



Drug Abuse in Sports

Introduction

Misuse of drugs by athletes to enhance performance has gained much attention in the past years. Stimulants, anabolic-androgenic steroids, erythropoietin (EPO) and other performance enhancing (ergogenic) substances are used by athletes to increase their competitive edge. Drug education and testing programs to eliminate the use of performance-enhancing drugs in sports have been initiated by amateur and professional sports authorities. The World Anti Doping Agency (WADA) and the US counterpart, USADA, coordinate and promote the fight against doping. On an international level, WADA interfaces with the International Olympic committee (IOC), the International Sports Federation (IF), the National Olympic committee and the athletes.

In the United States, mandatory drug testing programs were initiated in 1985 by the USOC and in 1986 by the NCAA. Drug testing and education programs in both organizations include confidentiality, informed consent, chain-of-custody of specimens and accurate laboratory testing. Drug testing programs have reduced the use of performance enhancing (ergogenic) substances in amateur sports and have received support from athletes, trainers, coaches and the general public.

Table 1 lists the major categories of substances banned by the IOC, USOC and the NCAA. Additional substances are banned for specific sports. The purpose of this article is to describe the most common substances abused by athletes, the reason for their abuse and the adverse effects associated with these agents.

Stimulants

The term stimulant applies to prescription, non-prescription and dietary supplements that produce both psychological and physical stimulation. Amphetamines have been shown to increase athletic performance in strength exercises (3-4%) and endurance (1.5%) in a dose of 14 mg/70kg body weight. Ephedrine (75-150 mg) has been shown to enhance athletic performance to the same degree as amphetamine (15-30 mg). In addition, amphetamines can increase alertness and aggressiveness and reduce fatigue. The downside of amphetamine use includes: insomnia, impaired decision making, increased potential for dehydration, anxiety, and tremor.

Adverse effects from central nervous system stimulants include headaches, anxiety, confusion and restlessness. Amphetamines and ephedrine also stimulate both alpha and beta adrenergic receptors leading to hypertension and tachyarrhythmias. Phenylpropanolamine when used alone primarily stimulates alpha adrenergic receptors leading to hypertension and reflex bradycardia. Regular use of amphetamines and related agents

Table 1
IOC/USOC Banned Substances

Prohibited Classes of Substances	IOC/USOC	NCAA
Stimulants	Prescription Illicit Non-prescription* Beta-2-agonists Strychnine	Prescription Illicit Non-prescription
Narcotics	All but codeine, dextromethorphan, dihydrocodeine, diphenoxylate, propoxyphene, tramadol	Permitted
Anabolic agents	Anabolic steroids Beta-2-agonists	Anabolic steroids Clenbuterol
Diuretics	All	All
Peptide Hormones, mimetics and analogues (and all releasing factors)	HCG, growth hormone, insulin, erythropoietin Gonadotropins, corticotropin and related substances	HCG, corticotropin, growth hormone and related releasing factors, erythropoietin, sermorelin
Street drugs	Cannabinoids	Heroin, THC

can precipitate withdrawal symptoms upon discontinuation. Tolerance develops after chronic use requiring higher doses to achieve the same effect. Long-term effects of amphetamines include malnutrition, and psychiatric disturbances.

Ephedrine is available without a prescription. It has been used as a precursor for the manufacture of methamphetamine resulting in restrictions for purchase in some states. Ephedrine, commonly used to treat nasal congestion, has a thermogenic (heat producing and weight loss) effect on the body at low doses. Ma Huang, found in many dietary supplements, is an herbal preparation that contains ephedra.

Phenylpropanolamine is a non-prescription sympathomimetic agent that was commonly used for weight loss. The FDA recently requested all manufacturers to discontinue marketing products containing phenylpropanolamine because of the potential for serious adverse effects, such as stroke.

Caffeine is a central nervous system stimulant. In addition, it has a diuretic effect that may worsen dehydration in hot conditions. Some products combine aspirin and caffeine, which theoretically enhances thermogenesis. Caffeine can also be a constituent in herbal products such as guarana. Acceptable urine caffeine concentrations are set by the individual sport

federations. Athletes are monitored and must control their caffeine intake to ideally achieve urinary concentrations of below 12mcg/ml. About 500-mg of caffeine ingested within 1 hour would approximate this urine concentration in a normal healthy adult male. One cup of regular coffee contains about 100-mg of caffeine that can produce a urine concentration of 1.5mcg/ml in 2-3 hours.

Narcotics

All narcotic analgesics except codeine and dihydrocodeine are banned by the IOC/USOC. Heroin (diacetylmorphine), is also included on the list of banned substances. Narcotics have no ergogenic properties. Potential benefits to athletes from narcotics included euphoria and increased pain threshold. The downside of narcotic use includes false feeling of invincibility, illusions of athletic prowess beyond an athletes inherent ability, failure to recognize injury, and physical and psychological dependence.

Anabolic-androgenic Agents

Anabolic-androgenic agents include both anabolic-androgenic steroids and beta-2-agonists. Anabolic-androgenic steroids are the most widely detected performance enhancing drugs in sports. Anabolic-androgenic steroids include; androstenediol, androstenedione, danazol, DHEA, nandrolone, oxandrolone, stanozolol and testosterone. The Canadian sprinter Ben Johnson was disqualified for life from the Olympics after he tested positive for anabolic-androgenic steroids for the second time in January 1993.

Testosterone and its synthetic derivatives have a core 17-carbon steroid chemical structure that gives them androgenic (masculinizing) as well as anabolic (protein building) properties. There is currently about 40 steroid-related products available world-wide. The mechanism of action of anabolic-androgenic steroids is to increase protein synthesis, lean body mass and nitrogen balance when administered under the correct conditions.

Anabolic-androgenic steroids facilitate protein synthesis through a series of complex reactions that are not well understood. Steroid hormones affect lean body mass by preventing protein breakdown in the muscles and maintaining the muscle mass. Anabolic-androgenic steroids promote nitrogen retention by shifting the nitrogen equilibrium resulting in better utilization of ingested proteins. However, this shift in equilibrium is only temporary. In order to increase lean body mass with concurrent use of steroids, individuals must have a dietary intake of up to 10,000 calories daily (mostly in terms of protein) and must maintain a rigorous weight-training program. Anabolic-androgenic steroids must be taken in doses of 10 to 100 times the therapeutic doses to produce ergogenic effects. Adverse effects are common at these doses.

The most common adverse effects associated with chronic use of anabolic-androgenic steroids include acne, sodium and water

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UPCC Update

The events of September 11, 2001 and subsequent anthrax exposures have brought forth the reality that the next terrorist attack is a matter of when it will occur, rather than if it will occur. Planning and preparing for an attack using a weapon of mass destruction (WMD) has been ongoing in our community. The UPCC has been actively involved in this process. The UPCC is represented on a number of state and local committees involved in planning and preparing for a WMD event. These include: the Chemical Stockpile Emergency Preparedness Program, Domestic Preparedness Health and Medical Working Group, and Health Alert Network that are coordinated through state agencies and the Metropolitan Medical Response System and the Terrorism Working group coordinated on a local level. The UPCC participates not only in the planning process but has actively participated in regular full-scale exercises to test its own internal capabilities to respond to a large scale incident.

The UPCC role in an actual WMD event is quite varied. For the public, the UPCC's role is to evaluate the callers situation and to make recommendations for treatment in place or referral depending on signs and symptoms, past medical history of individual, and location of individual. Decisions are based on the experience of the specialists in poison information, clinical and medical toxicologists on staff and with credible risk information from emergency response personnel at the scene. In many cases the person calling may not have been exposed. In this situation, the UPCC's role is to provide information to the caller and to try and reduce fears as much as possible to reduce mass hysteria and unnecessary self-referrals to area hospitals or the 911 system.

The UPCC's role with health professionals is to provide information, consultation and to assist in epidemiologic data collection. The UPCC has a high-speed facsimile that can disseminate information quickly to all of the acute-care hospitals in the state. The UPCC will use this system in a WMD event to communicate technical information to area hospitals. In some cases it may be information generated by the UPCC, in other cases the UPCC may be transmitting information from other public health agencies. In a chemical event, the UPCC staff are available to consult on the clinical toxicology of the agents and available treatment. The UPCC will also be working with area hospitals to help identify the number of patients in the health care system to report to the proper public health agencies.

The UPCC's role with emergency responders and for public health personnel is also multifaceted. The UPCC staff are available 24-hours a day to provide technical information. The UPCC staff are available to disseminate information from public health officials or emergency responders to other health professionals, the public and the media.

The UPCC has been actively involved in planning and preparing for a release of a chemical weapon since the start of the CSEPP program in 1990. As an active member of this program, the UPCC has been able to build strong relationships throughout the state. The UPCC has numerous resources on the issues associated with weapons involving chemical, biological and nuclear agents. We hope you will consider calling the UPCC with any questions involving WMD. Finally, the UPCC has a unique opportunity to potentially identify trends in the community through our surveillance system. The UPCC is in a unique position to provide sentinel event monitoring in the event a WMD is released in our community.

retention, and aggressive behavior. Hepatotoxicity due to steroids is usually reversible upon discontinuation of the drug. An elevation of transaminases without associated symptoms is the most common hepatic manifestation of anabolic- androgenic steroids. Prolonged use can lead to cholestasis, jaundice, peliosis hepatitis, hepatic tumors, and bleeding. A direct causal relationship has not been well defined due to lack of controlled epidemiologic studies.

Anabolic-androgenic steroids inhibit the release of gonadotropins from the pituitary gland, causing menstrual irregularities in women, inappropriate hair growth (hirsutism), deepening of the voice, and clitoral hypertrophy. These changes may be irreversible. Acne and changes in libido are seen in both sexes. In males, prolonged use causes a feedback inhibition of testosterone production from the testicles and suppression of the hypothalamic-pituitary-testicular axis resulting in suppression of spermatogenesis. Gynecomastia, prostate enlargement leading to urinary obstruction, testicular atrophy, decreased sperm counts and impotence occurs. Anabolic-androgenic steroids cause an increase in LDL and a decrease in HDL. This increases the risk for myocardial infarction and coronary heart disease. Extreme increases in blood pressure can occur suddenly. There are also several reports of strokes, pulmonary embolism, heart attacks and coronary artery thrombosis.

The use of anabolic-androgenic steroids results in stronger muscles but stiffer tendons that can lead to potential damage to the joints, muscle ruptures and strains. In growing teenagers, anabolic steroids cause premature closure of the growth plates, limiting their growth potential. Habituation is also postulated to be a problem for many steroid users and legally, most injectable steroids are in the controlled substance category.

Testing for anabolic-androgenic steroids can be a challenge. Athletes may exclusively use testosterone cypionate or other similar testosterone salts that cannot be differentiated by drug tests from natural testosterone in the body. However, the USOC and NCAA have devised methods by which they can indirectly detect these substances by evaluating the urine testosterone: epitestosterone (T:E) ratio. In addition, some precursors of the anabolic-androgenic steroids, such as androstenedione, are also banned substances even though they are not controlled by the

Kava Update

Kava, a dietary supplement, was reviewed in Utox Update, Volume 3, Number 3 in the Fall 2001. Since that report approximately 25 cases of hepatic toxicity associated with the use of kava have been reported from Europe. This includes hepatitis, cirrhosis and liver failure. Switzerland and Germany have proposed banning the sale of kava containing products. If you are aware of any cases of hepatotoxicity associated with the use of kava we encourage you to report them to the Utah Poison Control Center (1800-222-1222) or to FDA's MedWatch program (1800-332-1088).

drug enforcement agency. These precursors are commonly found in dietary supplements which are readily available in retail stores and heavily marketed. There are strict legal implications for the use of steroids by athletes and various enforcement, education and counseling programs are in place to deal with this misuse of anabolic agents.

Beta-2 Agonists

Beta-2 agonists have both stimulant effects and potential anabolic effects. Athletes with consistently high beta-2 agonist blood concentrations have demonstrated anabolic effects. For this reason, these oral and injectable forms of beta-2-agonists are banned by the USOC/IOC.

Diuretics

Diuretics are abused for two primary reasons: to quickly lose weight and to reduce the concentration of other banned substances. Potential deleterious effects include electrolyte imbalances, muscle cramps, dehydration and volume depletion.

Peptide Hormones, analogues, and compounds that mimic the effect of peptide hormones

Substances included:

- Chorionic Gonadotropin (hCG). Prohibited in males only.
- Pituitary and synthetic gonadotropins (LH). Prohibited in males only.
- Corticotropins (ACTH)
- Growth hormone (GH)
- Insulin-like Growth Factor (IGF-1)
- Erythropoietin (EPO)
- Insulin (Allowed only to treat certified insulin-dependent diabetes. Written notice is necessary.)

Athletes abuse GH to increase height and to enhance muscle mass. It can result in acromegaly, gigantism, metabolic and endocrine disorders. Corticotropins mimic the body's natural steroids (cortisol), and act to relieve pain and inflammation and create a sense of physical well-being. Potential deleterious effects of ACTH include the suppression of the body's immune system, which increases the risk for infection. Erythropoietin (EPO) is a peptide hormone naturally produced by the kidneys. It stimulates bone marrow to increase the number of red blood cells. This is clinically useful in patients with anemia of chronic disease and in cases where the kidney fails to produce EPO. EPO can increase endurance by increasing the oxygen carrying capacity of the blood. Excessive use of EPO leads to increased hematocrit and hypertension. Potentially life-threatening thrombosis has occurred in the setting of dehydration and elevated hematocrit.

Meet the UPCC Staff



John Stromness

John has been with the Utah Poison Control Center since December 1998. Prior to that he was the pharmacy supervisor at the VA Medical Center. He is married with 3 daughters, a golden retriever and a cat. John graduated from high school in Pittsburgh, PA and then joined the Air Force. He spent 9 years in the Air Force as a flight engineer flying C-

141's hauling Military cargo worldwide. After that he went to the University of Utah College of Pharmacy where he graduated with a Bachelors Degree in Pharmacy in 1982. **Favorite Poisons:** Aspirin and Jimson Weed (*Datura Stramonium*). **Hobbies:** Hiking, travel, reading and listening to jazz music.

Utah Poison Control Center Staff

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Associate Medical Director

Douglas E. Rollins, MD, PhD

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Outreach Education Provider

Heather Foulger, MS, CHES

UTOX Editors

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Barbara Insley Crouch, PharmD,

MSPH

Editorial Review Panel

Bradley D. Dahl, PharmD, RPh, CSPI*

Jennifer Grover, PharmD, RPh, CSPI*

Heather M. Foulger, MS, CHES

Please send comments and suggestions for future articles to the editor of UTOX Update at:

410 Chipeta Way, Suite 230

Salt Lake City, Utah 84108

Or e-mail at

barbara.crouch@hsc.utah.edu or

martin.caravati@hsc.utah.edu

*CSPI denotes Certified Specialist in Poison Information.

Other Prohibited Substances

The USOC and other sports federations have additional classes of substances that are prohibited in certain circumstances. For example, the USOC and IOC ban beta adrenergic blocking agents in athletes who compete in the biathlon. Ethanol, cannabinoids and local anesthetics are banned in certain circumstances. In addition to banned substances, there are also prohibited doping methods such as blood doping, use of plasma expanders or the use of substances to mask other banned substances.

Summary

It is unlikely that athletes will stop using drugs or doping methods to try and gain a competitive edge. Drug testing programs have been established by amateur and professional sports authorities to promote a safe and fair competitive environment. Clinicians who treat athletes should be familiar with the commonly abused substances and doping methods.

Urvi Pandya, PharmD Student

References

www.ncaa.org. Website of the National Collegiate Athletic Organization

www.wada-ama.org. Website of the World Anti Doping Agency

www.usantidoping.org. Website of the US Anti Doping Agency

Fuentes RJ, Rosenberg JM, Davis A. Glaxo Wellcome Athletic Drug Reference '96. Durham, NC: Clean Data Inc;1996.

Shahidi NT. A review of the chemistry, biological action, and clinical applications of anabolic-androgenic steroids. Clin Ther. 2001;23:1355-1390.

Chyka PA. Androgenic-Anabolic Steroids. In: Ford MD, Delaney KA, Ling LJ Erickson T, eds. Clinical Toxicology. Philadelphia, PA:WB Saunders Company; 2001:595-601.

Nationwide Toll-Free Number

The new national toll-free number 1-800-222-1222 was announced at a news conference held January 31, 2002 at Bright Horizons Day Care Center located at the University of Utah. Calling this number anywhere in the US will connect you with the poison control center for that area. The UPCC hotline can be accessed by this number when calling from within the state. Our other number remains operational.

Utah Poison Control Center

410 Chipeta Way, Suite 230

Salt Lake City, UT 84108

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