Supplements and Sports

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Use of performance-enhancing supplements occurs at all levels of sports, from professional athletes to junior high school students. Although some supplements do enhance athletic performance, many have no proven benefits and have serious adverse effects. Anabolic steroids and ephedrine have life-threatening adverse effects and are prohibited by the International Olympic Committee and the National Collegiate Athletic Association for use in competition. Blood transfusions, androstenedione, and dehydroepiandrosterone are also prohibited in competition. Caffeine, creatine, and sodium bicarbonate have been shown to enhance performance in certain contexts and have few adverse effects. No performance benefit has been shown with amino acids, beta-hydroxy-beta-methylbutyrate, chromium, human growth hormone, and iron. Carbohydrate-electrolyte beverages have no serious adverse effects and can aid performance when used for fluid replacement. Given the widespread use of performance-enhancing supplements, physicians should be prepared to counsel athletes of all ages about their effectiveness, safety, and legality. (*Am Fam Physician.* 2008;78(9):1039-1046. Copyright © 2008 American Academy of Family Physicians.)

ILLUSTRATION BY JOHN W. KARAPELOU

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Although the use of performance-enhancing supplements by professional athletes has been the focus of media attention, this practice affects sports at all levels. In a survey of 902 Iowa high school athletes, 8 percent of adolescent males and 2 percent of adolescent females reported using some type of supplement to improve performance, with many taking multiple supplements.[1] In 1995, approximately 375,000 adolescent males and 175,000 adolescent females reported that they had used anabolic steroids at least once.[2] Similarly, a survey of adult anabolic steroid users revealed that nearly four out of five were nonathletes attempting to achieve cosmetic benefits.[3] Family physicians need to know about the effectiveness, safety, and legality of popular supplements in order to counsel patients about their use. *Tables 1*[4-42] and *2*[14,15] review the evidence for 13 popular supplements.

Amino Acids

Amino acid supplements have not been demonstrated to enhance performance. Although daily dietary protein requirements are higher for athletes, the typical athlete's diet contains enough protein to meet this increased requirement without additional supplementation.[43] In clinical studies, time to exhaustion (endurance) was not increased by amino acid supplementation,[4] and marathon running times did not improve.[5] Likewise, a 10-week study of untrained persons did not demonstrate an increase in strength attributable to amino acid supplementation.[6]

Amino acid supplements cause gastrointestinal adverse effects, primarily diarrhea and stomach cramps.[44] These supplements are not currently prohibited by any sports governing agencies.

Anabolic Steroids

This category includes all synthetic derivatives of testosterone, oral and injectable. Anabolic steroids are performance enhancing and exert their effect by increasing muscle protein synthesis.[7] Short-term use of anabolic steroids increases strength and

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendations	*Evidence rating*	*References*
Evidence fails to show enhanced athletic performance with amino acids, beta-hydroxy-beta-methylbutyrate, chromium, human growth hormone, and iron.	B	4-6, 17, 18, 26, 27, 36-39
Evidence shows dangerous adverse effects with use of anabolic steroids, blood transfusion, erythropoietin, ephedrine, and pseudoephedrine.	B	19, 32, 33, 45-50
Evidence demonstrates a context-specific athletic performance enhancement with caffeine, carbohydrate-electrolyte beverages, creatine, and sodium bicarbonate.	B	21-25, 28, 29, 40-42

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

Table 1. Effectiveness and Legal Status of Supplements Used in Sports

Supplement	*Postulated effect*	*Evidence of effectiveness*	*Adverse effects*	*Legal status*
Amino acids[4-6]	Increase growth hormone levels	No effect	Minimal	Legal
Anabolic steroids[7-9]	Increase lean muscle mass	Effective	Significant and dangerous	Illegal
Androstenedione and dehydroepiandrosterone[10-13]	Increase testosterone and lean muscle mass	No effect	Significant	Prohibited by IOC[14] and NCAA[15] Androstenedione is illegal under the Anabolic Steroid Control Act of 2004[16]
Beta-hydroxy-beta-methylbutyrate[17,18]	Decrease protein breakdown and increase synthesis	No effect	None, but long-term evidence lacking	Legal
Blood transfusion and erythropoietin[19,20]	Increase endurance and oxygen delivery	Effective	Significant and dangerous	Prohibited by IOC[14] and NCAA[15]
Caffeine[21-23]	Increase energy and decrease fatigue	Effective	Minimal	Prohibited by IOC[14] and NCAA[15] above urinary concentrations of 12 mcg per mL and 15 mcg per mL, respectively
Carbohydrate-electrolyte beverages[24,25]	Increase energy and decrease fatigue	Effective	None	Legal
Chromium[26,27]	Increase lean muscle mass	No effect	Potentially dangerous, but long-term evidence lacking	Legal
Creatine[28,29]	Improve muscle energy and strength	Effective in limited contexts	Minimal	Legal
Ephedrine and pseudoephedrine[30-35]	Increase energy and decrease fatigue	Mixed, but mostly negative	Significant and dangerous	Prohibited by IOC[14] and NCAA[15]
Human growth hormone[36]	Increase muscle protein synthesis and strength	No effect; lack of evidence	Significant and dangerous	Illegal
Iron[37-39]	Increase energy and general performance	No effect unless deficiency is present	None below recommended dietary allowance dosing; toxicity above this level	Legal
Sodium bicarbonate[40-42]	Increased buffering capacity	Effective in limited contexts	Minimal	Legal

IOC = International Olympic Committee; NCAA = National Collegiate Athletic Association.

Information from references 4 through 42.

body weight,[8] with the increase in body weight attributed to an increase in lean mass without a decrease in fat mass.[9]

Reported adverse effects include decreased high-density lipoprotein (HDL) cholesterol levels,[45] elevated blood pressure,[46] gynecomastia,[47] aggressive behavior,[47] azospermia,[48] and virilization in women (e.g., menstrual irregularities).[49] Many of these effects are reversible upon cessation of steroid use.[45,46,48] Premature death has also been associated with anabolic steroid use, with suicide and acute myocardial infarction being the two most common causes.[50] Because of these potentially life-threatening adverse effects, the U.S. Congress classified anabolic steroids as a schedule III controlled substance. Their use is prohibited by the International Olympic Committee (IOC)[14] and the National Collegiate Athletic Association (NCAA).[15]

Table 2. Summary of Supplements, Effects, and IOC and NCAA Rulings on Usage

Supplements	*Effects*	*IOC and NCAA ruling*
Caffeine* Carbohydrate-electrolyte beverages Creatine Sodium bicarbonate	Performance enhancing, with minimal adverse effects	Allowed
Amino acids Beta-hydroxy-beta-methylbutyrate Chromium Iron†	Ineffective or lack of evidence of performance-enhancing effects	Allowed
Anabolic steroids Blood transfusion and erythopoietin	Performance enhancing, with dangerous adverse effects	Prohibited
Androstenedione and dehydroepiandrosterone Ephedrine and pseudoephedrine Human growth hormone	Ineffective or lack of evidence of performance-enhancing effects, with dangerous adverse effects	Prohibited

IOC = International Olympic Committee; NCAA = National Collegiate Athletic Association.

**—The IOC and NCAA prohibit urinary caffeine concentrations of more than 12 mcg per mL and 15 mcg per mL, respectively.*
†—*In persons who are not iron deficient.*

Information from references 14 and 15.

Androstenedione and Dehydroepiandrosterone

Despite being reclassified as an anabolic steroid by the U.S. Anabolic Steroid Control Act of 2004, androstenedione is more biochemically similar to dehydroepiandrosterone (DHEA), a precursor of testosterone.[16] Cholesterol is metabolized by multiple enzymes into testosterone via a number of androgenic intermediaries *(Figure 1)*, including these two. Thus, androstenedione and DHEA are marketed as being able to build muscle and increase strength by increasing serum testosterone. However, supplementation has not been shown to increase testosterone levels, strength, or performance in clinical studies.[10,11] Androstenedione supplementation was not able to increase strength as measured by a one-repetition maximal bench press[12] or by total weight lifted per workout.[11] DHEA did not increase mean strength over 12 weeks of supplementation.[13]

Adverse effects of androstenedione and DHEA include a sustained increase in serum estrogen[11] and an increase in serum luteinizing hormone.[10] The clinical significance of these hormonal changes have not been studied. Decreases in HDL cholesterol levels have been noted,[11] and one case of priapism following androstenedione ingestion has also been described.[51] The use of androstenedione and DHEA is prohibited by the IOC[14] and NCAA.[15] In addition, androstenedione is illegal under the Anabolic Steroid Control Act of 2004.[16]

Beta-hydroxy-beta-methylbutyrate

Beta-hydroxy-beta-methylbutyrate (HMB) has not been shown to have a performance enhancing effect in trained athletes. Six weeks of supplementation did not increase strength when combined with resistance training.[17] In addition, a randomized trial of 27 elite rugby players did not demonstrate that HMB had an effect on aerobic performance during a multistage fitness test or on anaerobic performance during a 60-second maximal cycle test.[18]

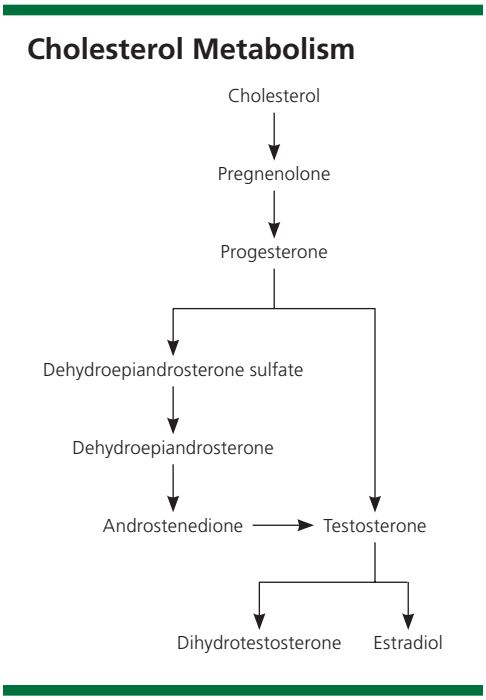

Figure 1. Summary of the endogenous metabolism of cholesterol into multiple hormones. Some of the intermediaries are used as supplements to promote physical performance.

With short-term use, no adverse effects of HMB supplementation have been noted. A six-week study in male athletes demonstrated no harmful effects of HMB ingestion on complete blood count; electrolyte, blood lipid, plasma urea, or plasma glucose levels; sperm count; or motility.[52] The IOC[14] and NCAA[15] currently do not prohibit the use of HMB supplements.

Blood Transfusions and Erythropoietin

The use of blood transfusions (also known as blood doping) or erythropoietin to increase oxygen delivery to exercising tissues has been demonstrated to improve performance in endurance sports, such as long-distance cycling. Early uncontrolled studies found that blood transfusions increased running time to exhaustion.[19] A double-blind, placebo-controlled study of 20 male athletes also revealed an increased time to exhaustion during cycling following administration of recombinant human erythropoietin for four weeks.[20]

Erythropoietin increases the risk of deep venous thrombosis, pulmonary embolism, and coronary and cerebral thrombosis.

Multiple risks are involved with blood transfusions and erythropoietin use. Transfusions carry a risk of transfusion reactions and bloodborne infections, such as human immunodeficiency virus and hepatitis. The increased blood viscosity that results from use of erythropoietin increases the risk of deep venous thrombosis, pulmonary embolism, and coronary and cerebral thrombosis.[19] Blood transfusions and erythropoietin use are prohibited by the IOC[14] and NCAA.[15]

Caffeine

Caffeine is classified as a stimulant and is performance enhancing. Persons were able to complete a cycling time trial significantly faster after caffeine ingestion,[21] and 2,000-meter rowing time was reduced by 1.2 percent after caffeine ingestion.[22] In both of these trials, increased performance was noted at urinary caffeine concentrations below the IOC allowable limit of 12 mcg per mL.[14] No effect of caffeine was noted during repeated sprints, such as sprinting that occurs during team sports; however, only 16 persons participated.[23]

Adverse effects of caffeine supplementation include possible anxiety, dependency, and withdrawal from central nervous system effects.[53] Although the IOC currently prohibits urinary caffeine concentrations of more than 12 mcg per mL,[14] the NCAA allows concentrations up to 15 mcg per mL.[15]

Carbohydrate-Electrolyte Beverages

Replacement of fluid lost during exercise with beverages containing carbohydrates and electrolytes has been shown to be beneficial for performance. Improvement in times for a 20-meter sprint and longer run times to fatigue were noted compared with placebo following intermittent high-intensity exercise when carbohydrate-electrolyte beverages were consumed during activity.[24] In the context of soccer, an increase in overall running distance and a 40 percent increase in the distance run at speed during the second half has been noted with carbohydrate-electrolyte beverages.[25]

For optimal performance, athletes should replace fluid lost from exercise with periodic consumption of carbohydrate-electrolyte beverages during activity. The optimal concentration of carbohydrate in these beverages is 5 to 7 percent because lower contents may not provide performance-enhancing benefits and larger percentages may cause abdominal discomfort secondary to more prolonged gastric emptying times.[25]

Chromium

Research does not support the claim that chromium supplementation improves performance. During high-intensity exercise, persons were not able to run longer when given a carbohydrate-electrolyte beverage containing chromium versus a carbohydrate-electrolyte beverage alone.[26] No increase in muscle strength was noted over a six-week period of supplementation.[27] However, these studies are limited by very small sample size.

The long-term effects of chromium supplementation have not been studied. Isolated cases of liver and renal dysfunction[54] and rhabdomyolysis[55] have been reported. Although use of chromium supplements is not currently regulated, physicians should advise athletes not to use them until research on long-term effects of supplementation has been conducted.

Creatine

A performance-enhancing effect of creatine supplementation has been demonstrated in certain contexts. In a meta-analysis of 16 controlled trials, creatine supplementation was found to increase maximal weight lifted by young men, but had no effect on women or persons older than 60 years.[28] Of note, studies were generally of low quality and may have overestimated the effect of creatine. A meta-analysis of 100 studies of varying designs found a performance benefit in the context of repetitive bursts of exercise lasting less than 30 seconds each, but no improvement in running or swimming ability.[29]

Adverse effects of short-term (three to five days) creatine supplementation include an increase in weight attributable to an increase in total body water.[56] A study of the effects of long-term (310 days) creatine supplementation in 175 persons revealed increased limb edema in the persons taking creatine at month two, but not thereafter, and demonstrated no increase in the occurrence of gastrointestinal discomfort, diarrhea, nausea, or renal dysfunction.[57] In younger, healthy persons, serum creatinine concentration is only minimally affected by creatine supplementation, but further studies of older persons and those with renal insufficiency are needed.[58]

Ephedrine and Pseudoephedrine

Although ephedrine and pseudoephedrine are classified as stimulants, they have different effects on performance. Ten-kilometer run time was decreased with ephedrine supplementation[30] and anaerobic performance was improved[31]; however, a meta-analysis of eight studies found insufficient evidence to support a performance benefit with ephedrine.[32] Crossover studies have failed to demonstrate an improvement in fatigue[33] or prolonged high-intensity cycling performance[34] with pseudoephedrine ingestion, but one small study did find a decrease in 1,500-meter running time.[35]

Serious adverse effects of these stimulants primarily involve the cardiovascular and central nervous systems. An analysis of 50 trials and 71 case reports of adverse events related to ephedrine reported a two- to threefold risk of psychiatric symptoms (e.g., agitation, anxiety, irritability), autonomic symptoms (e.g., tremor, insomnia), and heart palpitations.[32] Case studies of ephedrine report death, myocardial infarction, cerebrovascular accident, seizure, and psychosis.[32] Adverse effects of pseudoephedrine include nervousness, upset stomach, palpitations, and tremors.[59] The IOC[14] and NCAA[15] prohibit their use.

Human Growth Hormone

Popular over-the-counter supplements are often marketed as being able to increase endogenous levels of human growth hormone. However, human growth hormone is an injectable medication that is only available as a prescription. It has not been shown

to have a performance-enhancing effect. A recent systematic review of randomized controlled trials concluded that human growth hormone increases lean body mass, but has no beneficial effect on strength or exercise capacity in trained athletes.[36] Participants treated with growth hormone experienced higher rates of soft tissue edema, arthralgias, and carpal tunnel syndrome. One risk associated with the use of cadaveric-derived human growth hormone is Creutzfeldt-Jakob disease.[60] The IOC[14] and NCAA[15] prohibit the use of human growth hormone.

Iron

No performance benefit has been noted with iron supplementation in athletes who were not iron deficient. However, female athletes, distance runners, and vegetarians are often at risk of iron deficiency. A study of swimming performance during six months of training and iron supplementation in adolescents without iron deficiency failed to note a performance enhancement over placebo.[37]

A decrease in serum ferritin (a measure of iron status) without anemia commonly occurs in female athletes, but it has not been shown to negatively effect performance and usually can be corrected by careful dietary changes to increase iron intake.[38] Supplementation with iron in the context of iron deficiency without anemia was shown to be associated with improvements in muscle fatigability.[39] However, the study was limited by low power to detect a direct role of tissue iron status in the decreased fatigability.

Iron supplementation may result in hemochromatosis in susceptible persons, and it commonly causes constipation. In the context of deficiency or anemia, supplementation may be necessary, but only after nutritional consultation and dietary adjustments. Iron supplements are not prohibited by any sports governing agencies.

Sodium Bicarbonate

Supplementation with sodium bicarbonate appears to improve performance in certain contexts, but results of studies are conflicting. Following ingestion of sodium bicarbonate, a decrease in 1,500-meter race times has been noted.[40] Likewise, sodium bicarbonate improved performance during the second half of prolonged intermittent cycling.[41] However, in another study, no improvement was noted in 600-meter race times.[42]

There appear to be few adverse effects of sodium bicarbonate supplementation, with gastrointestinal distress (e.g., bloating, diarrhea) being the most prevalent.[61] The use of sodium bicarbonate is not currently prohibited by the IOC[14] or NCAA.[15]

Final Comments

The use of supplements for performance enhancement is widespread in athletes of all ages and levels of competition. One survey found that junior high school students who used anabolic steroids had less knowledge about the effects of steroids than students who did not.[62] Consequently, patients of all ages need to be counseled accurately on the effectiveness and safety of performance-enhancing supplements.

This article is one in a series on sports medicine created in collaboration with the American Medical Society for Sports Medicine. Coordinators of the series are Francis O'Connor, MD, Virginia Sports Medicine Institute, Fairfax, and Karl (Bert) Fields, MD, Moses Cone Family Physician Residency and Sports Medicine Fellowship, Greensboro, N.C.

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