

Sports Doping in the Adolescent: The Faustian Conundrum of Hors De Combat

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"He (it) cures most successfully in whom the people have the greatest confidence."

(Galen, 180 AD)

For thousands of years, humans have sought the use of medicines, herbs, and other chemicals to improve their lives in various ways. Some scholars have interpreted the story of Adam and Eve in Genesis (chapter 3) as a story of the original humans seeking to be strong (wise) like God.¹ Extensive pharmacopoeias have been developed in China and India over the past eons.² The first classifier of medicinal herbs is noted by historians as the Chinese emperor Shen-Nung 2737 BC, and there is a classic recorded painting of him holding *Ephedra* (machuang) leaves.³ An early historical record of medical treatments is the *Ebers Papyrus* (1500 BC), which lists more than 700 medicines of various origins (mineral, vegetable, and animal).^{2,4}

In recorded history, competitive athletes have used various mixtures of animal and plant origins, taken from known and unknown products, in attempts to improve their athletic performance and gain the perceived benefits of victory.⁵ For example, athletes during the Greek and Roman Games used wines, mushrooms, and opioids; stimulants (ie, strychnine) were popular at the beginning of the twentieth century. Galen, the famous Greek who became the physician to the gladiators of ancient Rome, observed the belief of athletes of his time (180 AD) that consuming mushrooms and herbal teas

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was beneficial to their overall performance.³ In 1886, a cyclist died during a race in France because of a stimulant overdose.³ Such sports doping practices have continued in advocates of sport and others to the present age, even though such practices have been banned by sports officials. For example, the death of a British athlete at the Tour de France in 1967 was attributed to the use of amphetamines complicated by a state of dehydration, and 9 riders were ruled ineligible for the Tour de France in 2006 because of suspected sports doping.⁶

Athletes of old and of today have been willing to take various chemicals even without any proof of their benefit, in hope of improving their general health or their sports performance.⁷ Over thousands of years, athletes have consulted experts from the ancient days of sorcery and alchemy to modern-day biochemistry and pharmacology to find effective yet safe performance-enhancing drugs.⁵ The milieu of “victory at any cost” that existed millennia ago continues to the present. In 1982, Goldman and colleagues^{8,9} asked 198 world-class athletes if they would take a chemical that would guarantee them success but would lead to their death in 5 years; in this survey, 52% reported they would take this chemical and this report remained at this level in repeat surveys between 1982 and 1995. Connor and Mazanov⁹ posed this Faustian bargain to members of the general public in Australia; they noted that only 2 of the 250 individuals surveyed agreed to take such a chemical. These sagacious members of the general public were not obsessed with victory at any cost.

As we enter a new millennium and century, it is sobering to realize that only a handful of the thousands of available herbal remedies of old or of modern chemistry have been shown to actually work as prescribed to better one’s health.^{2,4,10} Proof of improving sports performance with various chemicals (including herbs) is even more limited. Yet, today’s athletes are taking various products in ever-increasing numbers because they are driven to succeed to obtain the perceived glories of winning in contemporary society.

Agents that have been used in the hope of winning the game of sports and the game of life include anabolic steroids, anabolic-like agents, designer steroids, creatine, protein and amino acid supplements, minerals, antioxidants, stimulants, blood doping, erythropoietin, β -blockers, sodium bicarbonate and others **Tables 1** and **2**.^{11–21} For example, a survey of 13,914 college athletes published in 1997 noted a significant intake of creatine (13%), amino acids (8%) and dehydroepiandrosterone (DHEA) (1%).¹⁹ Supplement use in athletes ranges between 40% and 60%.^{20,21} The teenage athlete should be carefully counseled that there are few substances (if any) that consistently and safely improve the performance of a well-trained individual.

Table 1 Manufacturers' claims of ergogenic agents
Serve as an energy source
Decrease fatigue in sports events
Increase lean body mass and strength
Decrease adipose tissue
Alter weight in desirable directions
Improve aerobic capacity
Enhance motor capacity
Improve appearance
Enhance overall sports performance

Also, the use of these agents has considerable potential to cause physical and psychological damage. Misuse of drugs in this manner (or the sports doping phenomenon as it is called) should be discouraged. This discussion reviews some of these agents that are used. Our sports youth live in a modern-day Faustian dilemma often with the encouragement of coaches, trainers, parents, the media, and other members of society obsessed with success at any price.

PROTECTION FOR CONSUMERS

Some progress was made in the twentieth century to help consumers understand whether or not the medications or chemical agents they take are beneficial and safe. In 1906, the Pure Food and Drug Act required foods and drugs, which were sent between various states, to be provided with accurate labels. It was not required that medications be tested for safety until the 1938 Federal Food, Drug and Cosmetic Act (FFDCA). It was also not required that these drugs be proven effective for their intended use until the 1962 Harris-Kefauver Amendment of the FFDCA. However, the 1994 Dietary Supplement Health and Education Act (DSHEA) reversed some of these gains acquired over the previous 88 years. DSHEA allowed products classified as dietary supplements to avoid the scrutiny applied to drugs or medications. Thus, manufacturers of dietary supplements (defined as a vitamin, mineral, herb, other botanic, amino acid, metabolites of these products, related metabolites, related concentrations, or extracts or combinations) do not need to prove safety or efficacy of their products. All that is needed is to note that their products “maintain health or normal structure and function.”¹⁰

This has opened up the commercial floodgates to various agents used by athletes in the hope that the products they use are ergogenic (see [Table 1](#)).^{22–24} It is important for physicians and medical educators to be aware of these various products and to be willing to provide education to society and their patients about what is known and not known about these products.²⁵ With the legal floodgates open and the continuing drive for success in sports at any cost that permeates society in the United States and the world, Americans spent more than US\$12 billion on dietary supplements in 1999.^{18,26}

Research on these products remains limited and athletes rely on word of mouth from fellow sports enthusiasts, coaches, nutrition store personnel, advertisements, and other unscientific sources for information on what drugs, herbs, or other available agents will help them improve their athletic performance or their lives in general.²⁴ Most research has been done on adult men, who are involved in competitive athletics and not on teenage athletes. The potency and purity of nutritional agents are not known and the long-term effects of these various substances are also unknown at present. However, the use of ergogenic agents remains popular, and more than 30,000 individual commercial products are available throughout the world.^{20,27,28} Unproven claims (see [Table 1](#)) remain while the hope of victory burns strong in athletes of all ages whether competing at the high school (or below) level or at the Olympic level of competition.^{29,30}

DEFINITIONS

The term doping is derived from the Dutch word “dop” in reference to the practice of providing race horses with an opium mixture to act as a stimulant and enhance victory of the competing animal.¹⁷ Sports doping refers to the attempt of improvement or stimulation of sports performance in *Homo sapiens* in the eternal quest for victory at any cost. The promise of having a drug that is a true sports doping chemical often

Table 2
Drugs misused by athletes as ergogenic products

α -Lipoic acid
Anabolic steroids (DHEA, androstenedione)
Antioxidants (vitamin C, vitamin E, β -carotene)
Amphetamines
Bee pollen
β -blockers (ie, propranolol)
β -Hydroxy- β -methylbutyrate
Blood
Caffeine
Calcium
Carnitine
Choline
Chrysin
Chromium
Clenbuterol
Coenzyme Q ₁₀
Creatine
DSMO
Diuretics (furosemide, spironolactone, hydrochlorothiazide)
Engineered dietary supplements
Ephedrine
EPO
Folic acid
Ginkgo biloba
Ginseng
Glycerol
hGH
Inosine
IGF-I
Iron
Minerals: Boron Chromium Vanadium Iron Selenium Zinc
Niacin
Nicotine
Nonsteroidal antiinflammatory drugs (ibuprofen, mefenamic acid, naproxen, others)
Omega-3 fatty acids
Oxygen
Pantothenic acid
Phosphorus
Pyridoxine (vitamin B ₆)

Plant steroids (phytosteroids; γ -oryzanol; ferulic acid [FRAC])
Protein supplements
Riboflavin
Sodium bicarbonate
Sport drinks
Thiamin (vitamin B ₁)
Tribulus terrestris
Vitamin supplements
Vitamin B ₁₂ (cyanocobalamin)
Vitamin B ₁₅ (dimethylglycine)
Yohimbine (yohimbe)
Others
Various illicit drugs
Alcohol, marijuana, tobacco, methamphetamine, cocaine, GHB, GBL
Hallucinogens (lysergic acid diethylamide and phencyclidine-HCl)
Barbiturates, opiate narcotics, inhalants (volatile solvents, nitrous oxide, nitrites)

belies an eternal quest for the product having an ergogenic quality, and this term is derived from the Greek words *érgon* (to work) and *gennan* (to produce).

ANABOLIC STEROIDS

Anabolic steroids or anabolic-androgenic steroids (AAS) are a class of chemicals that are synthetic derivatives of testosterone and represent a drug class often abused by adolescent and adult athletes.³¹ The roots of their use can be traced over 6 millennia ago when ancient farmers noted the quieting or passive effects that castration had on animals.³² Testosterone was isolated in 1935 and developed to improve metabolism; it was used by athletes to gain strength as early as the 1940s. Concern over the use of anabolic steroids by athletes led to an inaugural definition of sports doping by the International Olympic Committee (IOC) in 1964, the banning of these drugs by the IOC, the start of antidoping programs by the IOC in 1967, and the first official testing for these chemicals at the 1976 Montreal Olympic Games.⁵

The term anabolic refers to the stimulation of protein synthesis, whereas androgenic implies the stimulation of male secondary sex characteristics. The terms steroids or steroid hormones refer to chemicals that are derived from cholesterol and include corticosteroids and sex hormones (ie, testosterone, estrogen, and progesterone). Anabolic steroids stimulate several receptors: androgen, estrogen, progesterin, and glucocorticoid. Some examples of oral and injectable anabolic steroids are listed in **Table 3**. The US Food and Drug Administration (FDA) has classified these chemicals as Schedule II drugs since 1990. Dianabol has been discontinued because of the high level of abuse noted by athletes. Adequate training and protein intake are necessary for maximal effect on protein synthesis in muscle tissue and the individual response is variable. Anabolic steroids have become the sine qua non of the Faustian bargain awaiting our youth.

Epidemiology

It is clear that many youth try anabolic steroids including one-third who are not athletes.^{31–35} Various studies over the past few decades confirm that 5% to 11% of high school boys and 0.5 to 2.5% of high school girls in the United States have tried anabolic steroids; of these, 50% used these chemicals before 16 years of age and

Table 3
Examples of anabolic steroids
Oral steroids
1. Oxandrolone (Oxandrin)
2. Oxymetholone (Anadrol)
3. Stanozolol (Winstrol)
Injectable steroids
1. Testosterone cypionate (Testim)
2. Testosterone enanthate (Depo-Testosterone)
3. Nandrolone phenpropionate (Durabolin)
4. Nandrolone decanoate (Deca-Durabolin)
Topical steroids
1. Testosterone gel (Androgel)
2. Testosterone transdermal (Androderm)

Data from Greydanus DE. Performance enhancing drugs and supplements In: DR Patel, DE Greydanus, R Baker, editors. Pediatric practice: sports medicine. New York: McGraw-Hill Medical Publishers; 2009. p. 63–77.

33% of these youth were not athletes.^{31,33,36–49} Approximately 80% of male body-builders and 40% of female body builders use these drugs in contrast to 20% of college athletes; 38% of users try the injectable forms. The mean start age is about 14 years with a range of 8 to 17 years. One study looked at 1881 high school students in Georgia and noted that 5.3% of ninth grade boys and 1.5% of ninth grade girls claimed they use or had used anabolic steroids.⁵⁰ A 1988 study of 3403 high school seniors nationally indicated that 6.6% responded they were or had used these chemicals; 38.3% were less than 16 years of age; of these, 47.1% indicated that the main reason for using these drugs was to improve their sports performance.³⁶ The 2008 Monitor the Future Study noted the annual prevalence rates had dropped; for boys in the 8th, 10th, and 12th grades, it was 1.2%, 1.9%, and 2.7%, respectively versus 0.6%, 0.5%, and 0.7% for girls.⁵¹ Several decades of research suggests a lifetime prevalence of 4% to 6% with teenage boys and 1.5% to 3% for teenage girls.⁵²

These youth have limited knowledge of the dangers of these drugs.^{41,53} Abuse of these chemicals may be increased in the nonathletic population versus the athletic adolescent population.⁵² Adolescents who take anabolic steroids may also be involved in other high-risk behaviors, including illicit drug use such as cocaine, alcohol, cigarettes, marijuana, smokeless tobacco, and various injectable drugs.^{43,47–55} Adolescents obtain these drugs from many sources, even from veterinary suppliers. Unless they have been banned (as in Olympic competition) and drug testing is in force, anabolic steroids are popular with all athletes. Although abuse of anabolic steroids by American professional athletes has decreased somewhat in recent years, the use of these and other drugs by famous athletes has long encouraged teenagers to try these substances.^{56–58} Youth often believe that these chemicals are natural hormones and are endorsed by their sports heroes.⁵⁴ Many teenagers are convinced that these drugs are valuable and worth any risk, even in very high doses.

Oral anabolic steroids are 17 α -alkylation chemicals that slow liver inactivation and cause much of the liver side effects of these drugs. The injectable forms are from 19 β -esterification processes and pose infectious disease risks, including hepatitis (B and C) and human immunodeficiency virus (HIV)/AIDS. The therapeutic doses of such drugs as used for treatment of various medical disorders are 8 to 30 mg depending on the particular drug being used. Because teenage athletes are often not afraid (nor informed) of risks, they may use prolonged and heavy (supraphysiologic) doses. They

may use these drugs in various combinations in a method called stacking, that is, cycles of 6 to 12 weeks on and then off.^{47,53,59} In 1 study, 18.2% used only 1 cycle, whereas 38.1% used oral and injectable anabolic steroids.⁶⁰ Increasing a drug dose in a cycle is called pyramiding, and doses may be 10 to more than 40 times the usual therapeutic doses.⁵⁹ While taking several drugs together (ie, stacking), some athletes use up to 200 mg per day. These athletes may not have any fear of side effects in their quest for ergogenic qualities or even in attempts to simply improve appearance.

Effects

Athletes use anabolic steroids in the hope of increasing lean body mass, strength, and/or aggressiveness; as noted, some only wish to improve appearance.^{33,61} Athletes at particular risk for the use of anabolic steroids include those engaged in sports such as weight lifting, shot putting, discus throwing, bodybuilding, sprinting, football, and wrestling. If athletes take high doses of anabolic steroids while undergoing heavy resistance training, there may be an increase in body weight (with increased water retention) and lean muscle mass. One controlled study looked at adult men taking 600 mg of intramuscular testosterone and noted that they gained significant size and strength.⁶² However, not all studies agree and the exact effects of anabolic steroids are complex and not fully defined. The effect of training is important because healthy volunteers who take these drugs without training show no increase in muscle strength or muscle size. Some experiments have noted that inexperienced weight lifters who take anabolic steroids may experience an increase in body weight but not strength. Whether or not athletes get a significant increase in athletic performance remains controversial, and individualized results are the norm.

Adverse Effects

Side effects of anabolic steroids are legion and reviewed in **Table 4**.^{33,45,46,63} Addiction to anabolic steroids may occur.^{38,44,48,56–67} One study of 164 steroid users identified 28% as being dependent on these drugs.⁶⁸ The maturation process may be accelerated in growing athletes with possible early closure of epiphyses and shortened ultimate adult height. An increase in tendon injuries has also been reported in teenagers on anabolic steroids. Liver complications are many and are related to the oral alkylated forms; these adverse effects include increase in liver function tests, peliosis hepatitis, cholestasis, hepatic failure, and hepatic neoplasms (benign and malignant). Risks for cardiovascular disorders occur, including hypertension, reports of cardiomyopathy, and various thrombotic phenomena such as myocardial infarctions, cerebrovascular accidents, and sudden death.^{69–73}

Masculinization of females may occur with changes such as hirsutism and clitoromegaly, both of which may be permanent; deepening of the voice is an irreversible effect of anabolic steroids in females. Amenorrhea, male-pattern baldness, and skin coarseness may also be seen in women; the skin changes may be permanent. Female athletes try to get a high enough dose to get the expected or desired results on muscle mass, but low enough to prevent unwanted side effects such as masculinization. Hair loss and severe acne may be seen in both sexes. Males may develop gynecomastia (partly irreversible) and prostatic enlargement (with possible increased risk for prostatic cancer). The reduction in testicular size is reversible, but abnormalities of germinal elements can persist for several weeks after cessation of anabolic steroids.

Use of Additional or Concomitant Doping Agents

Users of AAS may use other drugs as well.⁴⁸ For example, they may use human growth hormone (hGH), methamphetamine, or clenbuterol (see later discussion) to augment

Table 4 Anabolic steroids side effects
Fluid retention
Masculinization of females
Hirsutism
Clitoromegaly
Alopecia (males also)
Voice deepening
Other changes for females
Amenorrhea
Skin coarseness
Acne (both sexes; can be severe)
Growing athletes:
Acceleration of maturation
Early epiphyseal closure
Shortened ultimate adult height
Increase in tendon injuries
Psychological changes
See increase in:
Aggressiveness
Irritability
Depression
Gastric ulcers
Liver complications
Increase in liver function tests
Cholestasis
Peliosis hepatitis
Liver failure
Benign liver neoplasm
Malignant liver tumor (hepatocellular carcinoma)
Hyperglycemia (hyperinsulinemia)
Prostatic enlargement (possible increase risk for prostatic cancer)
Decrease in glycoproteins (follicle-stimulating hormone and luteinizing hormone) with:
Decreased spermatozoa
Decreased testosterone levels
Reduction in testicular size
Increase in tendon injuries
Reduction in high density lipoprotein, increased total cholesterol
Increased platelet aggregation, potential rise in cardiovascular disorders
Wilms tumor (at least 1 case report)

the anabolic effects of AAS. Human chorionic gonadotropin (HCG) may be added to raise testosterone synthesis and counter the anabolic steroid-induced effect of testicular atrophy. Diuretics (eg, furosemide, spironolactone, hydrochlorothiazide) may be used to reduce fluid retention, produce the desired rippled look, or dilute urine to subvert a drug-screening regimen. The use of diuretics to lose weight quickly is not an unusual plan of wrestlers. The use of such medications can result in increased weakness such that a wrestler can be injured by competing against a stronger opponent. Electrolyte dysfunction and other medical side effects of diuretics may complicate the picture. Pulmonary embolism has been reported in a high school wrestler using such a regimen.⁷⁴

Stimulants may be taken along with AAS to increase the drive for exercise and competition, whereas anti-acne medications are used to deal with the anabolic steroid-induced acne. Antiestrogens (as tamoxifen or clomiphene) may be used to prevent male feminization effects (ie, gynecomastia) of anabolic steroids. These athletes may use other drugs as well in the course of their training, such as antibiotics, corticosteroids (ie, prednisone), and analgesics (eg, morphine, propoxyphene, meperidine, oxycodone, and others). Narcotics and other illicit drugs are abused for their pleasure-granting effects as well. Corticotrophin (ACTH) is used to raise levels of internally produced corticosteroids and to produce a sense of euphoria.

Prevention

The use of anabolic steroids poses significant risks to the user/abuser and these chemicals have been banned by the (IOC), the National Collegiate Athletic Association (NCAA), the National Football League (NFL), and many other sporting associations. However, it is often difficult for the adolescent user to stop because many young people have difficulty understanding the consequences of their actions (concrete thinking) and have difficulty avoiding the win-at-all-cost attitude prevalent in the global sports milieu.^{29,30,41,56,57,75,76} It is important to educate youth about these sports doping agents.⁵⁹ Parents and coaches must be taught about these chemicals and they should not encourage the use of such potentially dangerous chemicals under the guise of "Winning is Everything!" Goldberg and colleagues^{77,78} have introduced the ATLAS model or the Adolescent Training and Learning to Avoid Steroids Program with some success.

Although there may be some medical indications for these drugs (ie, treatment of HIV-associated wasting or chronic renal failure), seeking to improve sports performance should not be one of the medical indications to use these drugs.^{11,44,79} Guidelines for following athletes who insist on taking anabolic steroids are provided by Blue and Lombardo.⁶⁴ The effort to ban anabolic steroids has now been complicated with the appearance of designer steroids, the first of which was norbolethone that was initially detected by a laboratory in Los Angeles in 2002.⁵ Other identified designer steroids include madol (desoxy-methyl testosterone) and tetrahydrogestrinone. Unfortunately, experts and amateurs in the biochemistry industry continue to produce such drugs, and the cat and mouse game between sports dopers and sports officials will continue in perpetuum.

Other Anabolic-like Agents

DHEA

DHEA is a mildly androgenic hormone naturally produced in the adrenal glands and testes. It is the precursor to testosterone (as well as dihydrotestosterone) and estrogen. Although DHEA is banned by the FDA and has no proven ergogenic effects, it is used by athletic teens and adults as an alternative to anabolic steroids.^{31,48,80} The ergogenic attempt is based on a hope and hype that DHEA will increase testosterone and an anabolic insulin-like growth factor (IGF-I). Despite animal studies having shown some DHEA-induced liver toxicity, it is marketed to adults (middle-aged and older) as an over-the-counter alternative to anabolic steroids with additional unproven claims of promoting euphoria, enhancing libido, delaying cardiovascular disease, preventing cancer, and boosting one's immunity.¹⁷ Research is limited on DHEA.⁶⁵ One study evaluated men (average age 24 years) who used 1600 mg per day for 4 weeks; serum testosterone levels were not altered.⁸¹ Another study called the Andro Project also noted no ergogenic qualities of DHEA.⁸²

DHEA is given at a dose of 50 to 100 mg per day for 6 to 12 months in oral or injectable forms, up to 1600 mg. Side effects may occur as with ingestion of sex hormones.

At doses of more than 100 mg/day, gynecomastia (irreversible) in men and hirsutism in women can occur; cancer (prostate or endometrial) may be worsened.⁸³ DHEA should be considered as an anabolic steroid and teenagers should be advised not to use it. The FDA has ruled it has no medical usage, and it has been banned by the National Hockey League, the IOC, the NFL, among others (**Tables 5** and **6**).

Androstenedione

Androstenedione is another androgen produced by the adrenal gland and testes; it is a precursor of estrogen and testosterone (as well as dihydrotestosterone) and is found in Scotch pine tree pollen.^{84–86} Androstenedione is available in Europe as a nasal spray and is used in the United States in a pill form. It is used as a T-booster in hope of increasing testosterone; serum testosterone/estrogen ratios are normalized within 1 day of stopping this drug. High doses (as 100–300 mg per day and 60 minutes before an event) may increase lean muscle mass and strength. Studies note that 300 mg of androstenedione increases testosterone, estrone, and estradiol levels more than 100 mg.²⁶ It is often used in combination with different anabolic steroids in various cycling methods.⁸⁰

Androstenedione is a banned chemical with unknown long-term safety. Side effects are the same as noted with anabolic steroids; the potency and safety of available products are unknown. It should be avoided with growing athletes and for those at risk for prostate or breast cancer. Androstenedione and other steroidal supplements may be packaged with various other chemicals, such as ephedrine, caffeine, saw palmetto, and others.⁶⁵ Although banned by the IOC, NFL and NCAA, androstendione remains a popular sports doping agent (see **Tables 5** and **6**).

Human growth hormone (hGH)

hGH has been used especially by power and speed athletes in attempts to increase lean muscle mass and strength, often in combination with anabolic steroids.^{11,31} However, ergogenic effects have not been proven, even when using supraphysiologic doses.⁸⁷ Although tests are available, it is difficult to detect all users and the user runs the risk of having an impure product obtained illegally.^{88,89} Recombinant DNA technology has provided recombinant hGH (rhGH) to those able to pay the high cost of this agent (more than US\$3000 per month).⁸⁹ A survey of more than 200 high school male athletes noted that 5% were on hGH.⁴⁸ The question of hGH purity as a natural product was previously raised with the development of Creutzfeld-Jacobs disease. Side effects of hGH supplementation may include jaw enlargement, gigantism,

Table 5 Banned substances and methods	
Main categories of prohibited substances	Anabolic agents Hormones and related substances (growth hormone, IGF-I, insulin, EPO) β2 agonists Hormone agonists and modulators Diuretics and other masking agents
Main categories of prohibited methods	Enhancement of oxygen transfer Chemical and physical manipulation Gene doping

Data from Greydanus DE, Patel DR. Sports doping: use of drugs and supplements to enhance performance. Int Public Health Journal 2009;1(4):2.

Table 6
Drugs banned from various sports competitions

Anabolic steroids (see Table 3)

Beta blockers

Clenbuterol

Metoprolol

Propranolol

Diuretics

Furosemide

Hydrochlorothiazide

Spirolactone

Narcotics

Dextropropoxyphene (Darvon)

Morphine

Meperidine (Demerol)

Peptide hormones

ACTH (corticotropin)

EPO

HCG

hGH

Stimulants

Amphetamines

Ephedrine

Others

Local anesthetics

Corticosteroids

Alcohol

Illicit drugs, including marijuana

hypertension, hyperglycemia, fluid retention, carpal tunnel syndrome, slipped capital femoral epiphysis, and pseudotumor cerebri.^{18,89} Although several amino acids (arginine, ornithine, lysine, and tryptophan) are used to induce release of hGH, doses usually used do not significantly raise hGH in the body.

γ-Hydroxybutyrate

γ-Hydroxybutyrate (GHB, Liquid Ecstasy, G, Georgia home boy) is a central nervous system depressant that leads to euphoria and lowering of inhibition.^{90,91} GHB is popular with body builders with the hype and hope of increasing growth hormone release during sleep and enhancing muscle growth. GHB can be made at home with recipes found on the Internet and with ingredients easily purchased. It is made as a clear liquid or white powder; tablets or capsules are available. It is also used as a date-rape pill to enhance sexual assault; as a colorless, odorless and tasteless liquid, it is easily slipped into party drinks to produce sedation and amnesia; effects are noted in 10 to 20 minutes and last for 4 hours. It is quickly cleared from the body and is hard to detect. Thus, it has become a popular date-rape drug. An overdose can lead to profound respiratory depression, coma, and death.

Because the United States government is cracking down on GHB use, some are taking GHB metabolites or precursors, such as γ-butyrolactone (GBL) and even the industrial solvent, 1,4-butanediol (BD). After ingestion of GBH, it becomes GHB. Some companies are substituting BD for GHB, even though BD has been declared a potentially life-threatening drug by the FDA. It is marketed as a dietary supplement in various sleep aid and muscle builder products. Although it is promoted to enhance

sexual performance, BD slows breathing and can lead to unconsciousness, emesis, seizures, and death.

Clenbuterol

Clenbuterol (Clensasma; Broncoterol) is a β_2 agonist bronchodilator (substituted phenylethanolamine) that is used with anabolic steroids in attempts to improve lean body mass and decrease adipose tissue.^{11,44,54,92–94} It is available in Europe, Central America, and South America. Clenbuterol can be given orally with full absorption, whereas aerosol and injection forms are also available. If used therapeutically for asthma, the dose is 0.02 to 0.04 mg per day; if used ergogenically, a dose of 0.02 to 0.16 mg per day is tried. Clenbuterol can be used in a 2-day on and 2-day off cycle for several weeks and then stopped before the athletic event, because it can be detected for 2 to 4 days after the last dose.

However, it is not proven that it increases muscle mass and reduces adipose tissue, certainly not to the extent attributed to anabolic steroids. Several side effects are observed, including tachycardia, headaches, anxiety, dizziness, nausea, tremor, and insomnia. Concern is raised that it may lead to arrhythmias, myocardial infarction, cardiac muscle hypertrophy, and cerebrovascular accidents. It is banned by many sport agencies, including the IOC, United States Olympic Committee, NCAA, and others (see **Tables 5** and **6**).

To avoid sanctions for using a medication (even with a prescription) at Olympic competition levels, rules of the World Anti-Doping Code must be followed in which the International Standard for Therapeutic Use Exemptions are used.⁹⁵ Sports doping has been viewed by authorities as being an unfair and unethical advantage in sports competition. The IOC developed a medical commission in 1967 and they have produced a list of substances that are prohibited for athletes to use as well as various antidoping regulations.⁹⁶ Specific screening for prohibited drugs was initiated at the 1972 Munich Olympic Games. In 1999, the World Anti-Doping Agency (WADA) was developed and this agency organized a worldwide effort to standardize and enforce antidoping regulations.³¹ WADA has published the 2009 World Anti-Doping Code listing categories of banned substances and methods used for doping; they provide a list of substances banned in competition and in specific sports (see **Table 5**).³¹ Athletes must be careful even with prescription drugs that are prescribed for them or misuse of medications that are being prescribed for someone else.⁹⁷

Others

IGF-I is a single-chain 70 amino acid polypeptide that contributes to the growth-enhancing effects of hGH.⁴⁸ Provision of injectable r-IGF-I produces similar effects to rhGH, and to the appreciation of female athletes, there is no virilization. This product's high cost (more than US\$3000 per month) limits its use. Anabolic phytosteroids (plant steroids) are marketed to athletes as plant extracts that have similar effects as anabolic steroids, but without the side effects. These products include γ -oryzanol, ferulic acid, β -sitosterol, and Smilax.¹⁸ There is no evidence for their ergogenic properties and their purity as purchased is not guaranteed. Potential adverse effects include hyperglycemia, respiratory problems, increased blood pressure, cardiomyopathy, and others.⁵ Insulin itself has been used in attempts to augment transport of glucose into muscle cells with potential adverse effects such as hypoglycemia, coma, and death.

CREATINE

Creatine is an essential amino acid synthesized from arginine, glycine, and methionine, mainly in the kidneys, and to a lesser extent in the liver and pancreas. It is

available in milk, meat, fish, and other foods, although meat and fish are the main food source and supply more than half of the daily requirement.^{27,28,31,80,90,98} The usual diet provides 1 to 2 g of creatine per day. It is a tasteless crystalline powder that is readily dissolved in liquids and is usually marketed as creatine monohydrate or with phosphorus.⁹⁹ At all levels of competition (from high school to professional), creatine is the most popular nutritional supplement sold today as an ergogenic agent.^{27,28,31,90,98,100–104} In a well-known 1997 study by the NCAA in which more than 1400 college athletes were surveyed, 32% had used creatine in the 12 months before the survey.⁹⁸ In a study of 520 British athletes, 36.1% reported use of creatine and many believed that they were able to train longer and/or maintain strength using creatine.¹⁰⁴ Although annual sales of creatine are more than US\$200 million, there remains little research on its effects on adolescents.^{12,17,103}

All but 5% of creatine is stored in skeletal muscle (especially the fast twitch, type II muscle), two-thirds as a phosphorylated form, and one-third as free creatine. This substance serves as an energy substrate for the contraction of skeletal muscle in the body. Cells with high-energy requirements use creatine in the form of phosphocreatine, which functions as a donor of phosphate to produce adenosine triphosphate from adenosine diphosphate. Cells in the skeletal muscles store enough phosphocreatine and adenosine triphosphate (ATP) for about 10 seconds of high-intensity action.^{80,100} The purpose of creatine supplementation is to increase resting phosphocreatine levels in muscles and free creatine to briefly postpone fatigue, with potential ergogenic results.^{99,100} Phosphocreatine maintains high energy ATP levels, acts as a proton buffer, and can lead to reduced glycolysis. When the phosphocreatine levels decrease, glycolysis increases. Maximal exercise eventually stops because of muscle fatigue, probably because of accumulation of lactate and hydrogen ions in addition to a decrease in ATP.

Is creatine an ergogenic supplement? Studies in adult athletes suggest there may be a 5% to 15% improvement in short-term (<30 seconds), repetitive/intermittent, high-intensity exercise.^{18,27,28,102,105–107} Some literature tends to suggest it is probably beneficial for those in power sports (ie, football, sprinters), but not for those in endurance sports (eg, swimming). However, not all the literature agrees that there is any improved sports performance.^{31,108–112} Some athletes may have a low intracellular concentration of creatine and thus may respond to it, whereas those with a higher level do not respond. Most in vivo studies show no improvement in sports performance.⁸⁰ Also, no studies report any improvement with long-term endurance activities.

The work of Harris and colleagues^{113,114} has led to the current practice of many athletes using a loading dose of 20 g per day (5 g four times a day) for 5 to 7 days followed by 2 to 5 g per day for maintenance. Other loading and maintenance doses are also used. For example, research suggests an equally beneficial effect may be seen with 3 g a day versus a loading dose of 20 g a day.¹¹⁵ The loading routine may maximize the amount of phosphocreatine in muscles, whereas a maintenance dose may keep muscles filled. Positive results are best with an active exercise program, although there is no need to take creatine specifically before or during exercise. Increased muscle mass may result because of fluid (water) retention and not increased protein synthesis.¹¹⁴ An increase of 0.7 to 3 kg in 1 month has been reported; weight gain can be maintained on 5 g per day of creatine during a 10-week period of detraining and maintained 4 weeks after its use is stopped.

Although creatine is generally regarded as safe, there may be side effects and risks, especially when consuming more than 20 g per day. The best-known effect is weight gain because of fluid (water) retention. Other adverse effects that are often cited but not proven include anecdotal reports of muscle cramps, strains, dehydration in hot/

humid weather, renal function deterioration, suppression of endogenous synthesis, and possible cardiac muscle hypertrophy. Other anecdotal concerns include abdominal pain, dyspnea, nausea, emesis, diarrhea, anxiety, fatigue, migraine headaches, seizures, myopathy, and atrial fibrillation.^{17,80} Long-term (ie, more than 1 year) effects are unknown and no studies are reported in children or adolescents.²⁰ Supplementation does reduce endogenous creatine production, with unknown results on the body. Although it is not banned by any major sports groups, the American College of Sports Medicine recommends that those less than 18 years of age should not use creatine.¹¹⁵

STIMULANTS

Ephedrine

Ephedrine is a medication that can have beneficial effects in disease states (eg, asthma), but which is not acceptable to various sports medicine committees because of potential harmful effects.^{18,20,116,117} It is an example of using a stimulant drug to seek improvement in one's performance in training or competition. Although not proven to be ergogenic, it has been used by various athletes in this regard. Other stimulants include amphetamine and caffeine. They are used to reduce the sense of being tired, lessen the feeling of pain, and heighten aggressiveness.⁴⁵ As noted earlier, stimulants have been used by athletes over the eons as performance-enhancing chemicals. The Incas in South America chewed coca leaves to help them run long distances.¹

In the case of ephedrine, many believe its sympathomimetic action gives the user an unfair advantage and is thus banned (see **Tables 5 and 6**). However, β_2 agonists such as terbutaline and salbutamol are accepted in the Olympics if the athlete has documented asthma and informs the Olympic Committee of their use. The purpose is to allow the athlete proper treatment of a verified disorder (ie, asthma), but not to allow him/her to gain an unfair advantage over the competitors (ie, using stimulants).

Ephedrine alkaloids are derived from ephedra herbs (also called ma huang). Athletes use dietary supplement products that contain ma huang to improve muscle tone and energy levels, although there is no proof of these claims.^{10,17} Negative effects have been identified, including more than 800 adverse reports that were investigated by the FDA between 1994 and 1997 (FDA, June 2, 1997). These incidents involved otherwise healthy young to middle-aged adults who developed various complications while on these products; these included hypertension, arrhythmias, anxiety, tremors, insomnia, seizures, paranoid psychoses, cerebrovascular accidents, myocardial infarctions, and death.¹¹⁸ The FDA recommended limiting consumers to 24 mg of ephedra alkaloids and wanted labels to limit these products to 7 days and alert the public to these potential problems if high doses were taken. No official government action in this regard has been taken and the FDA was requested to provide more data. Despite such adverse reports, more than US\$1 billion was spent by consumers of ephedra products in 2000.¹⁰

Caffeine

Caffeine is a xanthine derivative that is used by many athletes.^{31,119} In a study of 520 British athletes in which 36.1% reported use of creatine, caffeine use as a sports doping agent was reported by 23.8%.¹⁰⁴ It may improve performance in steady state endurance activities that rely on fat for fuel, because this chemical increases lipid metabolism. It increases the release of free fatty acids from adipocytes and stimulates catecholamine activity.^{44,120} Studies have noted that ingestion of 2 to 3 cups of coffee (100–150 mg of caffeine per cup) increases the endurance of individuals cycling to

exhaustion on bicycle ergometers. Coffee seems to reduce the perception of fatigue and allow further performance. However, an excessive amount increases sympathomimetic stimulation, which can interfere with overall athletic performance. Its diuretic effect can also interfere with such performance. Excessive amounts were banned from Olympic competition and is defined as more than 12 to 15 $\mu\text{g/mL}$ in the urine; this usually results from ingestion of 6 to 8 cups of coffee.¹⁸ This ban was recently lifted. Other sources of caffeine include tea, over-the-counter pills for sleepiness, and some analgesic pills that contain caffeine.

BLOOD DOPING AND EPO

Blood doping (bloodboosting or blood packing), in which athletes receive transfusions of their own blood, is an attempt to increase aerobic performance.^{31,121,122} It is impossible to detect by laboratory tests and the frequency of use among athletes is unknown. Hemoglobin levels may reach 19 to 20 g/dL, especially during intense competition (eg, cycling competition at high altitudes), which leads to dehydration.⁴⁴

EPO is a renal glycoprotein that stimulates red cell production.^{31,121,122} Recombinant EPO (rEPO) is used to increase aerobic capacity and thus has become popular with endurance athletes (eg, runners and cyclists).⁴⁴ rEPO is difficult to detect and has a half-life of 20 hours. As noted with blood doping, several side effects are reported, including increased blood viscosity, hypertension, coronary artery occlusion, cerebrovascular accidents, seizures, and sudden death. Dehydration from intense sports activity may trigger some of these complications. It is difficult to detect; it is as effective in increasing aerobic capacity as blood doping and its use is banned.^{121,122}

MISCELLANEOUS SPORTS DOPING AGENTS

β -Blockers (ie, propranolol, clonidine, metoprolol) have been used to reduce anxiety, lessen hand tremor, control tachycardia, and reduce hypertension. Hand control is important in sports such as archery and riflery; these athletes may also use benzodiazepines and barbiturates for relief of anxiety and insomnia.⁴⁴ These agents, like many others, are banned from many competitive sports (see **Tables 5** and **6**). Potential side effects of β -blockers include various well-known cardiovascular, hematologic, central nervous system, and gastrointestinal symptomatology.⁵

Ergolytic illicit drugs include alcohol (also used in small amounts for hand control), marijuana, nicotine, cocaine, amphetamines, and others.⁵⁵ Nicotine may improve central nervous system attention span in some, but may also worsen hand steadiness. Insulin has been misused in sports by some because of its anabolic and anticatabolic effects. Drug testing has been developed to detect this practice.¹²³ Selective androgen receptor moderators are a class of drugs with the potential for use and abuse as sports doping agents and drug testing technology is being developed to detect SARMs.¹²⁴ A selective progesterone receptor modulator is an agent that works on the progesterone receptor with an agonist action on some tissues and an antagonist action in others. Some athletes seek to use such unapproved and controversial chemicals with the eternal sports doping hope from advertised hype that improved sports performance will occur without undesirable side effects.

Sodium bicarbonate is an alkaline salt that has been used to delay fatigue during bouts of exercise that are limited by acidosis; this may be helpful in cases where the blood flow can increase to accommodate an increase in the by-products of increased muscles at work.^{17,44} Nonsteroidal antiinflammatory agents have been used to relieve pain and allow athletes to increase their performance despite painful injuries; this can lead to greater, more permanent injuries.⁴⁴ Such medications have

erroneously been used to quicken healing of muscle soreness after exercise. Side effects of such medications include gastrointestinal bleeding, reduced platelet aggregation, reduced renal perfusion, increased salt/water retention, and thermal regulation dysfunction with resultant heat illness. Another agent falsely used as an antiinflammatory agent by athletes is dimethyl sulfoxide (DMSO). This chemical has been available in over-the-counter preparations and is rubbed onto sore or injured areas. Its effectiveness as an antiinflammatory agent has never been proved by research and its production does not occur under standards acceptable for human use.

There are many other substances sold as ergogenic agents, such as ginkgo biloba, ginseng, yohimbine (yohimbe), coenzyme Q₁₀, and others as listed in [Table 1](#).^{17,125} Nutritional supplements in sports are reviewed in other articles.^{11,13,17,22,26,31,83,90} In a study of 520 British athletes in which 36.1% reported use of creatine, use of ginseng as a potential sports doping agent was reported by 8.3%.¹⁰⁴ Although their value in bettering health and improving sports performance remains controversial, their use continues by a population not willing to wait for scientific studies to provide helpful guidance. The purity and safety of these products are not guaranteed but this does not prevent youth and other athletes from using them in high amounts. Clinicians providing sports medicine care to youth, whether through anticipatory guidance or direct sports medicine management, should educate their young patients about the never-ending hype and hyperbole of these ergogenic products.^{11,17,25,126}

SUMMARY

The ancient Olympic Games took place from 776 BC to 393 AD and sports doping was quite common among athletes of ancient societies.⁵ The modern Olympic Games began in 1896 in Athens, Greece, under the influence of Baron Pierre de Coubertin who emphasized the need for sports to honor competition over winning.³ Unfortunately, the milieu of winning is everything persists and athletes will accept the Goldman challenge in their pursuit of performance-enhancing drugs. Most consumed agents do not improve performance, and risks of severe adverse effects continue to complicate the Faustian dilemma that athletes at all levels face in the early twenty-first century. It may have begun with an apple, but sports doping has now evolved into anabolic steroids, designer steroids, and other dangerous chemicals. Sports doping is also a part of the greater issue of illicit drug use that is so prevalent in youth and adults of the world.^{52,56,57} Our children and youth must be educated about proper exercise and nutrition. They are curious about using potential sports doping chemicals of all types.¹²⁷ We must teach our children and adolescents that sports doping is neither a safe nor effective way to succeed in the game of life on or off the field.¹²⁸ We need to reinstate Baron Pierre de Coubertin's view of competition over victory as the *raison d'être* for sports participation among our children and youth. Sports doping is an important cause of *hors de combat* in contemporary twenty first century sports society.

"When there is noble competition, there is victory"

(Aristotle, 4th Century BC)

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