



Contents lists available at ScienceDirect

Molecular and Cellular Endocrinology

journal homepage: www.elsevier.com/locate/mce

Detection of anabolic androgenic steroid use by elite athletes and by members of the general public

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ARTICLE INFO

Article history:

Received 20 September 2017

Accepted 20 September 2017

Available online xxx

Keywords:

Anabolic androgenic steroids

Testosterone

Sex steroids

Anti-doping

Biological passport

ABSTRACT

Because national and international sports competitions are sources of community pride and financial revenue, there have been great efforts to prevent and detect the use of performance-enhancing drugs such as anabolic androgenic steroids by elite athletes. The World Anti-Doping Agency and its national affiliate anti-doping agencies have created sophisticated monitoring systems and advanced testing techniques to detect the use of banned substances including anabolic androgenic steroids by participants in international and national athletic competitions. The creation of a longitudinal monitoring program known as the biological passport is a recent, important development in the efforts to prevent and detect the use of banned performance-enhancing drugs and methods. The biological passport program consists of the measurement of urinary and blood markers of anabolic androgenic steroid use (and other banned drugs or methods) at baseline and at random times. A panel of experts reviews the longitudinal data and interprets the likelihood of the use of banned drugs and methods. These advances in anti-doping appear to be highly effective, but some athletes persist in their efforts to cheat the detection process.

In addition, some members of the general public use anabolic androgenic steroids for a variety of reasons including to improve physical appearance or to enhance performance in athletics. Clinicians must depend on clinical acumen and the measurement of serum testosterone and gonadotropins to guide them in making a tentative diagnosis of anabolic androgenic steroid use. Definitive diagnosis requires that the patient disclose the use of the drugs.

Because anabolic androgenic steroids are effective for improving certain aspects of physical performance, some elite athletes (and members of the general public) will continue to use these drugs. Effective efforts to curtail the use of these drugs will require decreasing the ease of access to them, continued advancements in laboratory techniques, and perhaps a shift in societal approbation for athletic performance and muscular appearance.

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1. Introduction

Detection of unapproved use of anabolic androgenic steroids (AAS) is important in competitive sports where the governing agencies have opted to ban the use of these agents or to restrict the use of such drugs to specific, approved clinical scenarios through a process known as “therapeutic use exemption”. The rationale for restriction of the use of AAS is to prevent male and female athletes from achieving a competitive advantage via the performance-enhancing effects of AAS. In clinical practice, detection of AAS use is also important primarily when clinicians are evaluating men for management of side effects of AAS such as infertility. Because AAS remain readily available through non-prescription sources, clinicians also need to recognize and manage the use of AAS in men who are not elite athletes, but who are using AAS to increase musculature, improve performance in community athletic events or for non-evidence-based indications including improved sexual function or longevity (see [Table 1](#)).

In this review, I focus on the World Anti-Doping Association (WADA) process of screening and detection of the use of AAS or pharmacological agents that increase endogenous androgens. This WADA process is the basis for regulation of AAS use in many international athletic competitions including the Olympic games. Governing bodies of international and national sports athletics that wish to regulate the use of AAS in their sport generally agree to follow the WADA guidelines although they may apply internal rules about the frequency and type of monitoring. I will also discuss a pragmatic approach to the detection of AAS use in clinical practice.

The barriers to detection of AAS use are formidable for several reasons. First, there is significant variation in normal production and metabolism of sex steroid hormones in humans as well as a range of sensitivity to circulating sex steroid hormones. These natural variations lead to a broad range of circulating sex hormone concentrations in genotypic men and women with normal, congruent phenotypes and the establishment of normal ranges of serum hormone concentrations that are based on the statistics of normal distributions in populations and not on the physiology of an individual. Distinguishing between an athlete with naturally high

testosterone concentrations and an athlete using testosterone or testosterone precursor supplements is difficult. Second, measurement of AAS in blood and urine samples must be accurate and precise (i.e., measure AAS analytes correctly and reproducibly). There have been technological advancements that have dramatically improved the measurement of AAS, but there remain challenges, particularly as the development of novel, designer AAS advances rapidly. Third, collection of the biological sample for analysis must be done in a manner that reflects the individual's physiology. Collection of such biological samples is often inconvenient (e.g., early morning blood sample), invasive to privacy (e.g., witnessed urine collections to prevent substitution of a different urine sample) and costly (due to costs of locating, traveling to and collecting specimen athlete for random testing). Fourth, to avoid the possibility of tampering, the biological samples must be kept secure at every step of the process after collection: transportation, processing, testing and storage.

Finally, there are sociological barriers to creating effective screening and identification of AAS use in elite athletes. These barriers include extraordinary personal incentives for elite athletes to use AAS; a centimeter or a few milliseconds mean the difference between gold and adulation or ignominy. Many elite athletes who have spent years training will do almost anything to win. A survey of 212 participants in a Canadian national track meet demonstrated that greater than 5% of participants would take a legal performance-enhancing drug that would result in death within 5 years if the drug would guarantee an Olympic gold medal ([Connor et al., 2013](#)). In addition, greater than 10% of these elite athletes would take an illegal, but undetectable, performance-enhancing drug if the drug would guarantee an Olympic gold medal. With the personal stakes so high, athletes will attempt to cheat detection of AAS use with a variety of methods such as the following: 1) use of AAS with drugs that interfere with metabolism of AAS (e.g., known or novel aromatase inhibitors or 5- α reductase inhibitors) ([Ventura and Segura, 2010](#)); 2) use of AAS with diuretics or probenecid to lower urinary concentrations (by dilution or decreased excretion of acidic AAS conjugates respectively); 3) use of designer AAS that are not currently detectable; 4) discontinuous use of AAS with very

Table 1

Commonly used exogenous anabolic androgenic steroids and drugs that increase endogenous anabolic androgenic steroids.

Anabolic Androgenic Steroids (AAS)	Drugs that increase endogenous AAS
<u>Designer AAS</u>	<u>Gonadotropins</u>
Bolandiol	Human chorionic gonadotropin
Clostebol	Recombinant human luteinizing hormone
Danazol	
Drostanolol	<u>Aromatase inhibitors</u>
Dehydrochloromethyltestosterone	Aminoglutethimide
Gestrinone	Anastrozole
Metandienone	Exemestane
Metenolone	Formestane
Oxandrolone	Letrozole
Stanozol	Testolactone
Tetrahydrogestrinone	
Trenbolone	
<u>Endogenous AAS used as drugs</u>	<u>Selective estrogen receptor modulators</u>
Dihydrotestosterone	Clomiphene
Boldenone	Raloxifene
Nandrolone	Tamoxifene
Testosterone	Toremifene
	<u>Endogenous AAS precursors</u>
	Androstenedione
	Androsterone
	Boldione
	Dehydroepiandrosterone

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