



Performance-enhancing substances: What athletes are using

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■ ABSTRACT

Use of performance-enhancing substances is widespread among competitive athletes, whether professional or amateur, adolescent or adult. Some of these substances are legal and beneficial, but others are illegal or have adverse or unproven effects. This article describes the action and effects of these substances, their legality, and their potential for abuse.

HIGH-PROFILE CASES such as Mark McGwire's use of androstenedione in 1998 when he broke the home-run record, as well as revelations of drug use by athletes in the Sydney Olympics, have drawn attention to the questions and controversies about performance-enhancing drugs in competitive sports. Despite unresolved safety and efficacy issues, however, many athletes—not just Olympians and superstars—are using substances known or believed to enhance performance.

What are athletes using?

Performance-enhancing medications fall into several categories:

- Androgenic hormones and growth hormone for increasing muscle mass
- Protein and amino acid supplements for building muscle
- Beta-blockers to reduce anxiety
- Beta agonists, which may increase muscle mass
- Substances and techniques to increase the red blood cell count and oxygen capacity

- Stimulants to boost energy
- Vitamins and minerals.

Why do athletes take performance-enhancing substances?

Athletes naturally want to improve their performance and achieve greater success in competitive sports. In addition, other factors may be at work:

- Pressure from peers, coaches, trainers, and even physicians
- Legality and ease of use of some performance-enhancing substances
- Perception that drugs are a shortcut to achieving optimal performance
- Pressure to win
- Lack of fear of adverse effects.

Although the use of performance-enhancing substances in athletes is more common in men, use in women is on the rise. Professional and elite athletes are not the only ones who use these substances: the everyday weekend warrior is the most common user today. At this time, however, no data are available on how many older master's level athletes use these substances.

Avoid scare tactics

Physicians need to be aware of the effects of these substances, the laws and regulations governing their use, and their potential for abuse. We should also become familiar with the legal substances that may be beneficial, to provide solid advice for patients.

When dealing with an athlete whom you suspect may be using steroids, for example, it is important to be low-key but address the legal and health risks. "Scare tactics" are rarely effective in discouraging athletes from using these substances or persuading them to stop. Goldberg et al¹ showed that peer groups

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may be very effective in decreasing the use of steroids, at least in adolescents.

■ HORMONES AND DRUGS THAT BOOST HORMONE LEVELS

Androgenic hormones and drugs that boost these hormone levels help build muscle and strength but may also produce harmful physical and psychological effects. Human growth hormone is a nonandrogenic hormone that also helps build muscle. Most hormones and hormone boosters are banned by sports organizations.

Anabolic steroids

Anabolic steroids, the most commonly abused drugs in sports, have both anabolic effects (they promote growth of muscle tissue) and androgenic effects (they promote development of male secondary sexual characteristics). These drugs have been banned in almost all sports worldwide, and many organizations test for them in urine screens.

Anabolic steroids enhance muscle protein formation and may also decrease the rate of muscle tissue breakdown. As a result, they increase muscle mass and strength, but they have not been proven to improve sports performance. They help athletes recover from exercise more quickly, which can help them train more intensively. Among the androgenic effects of steroids is increased aggressiveness, which may cause social difficulties but may also help athletes train and perform more intensively.

Despite the illegality of steroids, more than 1 million Americans have used them. In 1985, the rate of use among college football players in division I schools was about 5%.² Twenty-five percent of those who have used anabolic steroids are adolescents; these adolescents are at risk for other drug use and high-risk behavior.

How athletes use steroids. Anabolic steroids are available in oral or injectable form. When testosterone is used for medical purposes such as promoting muscle growth in debilitating illnesses, the dosage is 5 to 10 mg; athletes, however, may use doses as high as 300 mg. In one delivery technique called "stacking," an athlete uses two or more

steroids simultaneously. In another technique, called "pyramiding," the dose is increased throughout a training cycle, then decreased.

Side effects of steroids. Steroids cause increased acne for both men and women. Women may experience deepening voices and growth of facial and body hair (masculinization). Because the body naturally converts excess testosterone into estrogen, men may develop feminizing traits such as breast enlargement.

Other side effects include testicular atrophy in men and clitoral enlargement in women. Enlargement of the prostate has also been documented, with unknown long-term effects. Possible cardiovascular effects include decreased levels of high-density lipoprotein and increased levels of low-density lipoprotein, stroke, hypertension, and accelerated coronary artery disease. Hepatic effects include tumors, peliosis hepatis, and occasionally jaundice, and orthopedic effects include an increased risk of tendon ruptures. Paradoxically, in adolescents, anabolic steroids can halt growth prematurely.

How athletes counter side effects. To counter some of these side effects, athletes often take other drugs while taking steroids. Some common options are human chorionic gonadotropin (HCG) to prevent atrophy of the testes, and antiestrogens such as tamoxifen to decrease gynecomastia. Also, to avoid detection, many athletes simultaneously use probenecid to decrease the urine concentration of the steroids.

Dehydroepiandrosterone (DHEA)

Dehydroepiandrosterone (DHEA) is a precursor to testosterone that stimulates protein anabolism to build muscle and increase strength. Most athletes who use DHEA state that they experience no side effects, but women may experience virilization.

The US Food and Drug Administration banned DHEA in 1996. DHEA is detected by urine tests for anabolic steroids.

Androstenedione and norandrostenediol

Androstenedione is a natural steroid hormone found in all animals and also in some plants. A metabolite of DHEA, "andro" is a direct precursor in the biosynthesis of testosterone. It is also an essential intermediate in the biosyn-

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thesis of other biologically active steroid hormones such as the highly androgenic steroid nandrolone.

Androstenedione increases blood levels of testosterone, increases energy, enhances recovery and growth from exercise, heightens sexual arousal and function, and enhances the sense of well-being. Serum testosterone starts rising about 15 minutes after oral administration, peaks at 1 to 1.5 hours, and stays elevated for about 3 hours.

Recently, a related but much more powerful steroid called **norandrostenediol** has become available. Some studies in athletes show that norandrostenediol supplements substantially increase muscle size, strength, and fat loss. Whereas androstenedione lasts only a few hours, norandrostenediol has a 3-week half-life.

Androstenedione is legal for sale as a nutritional supplement, but norandrostenediol is banned by the National Football League (NFL), National Collegiate Athletic Association (NCAA), and the International Olympic Committee (IOC).

How athletes use these hormones.

Androstenedione should be taken once a day before exercise to avoid prolonged exposure that may down-regulate normal testosterone production.

Side effects. These hormones carry some of the same side effects as anabolic steroids. When androstenedione is taken at regular intervals throughout the day, it produces constantly elevated testosterone levels but may induce the body to decrease natural testosterone production.

Tribulus terrestris

Tribulus terrestris, a legal herb used in traditional medicine to promote virilism, is a testosterone booster with a mechanism of action different from those of the more common hormones.³

Tribulus terrestris increases testosterone levels by more than 50% by increasing luteinizing hormone (LH) levels. Animal studies show that *Tribulus terrestris* increases sperm production and motility after 30 days of supplementation. Increased testosterone production and testicular maturation have also been reported.

A study of *Tribulus terrestris* found that 750 mg/day increased LH levels in healthy men by 72% and free testosterone by 41%. A study of impotent men showed that the herb increased LH, testosterone, sperm production, and sperm motility.

Side effects. No significant adverse effects have been reported. Some users report stomach upset, which can be prevented by taking the herb with food.

Chrysin

Chrysin is an isoflavone extracted from a plant in the passionflower family, *Passiflora caerulea*. It boosts testosterone levels by slowing the rate at which testosterone is converted to estrogen or dihydrotestosterone. Chrysin is legal and is often taken in conjunction with other testosterone boosters to prevent testosterone conversion and resultant feminizing side effects. Little is known about the side effects of chrysin.

Human growth hormone

Human growth hormone (HGH) is not a single substance but a family of structurally related proteins that promote the normal growth and maturation process by helping to generate insulin-like growth factors 1 and 2. It has many dangerous side effects and is banned by the IOC, the United States Olympic Committee (USOC), and the NCAA, although current drug screening cannot detect it.

Human growth hormone is legally used for replacement therapy in children deficient in growth hormone. Under natural conditions, levels of HGH rise in response to hypoglycemia and exercise. The largest surge occurs 90 minutes after sleep begins.

Athletes feel that HGH increases muscle mass, reduces recovery time between workouts, and increases strength. Studies show that athletes using HGH have significantly increased fat-free weight and decreased percentage of body fat.⁴ It has no androgenic effects.

How athletes use HGH. Athletes report taking up to 20 times the therapeutic dosage in hope of gaining some of the effects of anabolic steroids. The therapeutic dose is 0.06 mg/kg to 0.1 mg/kg three times a week.

Side effects include acromegaly, peripheral neuropathy, glucose intolerance, elevated cho-

**'Andro'
increases
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of testosterone**

lesterol and triglyceride levels, coronary artery disease, and cardiomyopathy. Musculoskeletal and cardiac effects may be irreversible.

■ PROTEIN AND AMINO ACIDS

Proteins and amino acids used by athletes are generally benign, but some may have side effects, and their efficacy as performance-enhancers is not proven. They have not been banned.

Protein

Resistance exercise increases the rate of protein synthesis. Many athletes may therefore need more than the US recommended daily allowance (RDA) of protein, which is 0.8 g/kg/day. Most athletes ingest more than enough protein and energy, but those on calorie-restricted diets, those who make poor food choices, and those who follow a vegetarian diet may need protein supplementation. Athletes who do not eat enough carbohydrates rapidly deplete glycogen during exercise and may rely more heavily on protein for energy.

One study suggests that even well-nourished athletes may benefit from extra protein.⁵ In this study, athletes who usually consumed about 1.3 g/kg/day of protein spent 4 weeks consuming an additional 2 g/kg/day. Whole body protein synthesis and lean body mass both rose. However, amino-acid oxidation also rose, suggesting that such high protein intake exceeds what was needed for muscle growth and was used for energy.

Athletes should be advised not to increase protein intake by eating high-fat foods such as red meat or whole eggs. An inexpensive and good source of protein is dry milk powder (casein), which provides all the necessary amino acids at less than half the cost of most commercial protein supplements.

Many commercial protein formulas are effective, but those that include such ingredients as whey protein or "special enzymes" have not been scientifically tested, so there are no data to support the contention that they promote muscle gain.

Creatine

Creatine, an amino acid synthesized from arginine and glycine in the liver, pancreas, and

kidneys, is naturally available in meats and fish. Creatine was brought to public attention in 1992 after athletes reported using it at the Barcelona Olympics. Creatine is not banned by the IOC or the NCAA and is relatively safe.

Creatine enhances skeletal muscle performance by increasing the bioavailability of phosphocreatine, which speeds the resynthesis of the power molecule adenosine triphosphate (ATP) to provide energy for brief spurts of high-intensity exercise. Creatine also buffers the intracellular hydrogen ions associated with lactate production and muscle fatigue during exercise. Thus, it increases the force of muscle contraction in short-duration and repetitive bursts of intense exercise.

How athletes use creatine. A 5-day loading period of 20 g/day increases creatine availability by 20% and significantly accelerates regeneration after intense muscle contraction.⁶ Unfortunately, high doses of creatine appear to decrease endogenous production of creatine. Ingestion with carbohydrates is thought to aid uptake in the muscle cells.

Side effects. Increases in muscle cramps, dizziness, and diarrhea have been reported. Some athletes have experienced elevated creatinine levels. If doses of creatine greater than 10 g/day are taken past the 5-day 20 g/day loading dose, athletes may be susceptible to injury to their liver and kidneys. Doses under 10 g/day appear to be tolerated by the kidneys without any long-term effects.^{7,8}

Beta-hydroxy-beta-methylbutyrate (HMB)

Beta-hydroxy-beta-methylbutyrate (HMB) is an amino acid metabolite that appears to suppress the protein breakdown that normally follows intense exercise. Although it has been patented, HMB is a natural metabolite of leucine and is found naturally in small amounts in catfish, citrus fruit, and breast milk. As a supplement, it is legal.

Supplementation with HMB may increase muscle strength and mass. Intensively trained athletes who use HMB supplements gain significantly more lean mass and strength than athletes who use a placebo.⁹ HMB may also accelerate fat loss from strenuous exercise. No side effects have been reported, but little is known about it.

Powdered milk is an inexpensive source of extra protein for athletes

How athletes use HMB. The usual dosage is 3 g per day.

Glutamine

The amino acid glutamine is found in many legal weight-gain supplements marketed to athletes. It appears to be an important metabolic nutrient that affects protein synthesis by increasing cell volume and osmotic pressure. Glutamine may also affect lymphocyte function. Research is needed to make further conclusions and determine effects and side effects.

L-carnitine

L-carnitine is an amino acid derivative once thought to improve sports performance by increasing the rate of fatty acid oxidation and decreasing muscle lactate levels. However, these claims have been disproved,¹⁰ and L-carnitine is now considered ineffective. Its use is legal.

■ BETA-BLOCKERS

Beta-blockers, which calm anxiety and enhance concentration, are prohibited in figure skating, archery, riflery, ski jumping, fencing, and diving.

These drugs depress the actions of epinephrine and norepinephrine, especially in the heart. They are thought to reduce the adverse effects of anxiety on fine motor control, steadying the arm in shooting events by reducing muscle tremors, and slowing the heart so there is time to fire between beats.

Beta-blockers decrease anxiety, tension, and heart rate. However, they can also decrease aerobic endurance, possibly through their effect on epinephrine.

How athletes use beta-blockers. Beta-blockers are usually taken 1 to 4 hours before competition to produce calmness.

Side effects include drowsiness, fatigue, nausea, and weakness. Fainting, hypotension, or congestive heart failure may occur.

■ BETA AGONISTS

Clenbuterol

Clenbuterol is a beta-adrenergic agonist that acts as a smooth muscle relaxant; it also increases lean muscle mass and decreases body

fat. Clenbuterol has dangerous side effects and is banned by the IOC, the USOC, and the NCAA. Urine tests can detect the substance up to 2 to 4 days after the last dose.

Chronic beta-agonist treatment is known to increase lipolysis and decrease lipogenesis dramatically in a process that increases the availability of fat for energy. In addition, it increases glycogenolysis from the liver, which may increase carbohydrate availability. Beta agonists also enhance protein anabolism.

Muscle growth can be measured after 2 days of use, and muscle weight increases 10% to 20% after 1 to 2 weeks.

How athletes use clenbuterol. Athletes often use clenbuterol on and off in 2-day cycles for 8 to 10 weeks, followed by a 10-to-12 week break.

Side effects include tremor, tachycardia, anxiety, palpitations, headache, nausea, anorexia, and insomnia. More serious side effects include cardiac muscle hypertrophy, myocardial infarction, and stroke.

■ STIMULANTS

Stimulants are popular for their obvious revitalizing effects and their ability to suppress appetite. However, ephedrine and excess caffeine are banned in many sports.

Ephedrine or *ma huang*

Ephedrine is structurally related to amphetamines and stimulates alpha- and beta-adrenergic receptors. It is found naturally in the plant genus *Ephedra* and in preparations of the Chinese traditional herb *ma huang*.

Although banned by the IOC and the NCAA, ephedrine has several effects that athletes find beneficial. It increases myocardial contraction, cardiac output, and blood pressure. A common component of diet drugs, ephedrine decreases appetite, which may be attractive to wrestlers trying to "cut weight." However, ephedrine has not been proven to cause weight loss in nonobese people. Ephedrine also produces a surge of energy and decreases the feeling of fatigue, which may be helpful for cyclists in long races.

Side effects. Ephedrine may be associated with temperature dysregulation and heat illness.

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Caffeine

Although caffeine is commonly available and legal, excess amounts (urinary levels ≥ 15 mg/dL) are grounds for disqualification by the NCAA.

Caffeine in pills or beverages increases cardiac output, and in prolonged aerobic endurance exercise, it may enhance performance. Blood levels peak 30 to 60 minutes after consumption, and caffeine's half-life in the body ranges from 2 to 12 hours. Caffeine may act either directly on cell functions or indirectly by increasing the release of epinephrine from the adrenal medulla or methylxanthines from the liver. Some have proposed that caffeine also increases lipolysis, increases circulating levels of free fatty acids, and spares glycogen.

MEASURES TO INCREASE RED BLOOD CELL COUNT

Techniques to elevate red blood cell count are banned but remain popular because they increase aerobic endurance by increasing the oxygen-carrying capacity of the blood.

Blood doping

Blood doping is the process of inducing erythrocythemia through a transfusion of blood or red blood cells. Rumors of blood doping were first heard in the 1972 and 1976 Olympics. In the 1984 Olympics, the United States cycling team admitted to blood doping. Blood doping is banned by the IOC, the USOC, and the NCAA.

How athletes use blood doping. The preferred technique for inducing erythrocythemia is an autologous transfusion. Athletes may draw blood, wait for hemoglobin levels and hematocrit to normalize, and then use the frozen blood.

Erythropoietin

Erythropoietin is a naturally occurring peptide hormone that induces red blood cell production. Recombinant erythropoietin (rEpo) is banned by most sports organizations. However, it is difficult to detect because very little is excreted in the urine and it has a half-life of only 4 to 5 hours if administered intravenously.

Recombinant erythropoietin is used for anemia associated with renal failure, HIV, or malignancy. It can increase oxygen consumption (VO_2 max) and treadmill run time.

Side effects. The abuse of recombinant erythropoietin poses a serious health threat. It raises hematocrit and blood viscosity. At hematocrit levels above 55%, the blood viscosity increases exponentially, leading to the risk of coronary or cerebral artery occlusions. Recombinant erythropoietin was thought to be involved in the mysterious deaths of several European cyclists between 1987 and 1990.

VITAMINS AND MINERALS

Many athletes supplement their diets with extra vitamins and minerals. These are legal and probably benign, although their benefit in many cases is not proven.

Antioxidants

Antioxidants most commonly used by athletes are vitamin C (ascorbic acid), vitamin E (alpha-tocopherol), and the vitamin A precursor beta-carotene. These vitamins may bolster antioxidant defenses and help prevent muscle and tissue damage during strenuous aerobic endurance training. However, they have not been shown to enhance sports performance.

How athletes use antioxidants. Doses vary, but 50,000 IU of beta-carotene, 2000 to 3000 mg of vitamin C, and 1,200 IU of vitamin E may provide a protective antioxidant effect.

Chromium

Chromium is an essential trace mineral present in various foods including mushrooms, prunes, and nuts. A normal diet includes only 50% to 60% of the US RDA of chromium. Although chromium supplementation is not banned by sports organizations, it is not recommended because of anecdotal reports of serious adverse effects, including anemia, chromosome damage, and interstitial nephritis.¹⁰

Chromium seems to function as a cofactor to enhance the action of insulin. Some studies have associated chromium supplements with a decreased percentage of body fat and increased lean mass among college athletes and students, whereas other studies do not.¹¹

Excess caffeine is banned in college sports



How athletes use chromium. The dosage for chromium supplementation is 200 to 400 µg/day for several months; to promote gastrointestinal absorption, chromium is bound to picolinate.

Vanadium

Vanadium is a nonessential mineral. Some people believe that it may produce insulin-like effects on glucose and protein metabolism, inhibiting protein degradation during exercise. It is thought to increase muscle mass. However, very little data are available on any sports-enhancing effects. Users report a strong cosmetic effect, saying that vanadium causes glycogen to be absorbed by the muscles, making them harder and bigger, and producing a “pumped” appearance.

How athletes use vanadium. Vanadium sulfate is taken for 12 weeks at a dose of 60 to 100 mg per day, although there is no RDA. Vanadium is legal.

Side effects. Users report gastrointestinal distress, primarily diarrhea.¹²

■ OTHER SUBSTANCES

Bicarbonate loading

Bicarbonate loading, “soda loading,” or “buffer boosting” is the taking of sodium bicarbonate to counteract buildup of lactic acid. Although bicarbonate loading is not specifically addressed in sports regulations, the IOC considers it blood doping.

Ingesting bicarbonate can increase the rate at which lactic acid is removed from muscle cells. Taking the equivalent of 11 Alka Seltzer tablets has been shown to prolong the time during which athletes can exercise before becoming exhausted.¹³

Side effects. The most common side effect is diarrhea several hours after ingestion. Adverse effects from chronic use are hypercalcemia, alkalosis, and nephrolithiasis. With increased alkalosis, oxygen may become less available to tissue.

Glycerol

Glycerol is a sweet, syrupy, alcoholic liquid derived commercially by hydrolyzing fats. It is thought to produce hyperhydration, which may help sports performance by increasing

blood volume and improving resistance to dehydration in stressful environmental conditions. It is also believed to increase exercise endurance and improve thermoregulation.¹⁴ It was approved by the IOC in 1997 after being reviewed by the USOC.

No studies show side effects with oral doses under 2.2 g/kg/day for less than 50 days. However, if glycerol is used intravenously, adverse reactions include hemolysis, renal damage, and hyperglycemia.¹⁵

Ginseng

Ginseng, prepared from the root of varieties of the ginseng plant grown in America and Asia, is used in traditional medicine as a purported energy booster and aphrodisiac. Current research does not support the effectiveness of ginseng in improving sports performance.¹⁶ However, many athletes believe that ginseng permits more intense training, reduces fatigue, and increases stamina. It has been proposed that ginseng activates the hypothalamic-pituitary-adrenal cortex axis, sustains muscle creatine phosphate during strenuous exercise, decreases lactic acid levels during exercise, and improves nitrogen and protein balance.

Side effects. Heavy and prolonged use of ginseng can produce side effects similar to those of corticosteroid poisoning: hypertension, hypotension, skin eruptions and acne, nervous disorders, tranquilizing effects, insomnia, edema, diarrhea, pounding sensation in the head, and ringing in the ears.

Ginseng is legal and is not banned by the USOC or the IOC.

■ DRUG TESTING

Both the USOC and the NCAA have developed drug testing and drug education programs to try to ensure safe and fair competition. Since 1968, drug testing has been mandatory at the international Olympic games. Most drug screens are performed on urine. Testing techniques include thin-layer chromatography, immunoassay, and high-performance liquid chromatography. Gas chromatography with mass spectrometry is the most precise testing method, but it is also the most expensive and is therefore generally used only for confirmation.

Users say vanadium gives them a ‘pumped’ appearance





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