepened voice, clitoromegaly, and loss of breast tissue, with elements of this virilization being irreversible.<sup>22</sup> Psychologically, steroid users may experience severe mood swings from depression to mania and aggression that cannot be channeled properly outside the athletic arena. Using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, the American Psychiatric Association’s standard for defining mental illnesses, it has been reported that nearly 50% of steroid users in a series met criteria for being dependent on or abusing steroids (Table 3).<sup>39</sup>

Apart from medical adverse effects, several investigators have documented social risks to steroid use. Middleman et al<sup>40</sup> documented an association with other high-risk activities such as driving under the influence, carrying weapons, and engaging in unsafe sexual practices by young users. Durant et al<sup>41</sup> also elaborated on the increased use of other illicit substances by youths who take steroids, including marijuana and alcohol.

### Legal/Sports Aspects

The Anti-Drug Abuse Act in 1988 first prohibited the distribution of steroids for any purpose other than treatment of a disease. This was followed by the Anabolic Steroid Control Act of 1990, which placed steroids under Schedule III of controlled substances. The illegal possession of anabolic steroids is punishable by 1 year in prison and/or a minimum \$1000 fine, with selling or intent to sell incurring a 5-year prison sentence and/or a \$250 000 fine. Steroids are banned from use by all major sporting leagues, although each governing body has individualized testing and penalization policies.

**TABLE 2 Common Anabolic-Androgenic Steroids**

Oral Steroids	Injectable Steroids
Anadrol (oxymetholone)	Deca-durabolin (nandrolone decanoate)
Oxandrin (oxandrolone)	Durabolin (nandrolone phenpropionate)
Dianabol (methandrostenolone)	Depo-testosterone (testosterone cypionate)
Winstrol (stanozolol)	Equipoise (boldenone undecylenate)

Adapted from the National Institute of Drug Abuse, National Institutes of Health, public domain.

**TABLE 3 Summary of DSM-IV Criteria for Substance Dependence/Abuse**

Dependence Criteria	Abuse Criteria
1a. Tolerance (using increasing amount)	1. Failing in role obligations
1b. Tolerance (dosing with less effect)	2. Using in hazardous situations
2a. Withdrawal symptoms experienced	3. Recurrent legal problems as a result of drug
2b. Withdrawal lessened via other drugs	4. Use despite psychosocial problems
3. Using more than intended	
4. Unable to cut down	
5. Significant time spent using drug	
6. Missing important events as a result of drug	
7. Use despite negative effects	
Diagnosed with $\geq 3$ criteria in 12 mo	Diagnosed with $\geq 1$ criteria in 12 mo

DSM-IV indicates *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. American Psychiatric Association 1994.

## Incidence

Estimates of high school steroid use range from 4% to 11% in boys and up to 3.3% of girls.<sup>1,25</sup> The landmark study in this area was performed by Buckley et al.<sup>2</sup> This nationwide survey of >3000 boys found that 6.6% of male high school seniors had tried steroids, with 67% beginning use by 16 years of age and 40% using multiple cycles. This was later confirmed in a survey of Indiana high school football players documenting a 6% use rate (mean age at first use: 14 years) and a 2003 nationwide Centers for Disease Control and Prevention data finding a 6.4% use of steroids by 12th-grade boys.<sup>1,42</sup> Subsequent publications have continued to document childhood steroid use with consistent findings of 2% to 3% of students using steroids in ages from 9 years to young teens, with numbers reaching 9% among middle school children who reported being gymnasts or weightlifters.<sup>38,43,44</sup> Unfortunately, even when examining only ninth-graders, one investigator found percentages that quickly reflected previous estimates for use over the entire high school population with 5.3% of boys and 1.5% of girls using steroids in a survey of nearly 2000 Georgia students.<sup>45</sup> The ongoing Monitoring the Future study, which has the largest nationwide cohort of nearly 50 000 students, showed a 1.3%, 2.3%, and 3.3% annual prevalence of male steroid users in the 8th, 10th, and 12th grades, respectively, in 2004. Girls in the 12th grade had a 1.7% use rate of steroids in the past year, whereas the Centers for Disease Control and Prevention found a 3.3% lifetime prevalence of steroid use in 12th-grade girls.<sup>1,46</sup> Although the numbers from the Monitoring the Future survey are more modest than other reports, it is important to remember that these numbers reflect the entire student population, not just athletes, and that a concerning trend was found with 12th-graders showing a steadily decreasing perceived risk of steroid use yearly since 1993, with now only 55% of seniors viewing occasional steroid use as a great risk.<sup>46</sup> Even in Buckley's initial work, it remains noteworthy to realize that nearly one third of young steroid users do not participate in formal school sports.<sup>2</sup>

In the 1980s, estimates of steroid use reached 20% for

division I college athletes.<sup>47</sup> Subsequently, the National Collegiate Athletic Association (NCAA) began surveying its athletes to better define the demographics of substance use in this population. The latest NCAA survey in 2001 polled >21 000 student athletes in all championship sports and all divisions.<sup>48</sup> They reported that 1.4% of these individuals used steroids in the past 12 months. Recent independent studies of college athletes, however, raise the possibility of underreporting to the NCAA as results show up to 9% of athletes using steroids on 1 campus.<sup>49</sup> Worrisome trends discovered by the NCAA included a change in utilization, with most athletes in 1997 using steroids to recover from injury, whereas current athletes mainly reported use to improve performance or appearance. Also, steroids were the only ergogenic drug class to increase in all collegiate divisions. Furthermore, steroid use was beginning earlier than in the past, with 42% of users reporting first use in high school and 15% beginning steroids in junior high or before.<sup>48</sup>

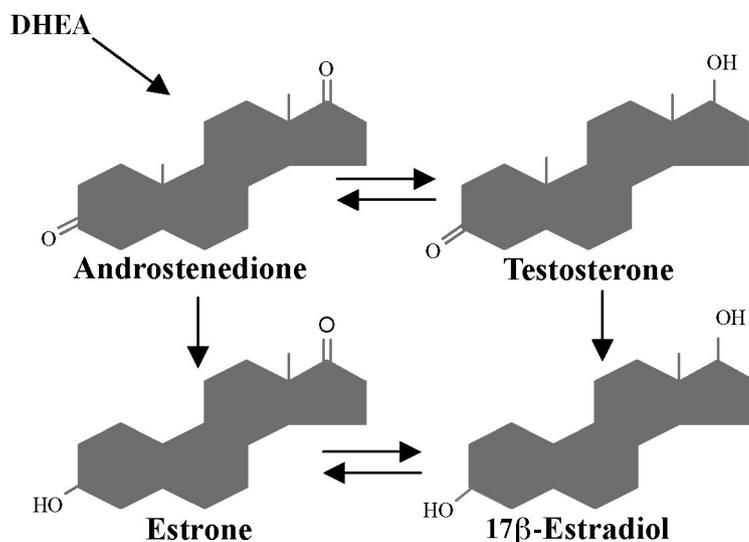
## STERIOD PRECURSORS (PROHORMONES)

### Physiology

Androstenedione and closely related dehydroepiandrosterone (DHEA) are 2 popular steroid precursors, or prohormones. DHEA is a weak androgen that is produced in the adrenal cortex, whereas androstenedione, a more potent anabolic-androgenic steroid, is made in the adrenal glands and gonads. DHEA is converted in the body to androstenedione, which then can be transformed into either testosterone or estrone (Fig 1).<sup>50</sup> Athletes use these substances with the belief that they will boost testosterone levels, thereby having ergogenic effects similar to anabolic steroids.

### Dosing

DHEA's recommended dosing is in a range of 50 to 100 mg/day for up to 1 year. The number of adverse effects increases at doses that exceed this amount, although athletes may well take more than the recommended amounts.<sup>51,52</sup> Although now off the supplement market,



**FIGURE 1**  
Steroid pathway for DHEA and androstenedione showing conversion to testosterone or estrone. Adapted with permission from DPC Company Web site. Available at: [www.dpcweb.com/documents/news%26views/fall\\_2003/images/androsteine.html](http://www.dpcweb.com/documents/news%26views/fall_2003/images/androsteine.html).

androstenedione's upper limit for dosing was 100 to 300 mg/day.

### Effects

In 1962, Mahesh and Greenblatt<sup>53</sup> published that androstenedione given to 2 female individuals resulted in increased testosterone levels. Since that time, there has been little support for these precursors having any ergogenic effects, although their popularity soared after Mark McGwire admitted to using androstenedione during his 1998 quest to break Roger Maris's single-season home run record. Leder et al<sup>54</sup> in 2000 reported that men who were given androstenedione showed increased testosterone levels, although this effect was seen only in the first few hours after initial use. Furthermore, the early boost in testosterone levels reached only the upper limit of normal for physiologic male individuals. Later, after several weeks of use, the only hormone change was increased estrogen.<sup>54</sup> Most studies have found no change in testosterone levels but have confirmed increasing estrogen levels in male individuals.<sup>4</sup> Specific to athletes, King et al<sup>55</sup> in 1999 published a series of 20 healthy male individuals with 8 weeks of standardized resistance training, whereby androstenedione was given in a double-blinded manner versus placebo. At the conclusion of the testing period, those who received the drug showed no change in any athletic measure or testosterone levels but were found to have significantly increased estrone and estradiol levels. In the literature to date, there is no convincing evidence that these prohormones have any true benefit for the athletes, and as Tokish et al<sup>20</sup> reported in 2004, "The marketing of this supplement's effectiveness far exceeds its science."

### Adverse Effects

Although androstenedione and DHEA are without proven benefit, they are not without risk. As they share

a metabolic pathway with anabolic steroids, they share several common adverse effects. These include adverse changes in lipid profiles as well as potential male gynecomastia and virilization of female individuals. Use of these substances may also downregulate endogenous testosterone over time.<sup>56</sup> In addition, priapism has been reported and animal studies have found resultant hyperplastic prostatic changes with use.<sup>57,58</sup> Finally, although DHEA is a legal supplement, impurities during production can place athletes at risk for testing positive for a banned substance.

### Legal/Sports Aspects

In 2004, a new Steroid Control Act that placed androstenedione under Schedule III of controlled substances effective January 2005 was signed. DHEA was not included in this act and remains an over-the-counter nutritional supplement. Androstenedione now is banned by all major sporting leagues, including Olympic and collegiate sports.

### Incidence

Sparse literature is available for evaluating use of androstenedione and DHEA. In 2002, Reeder et al<sup>59</sup> surveyed 475 high school students and found that 4% of this population of athletes and nonathletes used steroid precursors within the past year. Meanwhile, the NCAA's 2001 study found that 5.3% of their athletes admitted to use of androstenedione or DHEA in the past year.<sup>48</sup> The high number of adolescent users in Reeder's student body cohort suggests that these drugs are being used by adolescents and again raise concern that collegiate student athletes may be reluctant to report use to the NCAA.

## GROWTH HORMONE

### Physiology

Growth hormone is a polypeptide secreted by the somatotrope cells in the anterior pituitary. Secretion is pulsatile and gradually decreases after peaking during early adolescence. Growth hormone is converted in the liver into insulin-like growth factor 1, which has several effects throughout the body. Insulin-like growth factor 1 serves to increase protein synthesis, lipid catabolism, and bone growth.<sup>60</sup>

### Dosing

Growth hormone first was used in children who were growth hormone deficient. This was initially derived from cadavers and proved dangerous with the transmission of prion disease. Now, there is a biosynthetic growth hormone available. Growth hormone is produced only in injectable form. It may be used several times per month, and the cost of a 1-month supply can approach \$5000.<sup>61</sup> Athletes who take growth hormone often combine use with anabolic steroids.<sup>5</sup>

### Effects

Although growth hormone has many benefits for those who are congenitally deficient, it does not seem to hold similar promise for healthy young athletes. No conclusive evidence exists that growth hormone enhances athletic performance.<sup>62-64</sup> In fact, patients who have acromegaly with an excess of growth hormone may be the most accurate model for the athlete who is supplementing an already normal hormone level. Patients with acromegaly often have weaker muscles as a result of a growth hormone-induced myopathy and have demonstrated greater exercise tolerance after treatment to reduce growth hormone levels.<sup>65,66</sup> Even without proven performance benefit, this drug does have several effects that attract athletes. One is that growth hormone causes perceptible fluid shifts within bodily tissues with early use, causing individuals to feel that the drug is "doing something." Second, growth hormone has a repartitioning effect, which decreases subcutaneous fat, making it attractive to individuals who are aiming for a more toned appearance.<sup>67</sup>

### Adverse Effects

The initial use of growth hormone from cadavers risked transmission of prion diseases, but this has been resolved with the advent of synthetic growth hormone. However, injecting the synthetic form still carries with it the widely known risks of hepatitis and HIV transmission with the use of nonsterile needles. Additional risks include premature physeal closure, jaw enlargement, hypertension, and slipped capital femoral epiphysis.<sup>51</sup> Rare but severe risks also include reported papilledema with intracranial hypertension.<sup>9</sup>

### Legal/Sports Aspects

Growth hormone is a banned by all major sporting leagues. However, no reliable test to detect use by athletes has been developed.

### Incidence

Questioning younger athletes, Rickert et al<sup>5</sup> surveyed 224 boys who were in the 10th grade to assess high school growth hormone use. Nearly 5% reported using growth hormone, with 10 students indicating explicitly that it was for improving sports performance. More than half used growth hormone in conjunction with steroids, and 70% reported use more than once per month. Of concern was the fact that half of the students could not name a single risk associated with taking growth hormone.<sup>5</sup> The latest NCAA study found that 3.5% of athletes reported using growth hormone in the past 12 months.<sup>48</sup> It is interesting that this statistic was available in the raw data but was without mention in any published conclusions.

## NUTRITIONAL SUPPLEMENTS

Nutritional supplements can be purchased legally at any health store. Yearly sales in the United States approach \$12 billion to \$15 billion, with sport supplements being responsible for \$800 million.<sup>68,69</sup> Investigators at 1 university found that 88% of athletes used nutritional supplements, and among a high school cohort of 270 athletes, 58% had used some form of supplementation.<sup>70,71</sup> The 1994 Dietary Supplement Health and Education Act permanently changed the landscape for these substances. In this act, dietary supplements were defined as "a product (other than tobacco) that is intended to supplement the diet. It bears or contains 1 or more of the following dietary ingredients: a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance to supplement the diet by increasing the total daily intake; or a concentrate, a metabolite, constituent, extract, or combination of these ingredients. The product is intended for ingestion in pill, capsule, tablet, or liquid form. The product is not recommended for use as a conventional food or as the sole item of a meal or diet, and it is labeled as a dietary supplement."<sup>72</sup> Besides providing a generously inclusive definition, the act had several other implications. Specifically, Food and Drug Administration (FDA) approval is not necessary for a supplement to reach the marketplace. Remarkably, manufacturer claims do not need to be proven before appearing on labels. Claims require only a disclaimer that there is a "lack of proof," whereas the FDA now has the burden of proof in establishing that claims are actually false. Proper labeling requires simply that manufacturers list the ingredient(s) and the quantity enclosed, with the product having the strength and the identity that the substance is represented to have.<sup>72</sup> Although no specific criteria for this last requirement were made, the

US Pharmacopeia adheres to drugs' having 90% to 110% of the represented strength for ethical drug production.

The lack of regulation in supplement production can place the consumer at significant risk. Although documented by many investigators, Green et al,<sup>73</sup> in 2001, illustrated this point clearly. Sampling 2 to 4 capsules in every bottle of 12 supplement brands, he used liquid followed by gas chromatography to identify the true ingredients in each package. Stuningly, only 1 brand met the 1994 labeling requirements detailed above. Eleven of 12 brands contained less than the stated dose, 1 brand had 177% of the stated dose, and 2 brands contained none of a stated ingredient. Although taking an erroneous dose of a supplement can be risky, an even larger warning to athletes was born out in this study. One brand actually contained 10 mg of testosterone, which, as an anabolic steroid, is banned in the sporting arena. With the stringent rules adhered to by today's governing bodies of sports such as the NCAA, this type of contaminated supplement could cost the athlete immediate disqualification. By most leagues today, athletes are held strictly accountable for all substances that enter their bodies. A positive drug test is punishable regardless of whether the athlete knew that he or she was consuming the drug. Therefore, much caution is warranted when athletes consider using even "legal" nutritional supplements as manufacturing standards are not the same as pharmaceuticals.

## CREATINE

### Physiology

Creatine is formed from glycine, arginine, and methionine and is naturally produced by the liver, kidneys, and pancreas. After production, creatine is transported to muscle, heart, and brain, with 95% of bodily stores remaining in muscle. Creatine is also naturally present in the diet, mainly in meat and fish. The daily requirement of creatine is 2 g, with this amount provided half from endogenous production and half from normal diet.<sup>74</sup> Muscle creatine stores are in a balanced equilibrium with creatine and phosphocreatine interconverted via creatine kinase. Phosphocreatine provides energy to the muscle via its dephosphorylation, which donates a phosphate to adenosine diphosphate producing adenosine triphosphate (Fig 2). Aerobic recovery time then allows for the restoration of phosphocreatine.<sup>9</sup> Phosphocreatine availability is considered the limiting factor in short, high-intensity activities, as it provides muscle with the major energy source over the first 10 seconds of anaerobic activity after free adenosine triphosphate is consumed in the first 1 second of action (Fig 3).<sup>75,76</sup>

Investigations into the tissue level effects of oral creatine seem to show several changes. Supplementation can cause an ~20% increase in muscle phosphocreatine

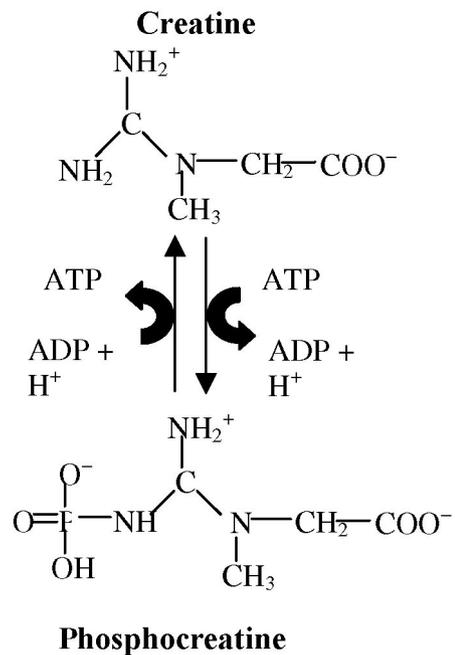


FIGURE 2

Interconversion of phosphocreatine and creatine producing adenosine triphosphate. Adapted with permission from Dr M. Jenkins, SportsMed Web. Available at: [www.rice.edu/~jenky/images/creatine.html](http://www.rice.edu/~jenky/images/creatine.html).

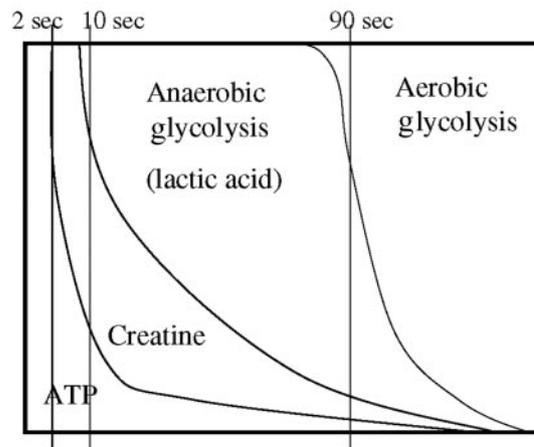


FIGURE 3

Time-dependent, dominant energy source for muscle activity. Adapted with permission from Dr M. Jenkins, SportsMed Web. Available at: [www.rice.edu/~jenky/images/creatine.html](http://www.rice.edu/~jenky/images/creatine.html).

stores, quicken the replenishment of phosphocreatine during recovery, and buffer lactic acid as hydrogen ions are consumed during the dephosphorylation of phosphocreatine, which potentially delays fatigue onset (Fig 2).<sup>77-79</sup>

### Dosing

Creatine is recommended to be taken first in a loading phase, with athletes consuming 5 g 4 times per day for the first 4 to 6 days. The standard dosing then is 2 g/day for the next 3 months. Creatine taken in excess of this

amount seems to be excreted via the kidneys.<sup>80</sup> A month of abstinence is standard practice after each use cycle. The Physician's Desk Reference notes that athletes should consume 6 to 8 glasses of water per day while taking creatine to prevent dehydration.<sup>81</sup> Absorption of oral creatine does vary with diet. Carbohydrate-rich fluids tend to increase creatine absorption, whereas caffeine impairs its uptake.<sup>82,83</sup>

### Effects

Creatine supplementation does appear to have athletic benefits. However, nearly 30% of athletes do not see benefits with creatine use, thereby falling into a category of "nonresponders" who are theorized to have already maximal phosphocreatine stores.<sup>9</sup> Most common, performance effects are seen in increasing strength and outcomes in short-duration, anaerobic events. Studies do not show improved endurance performance as expected given that prolonged muscle activity depends on aerobic glycolysis.<sup>84</sup> In a well-controlled setting, Volek et al<sup>85</sup> performed a double-blinded study that examined 12 weeks of creatine use including standard loading and maintenance phases in recreational weightlifters. In those athletes who were taking creatine, significant increases in fat-free body mass; bench press maximal lift; peak power production in sets of repeated jump squats; and biopsied type I, IIA, and IIAB muscle fibers were demonstrated.

### Adverse Effects

Athletes who take creatine commonly experience early weight gain of 1.6 to 2.4 kg, which can be detrimental in purely speed-based events. It is also common for athletes to report minor gastrointestinal discomfort and muscle cramps, although these generally do not curb use.<sup>4</sup> There have been 2 case reports of renal function compromise. One was an athlete who had previously diagnosed focal segmental glomerulosclerosis and experienced a transient 50% loss of glomerular filtration rate, and 1 previously healthy athlete reported transient interstitial nephritis.<sup>86,87</sup> However, at least 1 study of self-reported use over several years did not show adverse renal effects.<sup>88</sup> Three highly publicized deaths have occurred in college wrestlers who were known to take creatine, although official autopsy results indicated that dehydration and weight loss were at fault, not creatine.<sup>81</sup> Additional questions remain, as there are no data to judge the effects of supplementation on the other tissues that store creatine (heart and brain), the effects of chronic use, or the effects of creatine use in minors.

### Legal/Sports Aspects

Creatine remains a legal nutritional supplement today. Despite at least 1 brand's name, Teen Advantage, the American College of Sports Medicine has recommended explicitly that it is not to be used by anyone who is

younger than 18 years.<sup>79</sup> Collegiate teams, including trainers and coaches, are prohibited from supplying creatine or other supplements directly to their student athletes.

### Incidence

Questioning younger populations, 1 study found 8.2% of 14- to 18-year-olds using the supplement, with 75% of those users either unaware of how much creatine they consumed or taking more than the recommended amounts.<sup>89</sup> Meanwhile, looking at 10- to 18-year-olds, Metz et al<sup>90</sup> reported that 5.6% of that age group used creatine, with every grade from 6 to 12 involved. It was also noted that 12th-graders used creatine much like their collegiate counterparts, with that grade reporting 44% use. Current estimates of collegiate creatine use vary from 25% to 78% of athletes.<sup>48,91</sup>

## EPHEDRINE

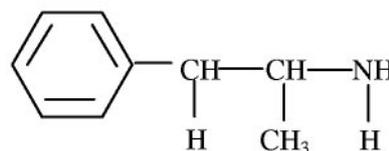
### Physiology

Ephedrine is a stimulant with a chemical structure closely related to amphetamine (Fig 4). It is derived from ephedra herbs also known as ma huang. It possesses  $\alpha$  and  $\beta$  adrenergic agonistic effects, enhances the release of norepinephrine, and stimulates the central nervous system.<sup>92</sup> Pseudoephedrine is closely related and also possesses central nervous system stimulant properties in addition to being a popular decongestant.<sup>93</sup>

### Dosing

Previously available ephedrine compounds included such brands as Metabolife356 and Ripped Fuel. Before being banned in 2004, the FDA recommended that daily ephedra alkaloid intake remain under 25 mg and not be continued longer than 1 week.<sup>94</sup> Pseudoephedrine in cold remedies is taken in maximal amount at 60 mg. Combining ephedrine with caffeine or its herbal form

### Amphetamine



### Ephedrine

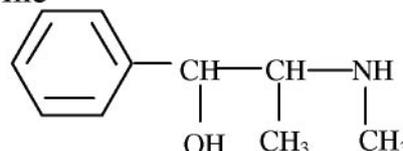


FIGURE 4  
Chemical structure of ephedrine.

guarana poses significant risk and was prohibited by the FDA in the 1980s.<sup>95</sup>

### Effects

Ephedrine traditionally has been used by athletes to provide quick energy and to aid in fat loss, consequently improving speed and appearance. The majority of studies that are available show no change in athletic performance with ephedrine use. A few investigations have reported improvements in quadriceps strength or stationary cycling, but these have involved high doses of ephedra compounds and sometimes were combined with caffeine, which poses significant risk to the athlete.<sup>96,97</sup>

### Adverse Effects

Bent et al<sup>98</sup> reported that ephedra accounted for 0.82% of herbal product sales but was implicated in 64% of adverse herbal reactions in the United States in 2001. Adverse reactions are wide ranging and include hypertension, arrhythmias, anxiety, tremors, insomnia, seizures, paranoid psychoses, cerebral vascular accident, myocardial infarction, and death.<sup>99</sup> In fact, in athletic performance studies, the most consistent finding is increased heart rate. Haller and Benowitz<sup>99</sup> in 2000 critically evaluated the 140 adverse events reported to the FDA from 1997 to 1999 and concluded that 62% of the adverse events reported were definitely or possibly related to the drug. In that series, 10 users were younger than 18 years, and there were 10 deaths and 13 cases of permanent disability. These included a 22-year-old man who was taking Ripped Force and sustained a cardiac arrest and was left with a permanent neurologic disability and a 15-year-old girl who was taking Ripped Fuel and sustained a fatal arrhythmia.

### Legal/Sports Aspects

In 2004, ephedrine was the first supplement removed from the market by the FDA since the 1994 supplement act. However, in April 2005 a US District Court judge ruled to overturn the ban, stating that the FDA had not proved that a 10-mg dose was dangerous. She ruled that "[the prior ban] would be directly contrary to the statutory language placing the burden of proof on the government. . . ." It is likely that this legal battle will continue with possible appeals by the FDA, although this ruling may open the door to ephedrine's return to the supplement marketplace. The International Olympic Committee, NCAA, Major League Baseball, National Basketball Association, and National Football League all have banned the systemic use of ephedrine products.

### Incidence

The NCAA has documented that its athletes in 2001 were using ephedra products earlier than in the past, with just >60% beginning use before college.<sup>48</sup> The

work of Kayton et al<sup>71</sup> in 2002 supported this claim, finding that among 270 high school athletes, 26% of girls and 12% of boys had tried ephedrine products. The NCAA data from 2001 reported a 3.9% incidence of ephedrine use in the past 12 months for men and women. When female sports were examined, there were marked increases from 1997, with 8.3% of gymnasts using ephedrine and 11.8% of ice hockey players using the drug compared with 1.1% and 0% rates 4 years earlier.<sup>48</sup> An even more recent look at collegiate use was published in 2004<sup>98</sup>, which examined 5 male ice hockey Division I teams and found that 38% used ephedrine and 46% using pseudoephedrine in cold remedies, hoping to boost performance.

### ADDRESSING THE PROBLEM

Approaches to combat the use of drugs by young athletes generally have fallen into 2 categories: (1) changes in rules and testing or (2) educational initiatives. Changes at the collegiate level now bar any supplement distribution directly from teams, and the NCAA uses rigorous drug testing of student-athletes. For high schools, the 1995 Supreme Court ruling in the case of *Vernonia versus Acton* authorized school drug testing for student athletes, maintaining that this does not violate participants' Fourth Amendment Rights. Data from the National Federation of State High School Associations indicate that only 13% of high schools perform drug testing on athletes.<sup>100</sup> However, only 29% of those schools reported testing for anabolic steroids, whereas the rest tested only for illicit substances such as marijuana, opiates, and alcohol. It is anticipated that high school drug testing may increase, because President Bush has promised \$23 million dollars for such testing.<sup>101</sup>

The second approach to combating youth drug use in sports has been educational programs that are designed to teach students about the facts and the myths of these substances. The model program for such interventions is the Adolescents Training and Learning to Avoid Steroids program.<sup>102,103</sup> This program involved >3000 high school football players, with the intervention group participating in interactive classroom sessions and exercise training sessions focusing on nutrition, drug effects, and drug refusal role playing. The control group received brochures with similar information. The sessions were led both by student athletes and by educators. At the conclusion of the study, testing showed the intervention group to be more knowledgeable of steroid and other drug effects. They were less likely to believe supplement ads and were more able to reject drug offers from peers. At the end of the season and 1 year later, supplement use was lower, there were fewer new steroid users, and students remained more knowledgeable about ergogenic drugs in the intervention group. Similar intervention specifically for female athletes also resulted in a significant reduction in use of diet pills, amphetamines, ana-

bolic steroids, supplements, and alcohol as well as safer sexual practices and wearing of seat belts.<sup>104</sup>

Dealing with young athletes poses several challenges. This age group is often developing rapidly, with physiologic changes that mimic those produced by several ergogenic drugs discussed. They are not likely to volunteer to physicians information about drug or supplement use. However, the pediatric community is poised to make a unique impact on this problem. Pediatricians are the primary contact for most young people with the medical community and are in a position to develop long-lasting relationships with their patients. Therefore, it is critical for pediatricians to be aware that drug use in sports is not only an adult problem. Physicians need to become educated about the drugs that are being used and the consequences of their use. One must be willing to ask about such ergogenic drug use in the same tone as other routine screening questions during office visits and preparticipation physicals. When young people do admit to using these substances, having a physician who is able to discuss openly the performance effects as well as the adverse effects of ergogenic drugs can be the first step in establishing that physician as a trustworthy source to approach should the young person consider using other drugs or begins to experience adverse effects of these drugs.<sup>105</sup> In this way, the entire medical community, not just physicians who formally care for athletic teams, can make a significant influence on youth drug use in sports.

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