Drug misuse in modern sport:
Are cheats still winning?

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Introduction

One sultry summer's day in Seoul on the occasion of the 1988 Olympic Games, the stadium rose to the performance of Canadian sprinter Ben Johnson, the fastest self-propelled man in the world. Few imagined that a monumental drug scandal was about to break. Overnight, Johnson, Olympic champion and hero of the hour, suddenly became the shame of sport when stanozolol, a prohibited anabolic androgenic steroid was detected in his urine. His coach and personal physician had simply underestimated the sensitivity of the Seoul laboratory and Johnson's misdemeanor confirmed that athletes in pursuit of kudos and huge sums of money were prepared to cheat. His gold medal returned, Johnson trundled ignominiously back to Canada to be greeted by a national inquiry into drug misuse in sport. Aspersions were subsequently cast upon a number of international performers, including Carl Lewis who had assumed Johnson's Olympic mantel.

Previously, in the 1970s, it had been the scientists of the former German Democratic Republic who orchestrated the use of performance enhancing drugs for female athletes, converting them into husky hirsute world-beaters.[1] Then in the early 1990s, China, a relative newcomer to international sport, employed similar tactics. In over 30 cases, Chinese swimmers and coaches were disciplined for the use of androgenic anabolic agents and other 'masking' substances.[2] And at the 1996 Atlanta Olympics, muscle-bound Irish swimmer Michelle Smith-de Bruin became the darling of the pool by unexpectedly winning three gold medals. Two years later she was banned from sport for the wilful contamination of an out-of-competition urine sample in an effort to avoid drug detection. Ironically her husband–coach was also a convicted, field events steroid abuser. This fuelled speculation that her sudden rise to international fame had been drug-assisted and, together with the scandals of the Tour de France,[2] conveyed the public perception that the drug cheats were winning. Since 1968, when the International Olympic Committee (IOC) implemented rudimentary drug testing at the Mexico City Olympics, some athletes, coaches and their advisors were still prepared to win at any cost.[2,3]

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Over the past decade, a need for consistent standards and stringent testing protocols spawned the formation of the World Anti-Doping Agency (WADA)[4,5,6] This accord between international sporting federations, the IOC and governmental agencies has assumed responsibility for publishing lists of banned drugs,[7] setting standards for laboratory accreditation, promoting athlete and coach education, considering thresholds for therapeutic exemption to use prohibited substances[8] and harmonising sanctions. WADA, from its Montreal base, is headed by a New Zealand lawyer and backed by strong political allegiances. National anti-doping agencies like the New Zealand Sports Drug Agency (NZSDA) are signatories to an international Code that binds sporting nations to consistent standards for testing athletes worldwide.[4] The NZSDA is funded by the New Zealand Government, governed by an Act of Parliament and overseen by a dedicated core of fulltime staff and a Board appointed by the Minister. Each year the NZSDA conducts approximately 1500 drug tests in and out of competition.

But 2004 was notable for two reasons. First was the revelation that an undetectable 'designer' steroid had been manufactured specifically for

use by athletes. By manipulating the androgenic steroid gestrinone, chemists at the BALCO Laboratory in San Francisco produced tetrahydrogestrinone (THG) used with impunity by a number of profiled USA track stars until a tip-off to the WADA-accredited laboratory in Los Angeles raised the alarm. Within months the laboratory had confirmed a reliable urine-based test for THG and several prominent athletes ducked for cover prior to the Olympics. This was the first time a drug without clinical application had been designed solely to enhance sports performance. And then, despite publicity, a record 24 sanctions were issued against athletes at the Athens Olympics for various drug-related misdemeanors.

The science of drugs in sport

To have the potential for misuse in sports, a drug must first possess an ergogenic potential. Among the more popular classes of misused drugs are anabolic androgenic steroids (AAS) and glycoproteins.

Anabolic androgenic steroids (AAS)

In the case of AAS the potential for ergogenesis is very easy to understand.[9,10,11] These agents are modelled on testosterone and have gained notoriety in weight lifting, bodybuilding, power lifting and field events where dosage regimes are reported to be as high as 10 to 100 times the accepted therapeutic range.[11] They may be injected in the form of testosterone esters in an oily base that reduces its rate of absorption, or they may be taken orally as 17-alpha-alkyl substituted derivatives of testosterone.

Power and 'strength-event' athletes have been known to consume combinations of anabolic agents simultaneously – a process known as stacking, or to gradually increase doses over a number of weeks (pyramiding). The desired side effects are increased muscle bulk, improved strength and heightened competitiveness with associated aggression.[3,9] However, these drugs are not without significant systemic side effects that implicate the endocrine, hepatic, vascular, dermatological and musculoskeletal systems as well as the psychological state of the athlete.[9,10,11]

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Glycoproteins

Amongst the group of banned glycoproteins are Luteinising Hormone (LH), Human Chorionic Gonadotrophin (hCG), Growth Hormone (hGH), Erythropoietin (EPO) Insulin-like Growth Factor (IGF-1), Mechano Growth Factors (MGF), insulin and corticotrophins. Frequently these agents are used simultaneously with other anabolic agents. The action of hCG is similar to LH in stimulating testosterone production. Epitestosterone levels are also increased by the use of hCG and this is helpful in masking the exogenous use of testosterone, which is reflected in an elevated testosterone/epitestosterone (T/E) ratio. A T/E ratio greater than 4:1 in urine requires further investigation to determine whether this is due to a physiological or pathological condition.

hGH enhances protein synthesis – a fact not lost on the sporting community already alert to the fact that a reliable test for this agent has only just been developed. And now that biosynthetic forms of hGH are available, the underground market in cadaver pituitary glands has evaporated. Anecdotal reports of Creutzfeldt-Jakob Disease associated with supplies of human pituitary hormone did not diminish the popularity of hGH.[3]

When exposed to hypoxic stimuli, the renal production of EPO increases dramatically. High altitude, and significant blood loss from trauma or surgery are such stimuli. Put simply, increased erythropoiesis infers an additional oxygen transport mechanism that translates into enhancement of aerobic sporting performance.[12,13] Some authorities place this improvement at between 10 and 15%. Recombinant DNA technology has made EPO readily available to wealthy professional athletes with improved performances that apparently justify its continued use. But the limiting effect of increasing the haematocrit is the relationship between blood viscosity and catastrophic thrombo-occlusive events that have been reported in Dutch and Belgium cyclists.[2]

Athletes carded for national and international representation represent a unique patient base with specific requirements for doping control

The list of banned drugs in sport

Every doctor has a professional responsibility to provide accurate information on banned drugs to any inquiring athlete. Athletes carded for national and international representation represent a unique patient base with specific requirements for doping control. It behoves every sports doctor to become fully cognisant with the WADA list of banned substances and the special requirements for therapeutic use exemption.[4] Reputations and livelihoods may depend upon accurate medical advice. This information is readily available from the MIMS New Ethicals Drugs Catalogue[14] containing the current list of banned substances and the New Zealand Sports Drug Agency (NZSDA) that provides a confidential drug information hotline (0800 378 437) and an informative website.[15] Athletes tempted by rich financial and social gains are prime targets for drug misuse or nutritional supplementation of dubious scientific validity and often

contaminated with banned substances or their precursors.[16,17]

WADA publishes the definitive list of banned substances annually and all relevant information may be found on its website.[18] Of recent bioethical interest has been the specific inclusion of gene doping, a matter beyond the scope of this review.[19] WADA also accredits laboratories permitted to analyse urine and blood samples from athletes.[4] Our nearest accredited laboratory is the Australian Government Analytical Laboratory in Sydney. Gas chromatography and high-resolution mass spectrometry are the analytical tools used to assess anonymous samples. Given the increasing legal grounds for contesting the outcome of analyses, the testing protocol has been closely scrutinised.

Substances on the banned list meet two of the following three criteria:

1. A proven potential to enhance athletic performance;
2. A potential danger to health;
3. Contravention of the 'spirit of sport'.

A summary of prohibited substances and methods

A. The following substances are prohibited at all times[7]

S1. Anabolic agents

All exogenous and endogenous anabolic androgenic steroids are included in this category. So too are other anabolic agents such as clenbuterol.

S2. Hormones and related substances

This group includes peptides hormones, EPO, hCG, hGH and LH.

Note that insulin is prohibited without a standard Therapeutic Use Exemption (TUE).

S3. Beta-2 agonists

Formoterol, salbutamol, salmeterol and terbutaline are permitted only by inhalation and with an accompanying abbreviated TUE. *All other beta-2 agonists are prohibited.*

S4. Agents with anti-oestrogenic activity

Aromatase inhibitors, clomiphene, cyclofenil and tamoxifen are all prohibited.

S5. Diuretics and other masking agents

All diuretics and agents such as probenecid, plasma expanding agents and finasteride (*Propecia*) are prohibited.

B. The following methods are prohibited at all times

M1. Enhancement of oxygen transfer.

This is includes 'blood doping' (autologous or homologous transfusion of blood).

M2. Chemical and physical manipulation.

This includes altering the integrity or validity of urine samples through intravenous infusions, catheterisation and urine substitution.

M3. Gene doping.

Including the non-therapeutic use of cells, genes, genetic elements or the modulation of gene expression to enhance athletic performance.

C. The following substances and methods are prohibited in competition only. They include all the above categories plus:

S6. Stimulants

All sympathomimetic agents are prohibited. *Note that pseudoephedrine and caffeine are no longer prohibited.*

S7. Narcotics

All major narcotic analgesics are prohibited (refer to the MIMS catalogue for a complete list)

Note that codeine, dextromethorphan, dextropropoxyphene, dihydrocodeine, diphenoxylate, phlcodine, propoxyphene and tramadol are permitted.

S8. Cannabinoids

S9. Glucocorticosteroids

All glucocorticosteroids are prohibited when administered orally, rectally, intravenously or intramuscularly. Their clinical use requires an abbreviated TUE.

Note that all other routes of glucocorticosteroid administration including dermatological application are permitted.

Therapeutic use exemption (TUE)

The World Anti-Doping Code makes specific provision for athletes and their physicians to apply for special dispensation to use banned substances for strict therapeutic purposes.[8] This provision is, however, governed by strict criteria and subject to the scrutiny of a committee of clinicians who consider each application on the evidence presented. Each application for TUE must be accompanied by specialist confirmation on the appropriate form. In New Zealand a committee of three experienced sports clinicians considers all applications for TUE submitted to the NZSDA.[15]

There are two types of TUE

(a) The Abbreviated TUE, required for inhaled beta-2 agonists and non-systemic glucocorticosteroids. Dermatological preparations of glucocorticosteroids do not require a TUE.

(b) The Standard TUE that must be used for all other prohibited substances. Common examples include insulin, methylphenidate (Ritalin) and oral or intramuscular glucocorticosteroids.

TUE is only granted in exceptional cases and the main criteria include:

1. An application submitted no less than 21 days before participation in an event.
2. Evidence that the athlete would experience significant impair-

ment to health if the prohibited substance was withheld.
3. Evidence that the use of the prohibited substance would produce no additional enhancement of performance other than that expected by the return to normal health following legitimate treatment.
4. The unavailability of any reasonable therapeutic alternative from the permitted list.

A retrospective TUE will only be granted in cases where emergency treatment or treatment of an acute medical condition has been necessary or due to exceptional circumstances where there was insufficient time or opportunity to submit a TUE application prior to doping control.[8]

The ultimate liability rests with the athlete and responsible medical advisors must be familiar with the current list of prohibited drugs in sport

Conclusions

The use of performance enhancing drugs has become one of the most vexatious problems facing modern sport. Mixed messages are frequently sent to young aspiring athletes who perceive a high international use of performance-enhancing drugs. WADA has issued a clear message of zero tolerance to the misuse of any banned substance. However the ultimate liability rests with the athlete and responsible medical advisors must be familiar with the current list of prohibited drugs in sport. A number of accessible resources including websites are available.[7,8,14,15,18]

Doctors prescribing for athletes require:
1. Knowledge and empathy for the unique demands of active patients
2. An understanding of and respect for the World Anti-Doping Code
3. The ability to resource the updated list of banned drugs for sport
4. A familiarity with the process of TUE application
5. A willingness to provide an appropriate and ethical duty of care.

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A Burner

'A "burner" is a common nerve injury resulting from trauma to the neck and shoulder, usually during sports participation. The injury is most often caused by traction or compression of the upper trunk of the brachial plexus or the fifth or sixth cervical nerve roots. Burners are typically transient, but they can cause prolonged weakness resulting in time loss from athletic participation. Furthermore, they often recur. Treatment consists of restoring range of motion, improving strength and providing protective equipment. Return to sports participation depends primarily on reestablishment of pain-free motion and full recovery of strength and functional status.'

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