

## ERGOGENIC DRUGS IN SPORTS

William D. Knopp, MD, Thomas W. Wang, MD,  
and Bernard R. Bach, Jr, MD

The use of pharmacologic agents to improve athletic performance, or "doping," has been reported as early as the third century BC.<sup>31</sup> "Doping" is described by the International Olympic Committee (IOC) as "the administration of or use by a competing athlete of any substance foreign to the body or any physiological substance taken in abnormal quantity or taken by an abnormal route of entry into the body with the sole intention of increasing in an artificial and unfair manner his/her performance in competition. When necessity demands medical treatment with any substance which because of its nature, dosage, or application is able to boost the athlete's performance in competition in an artificial and unfair manner, this too is regarded by the IOC as doping."<sup>51</sup>

Although there have been anecdotal reports of doping throughout history, it was not until the middle of the twentieth century that documentation of usage became more widespread. One of the reasons for this increased awareness of usage may be the fact that pharmacology has improved significantly. As more potent and effective drugs were developed, some athletes began to see the potential for artificially enhancing their own performance.

Legislation was prompted as rumors of ergogenic enhancement in sports increased. The IOC's Medical Commission was founded in 1967. One of their principal duties involved the investigation of possible drug

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From the MacNeal Hospital Family Practice Residency Program, Berwyn (WDK, TWW); and the Department of Orthopedic Surgery, and Sports Medicine Section, Rush Medical College, Rush Presbyterian-St. Luke's Medical Center, Chicago (BRB), Illinois

misuse by athletes. Official drug testing of athletes began with the 1968 Olympic games in Mexico City.<sup>31</sup>

Despite legislation and increased random testing, the use of pharmacologic agents has continued and actually increased. Reports now indicate that, even at the high school level, many athletes are using a variety of drugs to enhance performance.<sup>3</sup> These epidemiologic studies probably underassess the prevalence of drug use, given that their data are from self-reported questionnaires.

The goal of this article is to provide the practicing clinician with an account of the commonly used ergogenic substances used in doping by athletes. We will discuss these agents in the manner in which the IOC has developed their classification.

This article also focuses on doping classes and methods. Although the remaining topics are important, their ergogenic potential is limited. It should be noted that epitosterone has been used in the attempt to mask steroid use. Also, probenecid has been used to decrease renal excretion of banned substances. Local anesthetics, corticosteroids, and beta agonists may be used with certain limitations in some athletic events. The prescribing physician should be aware that restrictions exist and consult the appropriate organizing body.

## **DOPING CLASSES**

### **Stimulants**

Stimulants are used by athletes in the belief that they may reduce fatigue as well as increase alertness, response time, and strength. This category includes a variety of central nervous system stimulants as well as sympathomimetics.

#### *Amphetamines*

Amphetamines were first developed in 1920. Their vasoconstrictive properties were initially utilized for treatment of nasal congestion. The ergogenic qualities became more apparent during World War II, when amphetamines were commonly used by soldiers as a means of increasing alertness on patrol duty.<sup>31</sup> Although amphetamines are still commonly used today, studies have shown a decline in use between 1984 through 1988.<sup>52</sup>

Structurally, amphetamines are similar to endogenous catecholamines, such as epinephrine. Their mechanism of action is believed to be augmentation of neurotransmitter release, especially norepinephrine, thereby stimulating the sympathetic nervous system. Their peak effect

is usually noted in 1 to 2 hours.<sup>18</sup> Although there are conflicting reports as to whether athletic performance is enhanced by amphetamines, there may be a mild improvement in swimming or throwing sports, such as shot put.<sup>43</sup> There are also some reports of prolonging the time to exhaustion, but there is no effect on actual speed.<sup>9</sup>

In many studies, there does not appear to be an increase in overall capacity for aerobic activity, but there may be an increase in tolerance of strenuous exercise. The athlete may be able to prolong exercise time by blunting pain perception and the symptoms of fatigue and exhaustion. This decrease in ability to sense the body's limitations may lead to an increased incidence of heat injury. Amphetamines also increase aggression, increasing the potential for injury in contact sports.<sup>42</sup>

Side effects have included thermoregulatory difficulties, such as heatstroke. Neurologic symptoms include restlessness, tremor, irritability, insomnia, and increased aggressive behavior, as well as the potential for addiction. Cardiovascular effects include angina, dysrhythmias, headache, palpitations, changes in blood pressure, and changes in heart rate. Adverse gastrointestinal side effects include abdominal pain, vomiting, and decreased appetite. There have even been some reports of fatal ingestions with convulsions, coma, and cerebral hemorrhage.<sup>42</sup>

### *Caffeine*

Caffeine is a methylxanthine that occurs naturally in many species of plants, including coca, coffee beans, and tea leaves. It is also found in numerous cola drinks and chocolate. Caffeine acts through a variety of mechanisms. The most important central nervous system action is believed to result from its role as an adrenergic receptor antagonist. Other systemic effects may include increased muscle contractility from an increased permeability of the sarcoplasmic reticulum to calcium. Caffeine may also inhibit phosphodiesterases and potentiate the role of hormones as neurotransmitters.<sup>18</sup> Generally, caffeine will have an effect on the central nervous system at a concentration of 85 to 200 mg. At this point, it will decrease fatigue and improve the level of consciousness.<sup>31</sup> The ergogenic dose is believed to be between 250 and 350 mg.<sup>18</sup> The IOC considers a urine concentration of greater than 12  $\mu\text{g}/\text{mL}$  as consistent with doping. The National Collegiate Athletics Association's (NCAA) defined limit is 15  $\mu\text{g}/\text{mL}$ . As an example of the quantity of caffeine that this represents, an athlete would need to drink six to eight cups of coffee in one sitting and be tested within 2 to 3 hours to reach the required urine concentration.<sup>51</sup> Potentially, the amount of caffeine needed for the ergogenic benefits is far less than defined limits.

Studies with caffeine do not demonstrate an effect on large muscle groups in terms of strength and short-term performance; however, caf-

feine may improve endurance. In a study of nine cyclists, caffeine users were able to exercise 20% longer than in the control group. They also had significantly higher levels of plasma fatty acids and blood glycerol.<sup>11</sup> The theory is that caffeine increases lipolysis while sparing glycogen. Oxidation of fatty acids would then provide the initial energy source, leaving glycogen available for later use. Other studies have not reached the same conclusions.<sup>20</sup>

Side effects include anxiety, irritability, restlessness, tremor, headaches, insomnia, diuresis, gastrointestinal disturbances, and tachycardia. These effects may occur after just a few cups. If used to excess, caffeine can be lethal at a dose of 3 to 10 g, causing seizures, tachycardia, or ventricular dysrhythmias.<sup>18</sup>

### *Clenbuterol*

Clenbuterol is a  $\beta_2$  agonist used in Mexico and some European countries as a bronchodilator, and it is available in both oral and aerosolized forms. The FDA has not approved its use in the United States. Clenbuterol came to public awareness at the 1992 Summer Olympics in Barcelona when an American hammer thrower, Jud Logan, and shot-putter, Bonnie Dasse, were disqualified after testing positive for this substance. This drug has been studied extensively in laboratory animals and livestock as a repartitioning agent.<sup>30</sup> Reeds et al<sup>36</sup> demonstrated that young rats fed clenbuterol showed an increase in the protein and RNA in skeletal and cardiac muscle, as well as a reduction in fat deposition and an increase in energy expenditure. Similar studies have been reported in livestock that support these results. Athletes have extrapolated the results of these studies in hope of gaining the anabolic as well as fat-reducing qualities of this and other  $\beta_2$  agonists.<sup>33</sup> Di Pasquale<sup>13</sup> states that if it does have an anabolic effect, relative to steroids it is weak. DiPasquale<sup>13</sup> estimates that up to a third of elite athletes have tried this drug.

The mechanism of action has not been completely elucidated. Clenbuterol has been shown to cause skeletal and cardiac muscle hypertrophy, but not hyperplasia,<sup>16</sup> even in denervated muscle.<sup>59</sup> This occurs by suppression of both muscle synthesis and to a lesser degree muscle degradation, with the net result being muscle hypertrophy.<sup>35</sup> Clenbuterol directly stimulates lipolysis as well.<sup>30</sup> As a result of its lipolytic activity, it is currently being studied for use in obesity.<sup>49</sup> Clenbuterol also causes sympathetic stimulation of  $\beta_2$  receptors, causing peripheral and central effects similar to those of other  $\beta_2$  agonists. Athletes generally use the oral form of this drug at a starting dose of twice that used in the treatment of bronchospasm (0.0172 mg/kg).<sup>33</sup> Animal studies used doses of 0.33 to 2.0 mg/kg. Owing to rapid downregulation of receptors,

