

# Use of Ergogenic Aids by Athletes

Marc D. Silver, MD

## Abstract

"Ergogenic aid" is defined as any means of enhancing energy utilization, including energy production, control, and efficiency. Athletes frequently use ergogenic aids to improve their performance and increase their chances of winning in competition. It is estimated that between 1 and 3 million male and female athletes in the United States alone have used anabolic steroids. In response to the problem of drug use, many athletic organizations have established policies prohibiting the use of certain pharmacologic, physiologic, and nutritional aids by athletes and have implemented drug testing programs to monitor compliance. Therefore, it is important for physicians to be knowledgeable about the available ergogenic aids so they can appropriately treat and counsel the athletic patient.

J Am Acad Orthop Surg 2001;9:61-70

Sports have become phenomenally popular worldwide. Successful athletes frequently become instant celebrities, with lucrative commercial opportunities. Unfortunately, some of those athletes use illegal substances to give themselves a competitive edge. A 1997 poll in *Sports Illustrated*<sup>1</sup> asked current and aspiring US Olympic athletes two questions. The first was whether they would take a banned performance-enhancing drug if they were guaranteed to both win their athletic event and not get suspended for drug use. The second question was whether they would take the same substance if it would enhance their ability to win every competition for the next 5 years but then result in death. Remarkably, 98% responded "yes" to the first question, and more than 50% responded "yes" to the second question.

Because successful athletes are looked on as role models in our society, many people in the general population try to emulate their

actions, even when that involves taking substances with major side effects that can cause permanent physical harm and even death.<sup>2-4</sup> For example, it is estimated that as many as 3 million athletes in the United States have used anabolic steroids for non-medically prescribed applications.<sup>5</sup> Therefore, it is important for the physician, especially one who deals with athletes, to be knowledgeable about the various ergogenic aids available.

## Types of Ergogenic Aids

An "ergogenic aid" is defined as any means of enhancing energy production and utilization.<sup>6</sup> Ergogenic aids have been classified into five categories: (1) mechanical aids, such as lightweight racing shoes; (2) psychological aids, such as hypnosis; (3) physiologic aids, such as "blood doping" (administration of packed red blood cells); (4) pharmacologic aids, such as androgenic ste-

roid supplements; and (5) nutritional aids, such as creatine supplementation.<sup>6,7</sup> The latter three categories are of the most interest. Some of the more commonly used substances are highlighted in Table 1.

Ergogenic aids can be specifically tailored to enhance performance in a particular sport. For example, some athletes involved primarily in strength-dependent activities, such as weight lifting, use anabolic steroids to increase muscle mass. Some endurance athletes, such as marathon runners, use blood doping (also known as "blood boosting" and "blood packing") to increase their oxygen-carrying capacity.

## Historical Perspective

The first Olympic games took place in Greece in 776 BC. From sources documenting specific training and dietary regimens for athletes in ancient times,<sup>3,8</sup> we know that some of them ate hallucinogenic mushrooms and sesame seeds to enhance

---

*Dr. Silver is Assistant Clinical Professor of Orthopaedics and Rehabilitation, Yale University School of Medicine, New Haven, Conn.*

*Reprint requests: Dr. Silver, Department of Orthopaedics and Rehabilitation, Yale University School of Medicine, One Long Wharf Drive, New Haven, CT 06511.*

*Copyright 2001 by the American Academy of Orthopaedic Surgeons.*

---

**Table 1**  
**Common Ergogenic Aids**

Substance/Method	Proposed Mechanism of Action	Athletes' Expectation
Pharmacologic substances		
Anabolic steroids (e.g., metandione, mesterolone, nandrolone)	Induce protein synthesis in muscle, stimulate release of growth hormone, reverse effects of cortisol	Increase muscle mass, strength, lean body mass
Growth hormone	Accelerates incorporation of amino acids into proteins, stimulates utilization of lipids from adipose tissue	Increases muscle mass, strength, lean body mass
Recombinant human erythropoietin	Stimulates erythropoiesis (thought to increase oxygen uptake)	Increases endurance and time to exhaustion
Beta-blockers (e.g., metoprolol)	Has antitremor and antianxiety effects	Improve shooting scores
Stimulants (e.g., caffeine)		
	Stimulates sympathetic nervous system, stimulates intracellular utilization of free fatty acids as energy source	Increase endurance
Nutritional aids		
Creatine	Enhances intracellular production of ATP (needed for muscle contraction)	Increases strength and power performance
Vitamin A	Acts as an antioxidant	Decreases cellular damage
Vitamin C	Acts as an antioxidant	Decreases cellular damage
Vitamin E	Acts as an antioxidant	Decreases cellular damage
Carnitine	Thought to spare muscle glycogen breakdown and decrease lactic acid production	Increases endurance
Androstenedione	Induces protein synthesis in muscle, stimulates release of growth hormone, reverses effects of cortisol	Increases muscle mass, strength, lean body mass
Blood doping	Increases oxygen-carrying capacity of blood	Increases endurance

performance.<sup>9</sup> Although the modern Olympic games commenced in 1896, scientific and medical interest in the diet and training of Olympic athletes did not begin until 1922.<sup>8</sup>

In 1889, Charles Edward Brown-Séquard, a French physiologist, claimed to have reversed his own aging process by self-injecting tes-

ticular extracts.<sup>10</sup> Testosterone, the primary male hormone, was first synthesized in 1935, and in the 1940s, athletes began taking anabolic steroids to increase their muscle mass.<sup>10</sup> Throughout the 1950s and 1960s, amphetamines and anabolic steroids were used extensively in sports.<sup>7</sup> Concerned about that

trend, the International Olympic Committee (IOC) banned their use by Olympic athletes in the early 1960s. Formal drug testing began with the 1968 Olympics.<sup>7</sup> In 1988, Canadian Olympic sprinter Ben Johnson was stripped of his gold medal after testing revealed he had used an oral anabolic steroid; this

Adverse Effects	US Organizational Policies
Effects on multiple organ systems (e.g., hypertension, elevated lipoproteins and liver enzymes, increased risk of tendon and muscle injury, testicular or uterine atrophy, depression, psychosis, immunosuppression)	Banned by NCAA, NFL, and USOC
Acromegaly-like effects (e.g., heart disease, heart failure, glucose intolerance, hyperlipidemia, impotence, menstrual irregularities, myopathy, osteoporosis)	Banned by NCAA and USOC
Thromboembolic events, ischemic events, hyperkalemia	Banned by NCAA and USOC
Bronchospasm, diminished performance capacity, atrioventricular block, cardiac insufficiency, hypoglycemia, hallucinations, insomnia, depression, nightmares	Banned for certain sports (e.g., shooting) by NCAA and USOC
Anxiety, jitters, inability to focus, gastrointestinal discomfort, insomnia, irritability, cardiac arrhythmia, hallucinations	Maximum urinary concentration allowed by USOC, 12 µg/mL; maximum urinary concentration allowed by NCAA, 15 µg/mL
Muscle cramping, dehydration, gastrointestinal distress, nausea, seizures, possible effects on kidney function	No organizational policy
Drowsiness, headache, vomiting, papilledema, hair, skin, and nail changes	No organizational policy
Diarrhea, renal stones	No organizational policy
Muscle weakness, fatigue, headache, nausea	No organizational policy
Diarrhea	No organizational policy
Decreased high-density lipoprotein levels, increased estrogen levels	Banned by NCAA, USOC, and NFL
Allergic reaction, bacterial contamination, disease transmission, immune sensitization, polycythemia, ischemic events, thromboembolic events	Banned by NCAA and USOC

was the first time a gold medalist in track and field was disqualified from the Olympics for using illegal drugs.<sup>11</sup> Criminal investigations are proceeding against former German Democratic Republic sports officials for systematically using banned substances in their athletes' training programs.<sup>12</sup>

### Incidence of Use of Ergogenic Aids

Most studies of pharmacologic aids used by athletes have dealt with steroid use. The prevalence of self-reported use of anabolic steroids by adolescent athletes is as high as 11% for boys and 2.5% for girls.<sup>13</sup>

Buckley et al<sup>14</sup> found that 4.4% of all male high school seniors had initiated steroid use at 16 years of age or younger. In studies of adults, the prevalence of self-reported steroid use has been as high as 15%.<sup>15</sup> In projected-use studies, in which subjects were asked about the practices of other athletes, the preva-

lence was even higher.<sup>15</sup> In all age groups, the prevalence was always higher for males.<sup>15</sup> The greatest use of androgens is not by competitive athletes, but rather by recreational bodybuilders who take them for cosmetic purposes<sup>15</sup> and continue their use indefinitely in order to maintain their effects.<sup>16</sup> The National Football League (NFL) first tested for anabolic steroids in 1988 and announced that 6% of professional football players had taken them.<sup>11</sup>

There have been rumors that various national teams, especially European bicycling teams, use blood doping during competition, but the extent of this practice is largely unknown. Blood doping has been replaced primarily by administration of recombinant human erythropoietin (r-EPO), which is the recombinant form of a normal hormone that regulates erythropoiesis in the bone marrow. The lay sports literature reports widespread use of erythropoietin to elevate the red blood cell concentration in endurance athletes; however, there are no scientific data to quantify the extent of its use among competitive athletes.<sup>17</sup>

Nutritional supplements, such as creatine and vitamins, are considered legal ergogenic aids.<sup>7</sup> Although researchers disagree about their effectiveness, athletes consume certain nutrients, often in large doses, in the hope of enhancing their performance. A recent survey of 13,914 collegiate athletes revealed extensive use of nutritional supplements, such as creatine (13%), amino acid supplements (8%), and dehydroepiandrosterone (DHEA), which is a precursor to testosterone and estrogen (1%).<sup>18</sup> In a 1998 poll of 56 professional sports teams, creatine supplements were reportedly used by fewer than 25% of players on 36 teams, by 25% to 50% of players on 15 teams, and by more than 50% on 5 teams.<sup>19</sup> Use of creatine appears to be higher in profes-

sional football than in other team sports.<sup>20</sup>

## **Drug Testing**

To address the problem of potentially life-threatening use of drugs by athletes and use contrary to the ethics and ideals of fair competition, in 1963 the Council of Europe established the definition of doping, as follows:

The administration or use of substances in any form alien to the body or of physiological substances in abnormal amounts and with abnormal methods by healthy persons with the exclusive aim of attaining an artificial and unfair increase in performance in competition. Furthermore, various psychological measures to increase performance in sports must be regarded as doping. Where treatment with a medicine must be undergone, which as a result of its nature or dosage is capable of raising physiological capability beyond normal level, such treatment must be considered doping and shall rule out eligibility for competition.<sup>21</sup>

In 1967, the IOC established a medical commission, which was charged with enforcing the prohibition of illegal drug use (Table 2). In response to the Congressional hearings in 1973 on improper drug use in sports, major athletic organizations in the United States, including the National Collegiate Athletic Association (NCAA), the NFL, USA Track and Field, and the United States Olympic Committee (USOC), implemented drug programs.

The first drugs to be used for performance enhancement were stimulants, such as amphetamines. The initial testing for stimulants (using gas chromatography) occurred at the 1972 Olympic Games in Munich.<sup>21</sup> Widespread testing (using gas chromatography–mass spectrometry) for anabolic steroids in the urine began at the 1983 Pan-American Games.<sup>21</sup> Peptide hor-

mones, such as growth hormone, are detectable in the urine by means of immunoassay, but they are difficult to test for and to confirm as a positive result. Many of these compounds have a short half-life in the blood and a low concentration in the urine. With the greater availability made possible by the production of recombinant proteins, this class of compounds threatens to become the most abused.<sup>21</sup> Urine testing may reveal the presence of substances that are not performance-enhancing drugs themselves but that are used to mask the presence of banned substances. Diuretics can be used to reduce the urinary concentration of prohibited drugs. Probenecid and bromantan can also interfere with the detection of anabolic steroids.<sup>21</sup>

## **Anabolic Steroids**

Anabolic-androgenic steroids are synthetic derivatives of testosterone. In clinical practice, they are used to treat men with hypogonadism or impotence and to reverse the wasting effects of conditions such as burns and chronic debilitating illnesses.<sup>10</sup> Under appropriate conditions, administration of anabolic steroids can result in increases in muscle size and strength.<sup>13,16</sup> The benefits of anabolic-androgenic steroids are more notable in strength-dependent sports, such as weight lifting and football, than in aerobic sports.<sup>16</sup> Bodybuilders use anabolic steroids primarily to gain lean mass and lose body fat.<sup>9</sup>

### **Mechanism of Action**

Anabolic steroids induce protein synthesis in muscle cells, stimulate the release of endogenous growth hormone, and can reverse the effects of cortisol, a catabolic hormone.<sup>16</sup> Their psychological effect may allow a more intense and sustained workout.<sup>13</sup> The extent to which anabolic steroids can increase

**Table 2**  
**Substances and Methods Prohibited or Restricted by the USOC\***

Prohibited substances

Stimulants (e.g., amphetamines, caffeine [ $>12 \mu\text{g}/\text{mL}$  on urinary testing])  
 Narcotics (e.g., morphine, meperidine)  
 Anabolic agents (e.g., dehydroepiandrosterone, androstenedione)  
 Diuretics (e.g., furosemide, acetazolamide)  
 Peptide hormones, mimetics, and analogues (e.g., erythropoietin, growth hormone)  
 Over-the-counter medications containing prohibited stimulants  
 Desoxyephedrine (e.g., Vicks Inhaler)  
 Pseudoephedrine (e.g., Actifed, Co-Tylenol)  
 Phenylpropanolamine (e.g., Alka-Seltzer Plus, Contac, Dexatrim)  
 Ephedrine (e.g., Bronkaid, Collyrium With Ephedrine)  
 Ma-huang (e.g., "Mexican tea," "Bishop's tea," ephedra)  
 Propylhexedrin (e.g., Benzedrex inhaler)

Prohibited methods

Blood doping  
 Pharmacologic, chemical, and physical manipulation  
 Use of substances and methods that alter the integrity and validity of urine samples in drug testing (e.g., probenecid and bromantan)

Substances subject to certain restrictions

Alcohol  
 Cannabinoids  
 Local anesthetics  
 Corticosteroids  
 Beta-blockers  
 Specific  $\beta_2$ -agonists  
 Caffeine ( $<12 \text{ mg}/\text{mL}$  on urinary testing)

\* Source: *Drug Status Guide: Athlete Reference*. Colorado Springs, Colo: US Olympic Committee, May 1999.

strength and lean body mass and the factors that influence their effects are not yet completely understood or documented.<sup>9</sup> There is a lack of consensus as to the effect of anabolic steroids on humans because of differences in technique and methodology in the various studies that have been performed.

### Athletic Dosing

Some effects of exogenous anabolic steroid administration are reversible. For instance, once the athlete discontinues use of the anabolic steroid, the increased size and strength disappear. Anabolic steroids can be administered orally or parenterally. The injectable forms

are less hepatotoxic than the oral preparations; however, they are detectable via drug testing for a longer period of time.<sup>9,16</sup>

Athletes frequently use a combination of anabolic steroid preparations, a practice called "stacking."<sup>9,13,16</sup> Individuals often take anabolic steroids in 6- to 12-week cycles and may "pyramid" their administration by increasing the dose through the cycle.<sup>9,13</sup> Even though there is as yet no scientific proof of effectiveness, athletes often use cycling and pyramiding in the hope of maximizing the beneficial effects of anabolic steroids while minimizing their harmful effects.<sup>13</sup> Athletes may also use other drugs, such

as diuretics, antiestrogens, human chorionic gonadotropin, and antiacne medications, concurrently with anabolic steroids to counteract some of the more common adverse effects.

### Adverse Effects

Much of the information about the adverse effects of anabolic steroid administration is anecdotal or extrapolated from its effects in therapeutic use.<sup>5,13</sup> Organs and systems affected include the liver, reproductive system, musculoskeletal system, skin, cardiovascular system, and genitourinary system. Anabolic steroids also have psychological and immunologic effects<sup>13</sup> (Table 3). There is evidence that anabolic steroids can induce tendon rupture, osteonecrosis of the hip, psychosis, and suicidal behavior.<sup>16,24,25</sup> The masculinizing effects in women, such as male-pattern baldness and deepening of the voice, may be irreversible, as may growth retardation in children.<sup>13</sup> Synthetic steroid derivatives with primarily anabolic or virilizing activity have been manufactured. The degree of virilization depends on the dosage, duration of treatment, and particular steroid used.<sup>26</sup>

Although the incidence of serious side effects of anabolic steroid administration has been relatively low,<sup>22</sup> fatal effects have been documented. Athletes have died of hepatocarcinoma, myocardial infarction, and stroke as a consequence of prolonged steroid use. There has also been one reported case of a bodybuilder who contracted acquired immunodeficiency syndrome as a result of sharing needles for steroid injections.<sup>16</sup>

### Growth Hormone

Growth hormone is the most abundant substance produced by the pituitary gland, and it acts on most organs and tissues in the body.<sup>16</sup>

**Table 3**  
**Adverse Effects of Anabolic Steroids<sup>16,22,23</sup>**

Cardiovascular	Liver
Hypertension	Elevated liver enzymes
Thrombosis	Hepatocellular damage
Increased total cholesterol	Hepatocarcinoma
Increased low-density lipoprotein	Hepatoadenoma
Decreased high-density lipoprotein	Urinary system
Endocrine	Wilms' tumor
Decreased glucose tolerance and thyroid function	Immunologic
Masculinization in women	Decreased immunoglobulins
Musculoskeletal	Hepatitis B and C infection (from shared needles)
Premature physeal arrest	HIV infection (from shared needles)
Increased risk of tendon or muscle injury	Integument
Bilateral hip osteonecrosis	Acne
Male reproductive system	Hirsutism
Abnormal spermatogenesis	Male-pattern baldness
Testicular atrophy	Edema
Gynecomastia	Coarsening of skin
Impotence	Psychological
Priapism	Mood swings
Prostatic carcinoma	Irritability
Prostatic hypertrophy	Aggressiveness
Female reproductive system	Increased libido
Menstrual abnormalities	Psychosis
Uterine atrophy	Depression
Breast atrophy	Addiction
Teratogenicity	Suicide

Overproduction leads to gigantism or acromegaly; underproduction causes dwarfism. Some athletes use growth hormone because it increases muscle mass and is more difficult to detect than anabolic steroids.<sup>25</sup>

### **Mechanism of Action**

Growth hormone has an anabolic effect on the body, accelerating incorporation of amino acids into proteins. In addition, growth hormone stimulates utilization of lipids from adipose tissue as an energy source, thereby sparing muscle glycogen.<sup>16</sup> Although strength and performance may improve with the use of growth hormones, no one has yet investigated the ergogenic effects of growth hormone administration on athletes.<sup>16</sup>

### **Adverse Effects**

The adverse effects of exogenous administration of growth hormone in athletes can be extrapolated from the findings in patients with endogenous oversecretion of this hormone. These include gigantism in children and acromegaly in adults. Acromegaly can lead to heart disease or cardiac failure, glucose intolerance, hyperlipidemia, impotence, menstrual irregularities, myopathy, osteoporosis, and death.<sup>16,25</sup>

### **Caffeine**

Caffeine has a stimulant effect on the body and is used by athletes to improve endurance performance. Several studies have demonstrated

increased endurance with specific amounts of caffeine ingestion.<sup>27</sup> Caffeine taken in doses of 3 to 9 mg per kilogram of body weight appears to enhance performance of both prolonged endurance exercise and more intense short-duration exercise (lasting up to 5 minutes). Most of these results are based on laboratory tests on athletes; more studies during actual sports competition are needed.<sup>28</sup>

### **Mechanism of Action**

Although the mechanism of its effects is not entirely known, caffeine may stimulate the sympathetic nervous system. Another theory is that caffeine enhances intracellular utilization of free fatty acids as an energy source, thereby sparing muscle glycogen stores.<sup>6,27</sup>

### **Adverse Effects**

Some of the potential side effects of caffeine ingestion include anxiety, jitters, inability to focus, gastrointestinal discomfort, insomnia, and irritability. At higher doses, cardiac arrhythmia and hallucinations may occur.<sup>28</sup> The IOC currently allows only low levels of caffeine ingestion by athletes. By limiting coffee consumption to a maximum of three cups throughout the day, most athletes remain safely under the limit of a urinary concentration of 12 µg/mL.<sup>29</sup>

### **Recombinant Human Erythropoietin**

As mentioned previously, the earlier practice of blood doping by administration of packed red blood cells has been largely replaced by the use of r-EPO. The objective is to enhance performance.

### **Mechanism of Action**

Recombinant human erythropoietin, like the naturally occurring substance, regulates erythropoiesis

in the bone marrow. The rate at which the hematocrit increases depends on the dose of r-EPO.<sup>30</sup> Ekblom and Berglund<sup>31</sup> demonstrated increased maximum oxygen consumption and increased time to exhaustion in male athletes after 6 weeks of r-EPO administration.

### Adverse Effects

Risks from r-EPO administration include hyperviscosity of the blood, which leads to ischemic and thromboembolic events, hypertension, flu-like symptoms, and hyperkalemia.<sup>32</sup> The use of r-EPO has been banned by the IOC since 1990. Unfortunately, it is extremely difficult to detect with current testing standards.

### Beta-Blockers

Beta-blockers are used by athletes in certain sports (e.g., riflery and archery) for their antianxiety and antitremor effects.<sup>23</sup> Beta-blockers are clinically used primarily for the treatment of hypertension, angina pectoris, and cardiac arrhythmias.<sup>23</sup>

### Mechanism of Action

There are two types of beta-receptors in the body:  $\beta_1$ -receptors primarily mediate cardiac stimulation and intestinal motility, and  $\beta_2$ -receptors primarily mediate bronchodilation and relaxation of vascular and uterine smooth muscle.<sup>33</sup> Beta-blockers were added to the IOC list of prohibited substances in 1986, when it was discovered that their use by marksmen improved their pistol shooting scores.<sup>34</sup> In the study by Kruse et al,<sup>34</sup> athletes given metoprolol, a  $\beta_1$ -receptor blocker, showed improvement in their shooting performance compared with those who received placebo. This effect was considered to be primarily due to the ability of the drug to decrease hand tremors. Increases in heart rate and systolic blood pressure were eliminated,

which might also explain improved performance.

### Adverse Effects

Beta-blockers have an ergolytic effect on endurance athletes and affect thermoregulation during exercise.<sup>35</sup> Beta-blockers can induce bronchospasm and cause atrioventricular block, cardiac insufficiency, hypoglycemia, hallucinations, insomnia, depression, and nightmares.<sup>33</sup>

### Creatine

The use of creatine by athletes increased after Harris et al showed in 1992 that administration of high doses of creatine resulted in a 20% increase in skeletal muscle creatine concentration.<sup>36</sup> Creatine has become popular among football players and athletes in power sports who are seeking to increase strength.<sup>18</sup>

### Mechanism of Action

Creatine is an amino acid derivative found in skeletal muscle, cardiac muscle, and brain, retinal, testicular, and other tissues.<sup>7,36</sup> Creatine is synthesized primarily by the liver, kidneys, and pancreas, and is excreted by the kidneys.<sup>21</sup> Total creatine in skeletal muscle is the sum of free creatine and phosphocreatine (PCr), both of which are important in the production of adenosine triphosphate (ATP) during anaerobic activity. Oral creatine supplementation is considered ergogenic because of its potential to enhance ATP production during exercise.<sup>18</sup> Theoretically, this can be accomplished by increasing PCr availability, accelerating PCr resynthesis, and improving the pH-buffering capacity of muscle.<sup>18</sup> The buffering action may allow improved tolerance of anaerobic metabolism, thereby lengthening its potential ergogenic effect.<sup>18</sup>

Research on the ergogenic effect of creatine supplements has pro-

vided mixed results.<sup>18</sup> Several studies carried out on untrained subjects under laboratory conditions have shown that oral creatine supplementation can improve sprint and power performances during repeated short-duration bouts of high-intensity exercise.<sup>37,38</sup> However, studies performed on highly trained or elite athletes engaging in a high-intensity sprint activity showed no performance improvement.<sup>37</sup> The majority of available data concerning creatine supplementation and endurance exercise suggest that it does not improve performance.<sup>18,37</sup>

### Athletic Dosing

The athlete typically starts with a loading dose of creatine ranging from 15 to 30 g per day for the first week. Afterward, a maintenance dose of 2 to 5 g/day is taken for as long as 3 months. A month's supply typically costs \$30 to \$50.<sup>19</sup> The athlete then discontinues creatine supplementation for 1 month to allow the creatine level to return to baseline before resuming the cycle again.<sup>20</sup> Risks are thought to be minimized with this regimen. There are no added benefits of increasing creatine intake above this level. Skeletal muscle has a specific maximum creatine storage capacity; supplemental creatine that exceeds this maximum is excreted by the kidneys.<sup>39</sup>

### Adverse Effects

Short-term creatine supplementation for as long as 8 weeks has not been associated with major health risks.<sup>38</sup> However, creatine supplementation can cause weight gain due to an increase in cellular water in muscle and possibly increased protein synthesis within muscle.<sup>18</sup> Some of the observed side effects of long-term use include muscle cramping, dehydration, gastrointestinal distress, nausea, and seizures.<sup>20</sup> There is also concern about

the effects of creatine supplementation on kidney function.<sup>20,36</sup> Therefore, creatine supplementation should not be used by persons with underlying kidney disease or potential for renal dysfunction.<sup>36</sup> More studies are needed to fully understand the long-term effects of chronic creatine supplementation.

## **Vitamins**

Vitamins are generally classified as water-soluble or fat-soluble. Water-soluble vitamins (e.g., vitamins B and C) are metabolized and excreted in the urine. Fat-soluble vitamins (e.g., vitamins A, D, E, and K) are stored in the liver and metabolized more slowly. The fat-soluble vitamins, therefore, are potentially more toxic when consumed in large amounts. In general, most athletes who eat well-balanced meals and have no dietary restrictions do not benefit from vitamin supplementation.<sup>6,18</sup>

### **Mechanism of Action**

Some of the more common vitamin supplements taken by athletes include vitamin E ( $\alpha$ -tocopherol), vitamin C (ascorbic acid), and vitamin A precursor (beta carotene). The belief is that these vitamins are antioxidants and therefore are able to act as free-radical scavengers, especially with the increase in free-radical production during exercise. Studies of the effects of antioxidant supplementation have had varied results.<sup>18</sup> Current research does not support their use to benefit performance.<sup>40</sup>

### **Adverse Effects**

Some of the adverse side effects of overconsumption of vitamin A include drowsiness, headache, vomiting, papilledema, hair loss, scaly skin, brittle nails, hepatosplenomegaly, anorexia, and irritability. Excessive intake of vitamin E can

cause muscle weakness, fatigue, headache, and nausea. Excessive intake of vitamin C can lead to diarrhea and renal stone formation.<sup>41</sup>

## **Carnitine**

Carnitine is a quaternary amine that exists in several forms in the body. L-Carnitine is the physiologically active form. Carnitine supplementation is believed to reduce muscle glycogen breakdown and lead to a decrease in lactic acid production during exercise, thereby primarily benefiting the endurance athlete.<sup>6,18</sup> Studies of carnitine and athletic performance have been inconclusive.<sup>18,27</sup> Large doses of carnitine can cause diarrhea, which is obviously a considerable distraction from top athletic performance.

## **Androstenedione**

Androstenedione, an androgen produced in small quantities by the adrenal glands and gonads, received a lot of attention in 1998, when professional baseball player Mark McGwire admitted consuming this nutritional supplement during his record-setting season.

### **Mechanism of Action**

Androstenedione has little intrinsic activity but is a direct precursor of testosterone, a potent androgen. Androstenedione is also produced by some plants, from which can be derived a natural alternative to anabolic steroids. It is sold as a nonprescription nutritional supplement. Users and manufacturers of androstenedione supplements claim that they encourage the buildup of muscle mass and promote rapid recovery from injury.<sup>42</sup> Whether this claim is true is unknown, as there is almost no published information available on the effects of taking androstene-

dione.<sup>43</sup> A recent study by King et al<sup>44</sup> showed no increase in muscle mass or increased testosterone levels in men given daily doses of 300 mg of androstenedione compared with control subjects given placebo.

### **Adverse Effects**

King et al<sup>44</sup> found decreased levels of high-density lipoprotein and elevated levels of estrogens in subjects who received androstenedione. Low levels of high-density lipoprotein can contribute to cardiovascular disease risk. Increased concentrations of estrogens may increase the risk of cardiovascular disease, breast cancer, pancreatic cancer, and gynecomastia. Several athletic organizations, including the NCAA, NFL, USOC, and IOC, have banned the use of androstenedione. Major-league baseball and some other athletic organizations still permit its use.

## **Blood Doping**

There have been several highly publicized scandals involving blood doping in endurance athletes.<sup>45,46</sup> The practice has been prohibited by the IOC. (The conceptually related practice of training at high altitudes in order to elevate hemoglobin concentration is considered to be a legitimate way to enhance performance.)

### **Mechanism of Action**

Red blood cell infusions are classified as ergogenic because they increase the oxygen-carrying capacity of the blood and thereby increase the performance of the working muscles.<sup>45</sup> The effectiveness of blood doping indicates that it does improve athletic performance.<sup>3,7,30,45,46</sup> It has been hypothesized that blood doping benefits the endurance athlete, who depends primarily on the aerobic cycle for energy, rather than the sprinter,

who depends primarily on the anaerobic cycle for energy.<sup>45</sup>

### Adverse Effects

Risks as a result of blood transfusions include allergic reactions, bacterial contamination, disease transmission, and immune sensitization.<sup>46</sup> Autologous transfusion minimizes the obvious risks, but there is still the potential of harm, especially if the storage and transfusion are performed in suboptimal conditions.<sup>30</sup> In addition, overtransfusion can lead to polycythemia, which can cause decreased

blood flow and subsequent ischemic episodes and thromboembolic events.<sup>45,47</sup>

### Summary

Unfortunately, some athletes have developed a "win at any cost" mentality. They are willing to do whatever is needed to enhance their chances of victory, even if it is both illegal and potentially physically harmful. Use of certain ergogenic aids may threaten their careers and certainly flouts the spirit of fair com-

petition. Nutritional supplements are marketed to athletic individuals as a way of enhancing sports performance, even though many of these claims have not been proved scientifically and their production is largely unregulated. It is important that physicians be knowledgeable about the various ergogenic aids that are available, so that they can advise and treat athletes appropriately.

**Acknowledgment:** The author wishes to thank Peter Jokl, MD, for his guidance and advice during the preparation of this manuscript.

### References

- Bamberger M, Yaeger D: Over the edge. *Sports Illustrated* Apr 14, 1997;86:60-64.
- Gunby P: Olympics drug testing: Basis for future study. *JAMA* 1984; 252:454-455, 459-460.
- Mangi RJ, Jokl P: Drugs and sport. *Conn Med* 1981;45:637-641.
- Beckett AH, Cowan DA: Misuse of drugs in sport. *Br J Sports Med* 1979; 12:185-194.
- Street C, Antonio J, Cudlipp D: Androgen use by athletes: A reevaluation of the health risks. *Can J Appl Physiol* 1996;21:421-440.
- Williams MH: Ergogenic and ergolytic substances. *Med Sci Sports Exerc* 1992;24(suppl 9):S344-S348.
- Williams MH: The use of nutritional ergogenic aids in sports: Is it an ethical issue? *Int J Sport Nutr* 1994;4:120-131.
- Grivetti LE, Applegate EA: From Olympia to Atlanta: A cultural-historical perspective on diet and athletic training. *J Nutr* 1997;127 (suppl 5):860S-868S.
- Yesalis CE, Bahrke MS: Anabolic-androgenic steroids: Current issues. *Sports Med* 1995;19:326-340.
- Hoberman JM, Yesalis CE: The history of synthetic testosterone. *Sci Am* 1995; 272:76-81.
- Cowart VS: Accord on drug testing, sanctions sought before 1992 Olympics in Europe. *JAMA* 1988;260:3397-3398.
- Bahr R, Stray-Gundersen J: Time to get tough on doping! *Br J Sports Med* 1999;33:75-76.
- American Academy of Pediatrics Committee on Sports Medicine and Fitness: Adolescents and anabolic steroids: A subject review. *Pediatrics* 1997; 99:904-908.
- Buckley WE, Yesalis CE III, Friedl KE, Anderson WA, Streit AL, Wright JE: Estimated prevalence of anabolic steroid use among male high school seniors. *JAMA* 1988;260:3441-3445.
- Laure P: Epidemiologic approach of doping in sport: A review. *J Sports Med Phys Fitness* 1997;37:218-224.
- Haupt HA: Anabolic steroids and growth hormone. *Am J Sports Med* 1993;21:468-474.
- Catlin DH, Murray TH: Performance-enhancing drugs, fair competition, and Olympic sport. *JAMA* 1996;276:231-237.
- Johnson WA, Landry GL: Nutritional supplements: Fact vs. fiction. *Adolesc Med* 1998;9:501-513.
- Strauss G, Mihoces G: Jury still out on creatine use: Pro teams' disapproval rate is high on use of popular dietary supplement. *USA Today*, June 4, 1998:1C.
- Feldman EB: Creatine: A dietary supplement and ergogenic aid. *Nutr Rev* 1999;57:45-50.
- Bowers LD: Athletic drug testing. *Clin Sports Med* 1998;17:299-318.
- Bahrke MS, Yesalis CE, Brower KJ: Anabolic-androgenic steroid abuse and performance-enhancing drugs among adolescents. *Child Adolesc Psychiatr Clin North Am* 1998;7:821-838.
- Bell AT: The use of ergogenic aids in athletics, in Zachazewski JE, Magee DJ, Quillen WS (eds): *Athletic Injuries and Rehabilitation*. Philadelphia: WB Saunders, 1996, pp 293-313.
- Pettine KA: Association of anabolic steroids and avascular necrosis of femoral heads. *Am J Sports Med* 1991;19:96-98.
- Risser WL: Sports medicine. *Pediatr Rev* 1993;14:424-431.
- Schwartz FL, Miller RJ: Androgens and anabolic steroids, in Craig CR, Stitzel RE (eds): *Modern Pharmacology*, 2nd ed. Boston: Little, Brown, 1986, pp 905-924.
- Clarkson PM: Nutrition for improved sports performance: Current issues on ergogenic aids. *Sports Med* 1996;21: 393-401.
- Spriet LL: Caffeine and performance. *Int J Sport Nutr* 1995;5 (suppl):S84-S99.
- Sando BG: Is it legal? Prescribing for the athlete. *Aust Fam Physician* 1999; 28:549-553.
- Adamson JW, Vapnek D: Recombinant erythropoietin to improve athletic performance [letter]. *N Engl J Med* 1991;324:698-699.
- Eklom B, Berglund B: Effect of erythropoietin administration on maximal aerobic power in man. *Scand J Med Sci Sports* 1991;1:125-130.
- Stricker PR: Other ergogenic agents. *Clin Sports Med* 1998;17:283-297.
- Westfall DP: Adrenoceptor antagonists, in Craig CR, Stitzel RE (eds): *Modern Pharmacology*, 2nd ed. Boston: Little, Brown, 1986, pp 174-192.
- Kruse P, Ladefoged J, Nielsen U, Paulev PE, Sørensen JP:  $\beta$ -Blockade used in precision sports: Effect on pistol shooting performance. *J Appl Physiol* 1986;61:417-420.
- Eichner ER: Ergolytic drugs in medicine and sports. *Am J Med* 1993;94:205-211.
- Juhn MS: Oral creatine supplementa-

- tion: Separating fact from hype. *Phys Sportsmed* 1999;27:47-56.
37. Mujika I, Padilla S: Creatine supplementation as an ergogenic aid for sports performance in highly trained athletes: A critical review. *Int J Sports Med* 1997;18:491-496.
  38. Williams MH, Branch JD: Creatine supplementation and exercise performance: An update. *J Am Coll Nutr* 1998;17:216-234.
  39. Clark JF: Creatine: A review of its nutritional applications in sport. *Nutrition* 1998;14:322-324.
  40. Williams MH: Nutritional supplements for strength trained athletes. *Sports Sci Exchange* 1993;6:1-6.
  41. Barone S: Vitamins, in Craig CR, Stitzel RE (eds): *Modern Pharmacology*, 2nd ed. Boston: Little, Brown, 1986, pp 1066-1075.
  42. Josefson D: Concern raised about performance enhancing drugs in the US. *BMJ* 1998;317:702.
  43. Creatine and androstenedione: Two "dietary supplements." *Med Lett Drugs Ther* 1998;40:105-106.
  44. King DS, Sharp RL, Vukovich MD, et al: Effect of oral androstenedione on serum testosterone and adaptations to resistance training in young men: A randomized controlled trial. *JAMA* 1999;281:2020-2028.
  45. Brien AJ, Simon TL: The effects of red blood cell infusion on 10-km race time. *JAMA* 1987;257:2761-2765.
  46. Klein HG: Blood transfusion and athletics: Games people play. *N Engl J Med* 1985;312:854-856.
  47. Marx JJM, Vergouwen PCJ: Packed-cell volume in elite athletes [letter]. *Lancet* 1998;352:451.