



## 4. The use and misuse of performance-enhancing substances in sport

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*Doctors need to know if a patient is an athlete subject to drug testing, and to be aware of the legal situation surrounding drugs they prescribe such patients*

Certain drugs have the potential to increase athletic performance, but they carry the risk of side effects, which may include death and life-long morbidity. Examples include a cyclist dying from stimulant misuse during the 1960 Rome Olympics, and deaths from cardiovascular disease and various cancers resulting from use of anabolic steroids,<sup>1</sup> as well as the permanent androgenising effects of these drugs, including infertility, which affect many female Eastern bloc former athletes. Prohibitions on the use of dangerous performance-enhancing drugs have been introduced in almost all elite-level sports over the past 4 decades. Antidoping laws attempt to minimise the numbers of athletes engaging in doping, although the enforcement of antidoping laws is,



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### ABSTRACT

- Antidoping laws generally exist in order to provide a safe and fair environment for participation in sport.
- These laws should prevent and protect athletes from subjecting themselves to health risks through the use of unsafe, but performance-enhancing drugs.
- Because of difficulties in proving intent to cheat, the World Anti-Doping Agency enforces a principle of strict liability for positive test results for banned substances.
- An area of major controversy with respect to liability is the "sports supplement" industry, which is poorly regulated when compared with prescription drugs yet is a potential source of doping violations.
- Medical practitioners can be found guilty of anti-doping violations if they traffic banned drugs, prescribe these to athletes or otherwise assist athletes in taking banned substances.
- Medical practitioners are also now required to complete paperwork (therapeutic use exemption forms) to enable athletes to take banned substances which are required on medical grounds for specific illnesses.

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predictably, not 100% successful.<sup>2-4</sup> Because there is a perception that it is impossible to fully enforce antidoping laws, some commentators argue that these laws be relaxed to create an "open" but arguably more "even" playing field.<sup>4</sup> However, sport without antidoping laws would disadvantage further those athletes who wanted to compete at an elite level without risking their health.

The recently formed World Anti-Doping Agency (WADA) is responsible for developing and implementing uniform antidoping standards worldwide (both with respect to lists of banned drugs and penalties for misusing them). The World Anti-Doping Code ("WADA Code") was adopted after consultation with governments, sporting bodies, national antidoping agencies and other relevant parties in 2003 by all Olympic Committees, many nations and many elite sports associations.

A substance can be included on the World Anti-Doping Code Prohibited List if it meets two of the three major criteria defined by WADA, or if it is a potential masking agent. The three criteria are that the substance is performance-enhancing, that there are health risks to the athlete with use of the substance and that use of the substance violates the spirit of sport. The need for two out of the three criteria means that the WADA Code can ban "social drugs" such as marijuana (even though they are not performance-enhancing) but can permit the use of a drug such as caffeine (even though low levels of this drug are performance-enhancing).

Antidoping laws do not just relate to positive tests for prohibited substances. Refusing to submit to testing procedures, tampering

**1 Samples for drug testing must be collected according to a rigorous protocol to prove that detected substances were definitely found within an athlete's system**



with samples (before or after they are submitted), possession and/or trafficking illegal substances, and refusal to supply accurate regular whereabouts information to authorities (to allow for regular unannounced out of competition testing) can lead to doping infringements. Therefore, doctors who may potentially prescribe or otherwise assist athletes in taking banned drugs may also be subject to doping sanctions and suspended from involvement in elite sport.

**The burden of proof in doping charges**

With respect to the doping charge of “the presence of a prohibited substance or its metabolites or markers in an athlete’s bodily specimen”, an athlete is found guilty irrespective of whether there was a proven or even suspected intention to ingest the substance or cheat. Such strict liability does not necessarily apply to some other doping charges (eg, trafficking illegal substances), in which various burdens of proof must be met.

WADA enforces the principle of strict liability because there is generally no reasonable doubt that a drug discovered within an athlete’s urine or blood sample (taken under strict protocols; see Box 1) was present within the athlete’s system, while it would be

far too difficult, in most cases, to prove intent to cheat beyond reasonable doubt. Strict liability for doping offences is controversial, although the WADA Code does allow consideration of the unique circumstances of each case. If an athlete can *prove no fault or negligence* (in exceptional circumstances, such as a case of *proven drink spiking*) it is possible that suspensions can be downgraded or waived. These exceptional circumstances do not generally include cases where the athlete was given a prohibited substance by his or her personal physician or trainer without disclosure to the athlete.<sup>5</sup>

In cases in Australia, even before the adoption of the WADA Code, where an athlete has claimed inadvertent doping and his or her claims *were* verified, it has been rare to completely vindicate the athlete. There have been occurrences where medical practitioners have prescribed banned drugs for athletes for medical indications and have recorded the prescription in the notes, which have subsequently led to positive tests. Three case histories involving Australian professional cricket players are presented in Box 2 showing the response of drugs tribunals to the various explanations provided by the players.

**Responsibilities of treating medical practitioners**

The case in Box 2, in which a general practitioner prescribed probenecid for a professional player, which resulted in a doping violation, highlights the need for every medical practitioner, whether interested in sports medicine or not, to be aware that doping laws exist for athletes. Athletes are also responsible for informing every treating medical practitioner that they are subject to doping restrictions. Doctors unfamiliar with drugs on the most recent banned list must check with the Australian Sports Drug Agency (ASDA, via their hotline [1800 020 506] or their website <<http://www.asda.org.au/>>), before prescribing. To date, there has been no reported litigation involving athletes taking action against medical practitioners for prescribing banned drugs which led to suspensions. In scenarios where a doctor was either unaware of the “testable” status of an athlete or where a drug was administered as part of emergency treatment, it is unlikely that a doctor would be considered negligent for prescribing a banned drug. However, if a patient asked a doctor to check the legal status of a drug and an error was made, then the doctor may be held responsible for this

**2 Case histories involving Australian cricket players**

Drug	Circumstance	Penalty	Rationale
Probenecid (potential masking agent)	Patient treated for an abscess by a medical practitioner who was unaware that the player was subject to drug testing. Given probenecid to enhance penicillin action	1-month suspension and \$2000 fine	Because there was a clear indication for probenecid and because the drug was not performance-enhancing (but classified as a masking agent), leniency was exercised (but the player was not found innocent because the definition of guilt in the code is the presence of a substance). The player admitted to failing to notify the doctor that he was subject to drug testing
Nandrolone (anabolic steroid)	Patient was prescribed injectable nandrolone to assist in the recovery from a chronic back condition when not playing professional cricket, although the drug was detected after he returned to professional play	18-month suspension	Very little sympathy was extended to the player for the explanation that he was prescribed an anabolic steroid for medical indications, as the drug was clearly performance-enhancing and the indication for the drug was dubious
Diuretic (masking agent)	Patient took a diuretic (prescribed for another person) for weight loss	12-month suspension	Controversial case as the player was given a severe, but not maximum, penalty, suggesting that the tribunal offered some “discount” for his explanation and the fact that the drug was a masking agent rather than performance-enhancing; however, he was still found liable for the positive test

**3 Evidence base\* for the status of certain drugs on the World Anti-Doping Code Prohibited List 2005**

Drug category	Common therapeutic use(s)	Current status	Rationale for current status
$\beta_2$ -agonists	Asthma	Banned, but an abbreviated TUE form acceptable for exemption for inhaled use	Oral salbutamol in high doses enhances performance (Level 2 evidence) <sup>7</sup>
Corticosteroids	Asthma (oral/inhalers); certain injuries (local injections)	Banned, but therapeutic exemptions may be granted	Suspected of being taken indiscriminately in ultra-endurance events during competition to induce a sense of euphoria and perhaps to mask pain (controversial Level 4 evidence); no anabolic effects
Anabolic steroids	Very rare (eg, after surgery for pituitary tumour)	Banned. Need full TUE from medical panel for exemption, which would only be granted in extreme cases	Performance-enhancing and dangerous when misused (Level 1 evidence) <sup>1</sup>
Amphetamines	Attention deficit hyperactivity disorder, narcolepsy	Banned. Need full TUE from medical panel for exemption	Controversial category, as very likely to be performance-enhancing and unsafe in high doses (Level 4 evidence). Therapeutic uses are genuine but hard to diagnose objectively <sup>8</sup>
Finasteride	Hair loss; prostate disorders	Recently banned as a masking agent. Need full TUE from medical panel for exemption	Potential masking agent
Pseudoephedrine	Very common component of over-the-counter cold and flu medications	Has recently been removed from the banned list	No performance-enhancing effects from a standard dose (Level 2 evidence) <sup>9</sup>
Caffeine	No medical use, but common in many foods	All restrictions on caffeine have recently been removed	Impractical to ban and a fairly safe drug, despite some potential performance benefits (Level 1 evidence) <sup>10</sup>
Local anaesthetic injections	Suturing of wounds; minimising pain from an injury	Legal	No advantage conferred over uninjured athletes (Level 4 evidence); impractical to enforce ban <sup>11</sup>

\* Evidence rated according to National Health and Medical Research Council levels of evidence.<sup>6</sup> TUE = therapeutic use exemption. ◆

mistake. When prescribing drugs for athletes, a similar principle applies to that of treating pregnant women: “if in doubt about the status of a drug, check it or do not use it”. Practitioners are also advised to have some system of recording on a patient’s file whether he or she is subject to sports drug testing.

### Success in policing of antidoping laws

Many of the women’s track world records from the 1980s still stand. They were set in a period where both drug testing programs and the ability to detect anabolic steroids were nowhere near as advanced as they are today. It is impossible to be certain that a specific world record was only achieved with doping (other than cases where confessions were made). However, the fact that world-class standards have dropped in women’s track events over the past 15 years is probably attributable to the decreased use of performance-enhancing agents over that time, as antidoping measures have become more successful.

The fact that most records in men’s track events and in other disciplines such as swimming and cycling have been broken since the 1980s can be explained with a variety of hypotheses, including that the relative performance advantage in these events for using anabolic steroids is not as great as for women’s track events. There is an expectation that world records will gradually improve over time as training advances are made.

It has recently been revealed that many athletes from East Germany in the 1970s and 1980s were regularly prescribed anabolic steroids, yet calls by some commentators to have retrospective changes made to the record books have not been heeded. This is sensible, as it is perhaps counterproductive to rewrite history many

years after the event. If an athlete wins an event under the drug-testing regimen of the day, any later declaration that he or she was able to beat the system of the time does not necessarily mean that he or she was the only athlete in that event doing so. It may also be helpful for improving the approach towards drugs in sport that athletes can confess years after an event, without the threat of [potential] retrospective erasing of results.

### Blood doping and erythropoietin: should direct or indirect testing be used?

Blood doping (transfusions of either donor blood or one’s own stored blood) to enhance performance in endurance events has probably now been superseded by erythropoietin (EPO). EPO increases red blood cell indices, such as haemoglobin concentration, and hence endurance. In certain sports, the “average” haemoglobin levels of competitors have increased significantly in recent years, which is highly suggestive of blood doping or EPO use.<sup>2,3</sup> EPO is considered a very difficult drug to detect: it exists naturally within the body and has a short half-life of a few hours, while its effects on red blood cell counts last for over a month. Thus, rather than relying solely on detecting EPO directly, athletes in sports such as cycling and cross-country skiing (where EPO misuse is thought to have been common) are banned from competing if their red blood cell indices are raised beyond certain levels (possibly consistent with, but not definitive of, EPO use). These tests are done just before competition and exclusion from that event is based on the potential risk to health.

While seen by some as a sensible method of minimising harm,<sup>4</sup> “banning” according to haematological indices means that the

principle of strict liability cannot be adhered to. Medical conditions, such as polycythaemia rubra vera, can cause similar haematological changes. Thus, affected athletes are not subject to doping sanctions, but are merely designated “unfit” to participate in the current competition. Similarly, wheelchair athletes with spinal cord injuries who have high blood pressure before an event are prevented from competing at the Paralympics, without prospective suspension, as the elevated blood pressure may be self-induced (illegal “boosting” to improve performance) or the result of a concurrent medical condition.



### Therapeutic use exemptions (TUEs)

The WADA Code has a process for granting exemptions for the legitimate medical use of banned substances. All applications must be prospective and registered (except in emergency situations). Some medications are banned (see Box 3) with the proviso that they may be used for certain medical indications, which require that the relevant body is notified before their use. Under the WADA Code, prospective approval to take a banned drug through the therapeutic use exemption (TUE) process for a documented medical condition is currently provided if:

- the condition poses significant impairment to health; and
- there is no additional enhancement of performance (other than return to normal state of health following treatment of the legitimate medical condition); and
- no reasonable therapeutic alternative exists to treat the condition.

The TUE process is generally simple for specific commonly-exempted drugs (inhaled  $\beta_2$ -agonists for the treatment of asthma and non-systemic glucocorticosteroids) with automatic approval being considered “granted” once a correctly lodged form is received by the relevant national or international sporting body. However, incorrect lodgement of paperwork can result in a guilty verdict under the principle of strict liability. This has already occurred in the case of an Austrian tennis player who was banned for 3 months in late 2004 for testing positive to a corticosteroid, injected by a doctor for a wrist injury.

Less commonly-exempted drugs (with greater potential for misuse and performance enhancement) must be assessed by an expert panel. In Australia, these requests for TUEs are handled by an independent panel called the Australian Sports Drug Medical Advisory Committee (see <http://www.asdmac.org.au>). Medical practitioners can also ring for advice, particularly in emergency situations, and may be able to speak directly to one of the medical practitioners on the committee. TUEs are commonly granted for the use of oral glucocorticosteroids to treat severe asthma or inflammatory bowel disease. All applications require full docu-

mentation, including specialist opinions and results of investigations. A TUE would never be granted to help elevate a slightly “below normal” testosterone level in an otherwise healthy adult. It has been noted that athletes will go to extraordinary lengths to appear to have conditions for which anabolic steroids are indicated, because of the known beneficial effects on performance.<sup>12</sup>

The legality of the various stimulants presents a further area of controversy. A Romanian gymnast was stripped of a gold medal at the Sydney Olympics after

testing positive for pseudoephedrine, which was banned at the time, but pseudoephedrine has been recently removed from the banned list (Box 3). The most contentious TUE decisions with respect to stimulants are for conditions such as narcolepsy and attention deficit hyperactivity disorder (ADHD). While these conditions improve markedly with stimulant medication,<sup>13</sup> a recent review cautioned against awarding TUEs for stimulants on the basis that symptoms are difficult to verify “objectively”, making it possible for athletes to allege having symptoms of narcolepsy and ADHD to gain access to performance enhancing stimulants.<sup>8</sup>

### The use of “legal” supplements

While most over-the-counter supplements are considered “legal” within anti-doping codes, some controversies exist because they may enhance athletic performance. While there is no scientific evidence to support the benefits claimed for most products, there is substantial proof that some *can* enhance specific performance outcomes when used according to specific protocols.<sup>14</sup> For instance, certain athletes taking bicarbonate/citrate, creatine and/or caffeine can exercise at higher work rates or for longer before experiencing fatigue.<sup>10,15,16</sup> WADA has taken a pragmatic approach, considering that such ingredients occur naturally in food, and that manufactured products simply represent a practical way for athletes to consume a desired dose.

By contrast, the WADA Code bans prohormones, including androstenedione, dehydroepiandrosterone, and 19-norandrostenedione, which can be converted in the body to testosterone or the anabolic steroid nandrolone.<sup>17</sup> Over recent years there has been controversy relating to their legality in professional baseball in the United States. Since the Dietary Supplement Health and Education Act (1994) was passed in the United States, products containing prohormones have been marketed as over-the-counter dietary supplements there. Even in countries like Australia where prohormones do not enjoy this liberalised status, they may be available to athletes through Internet or mail-order sales.

There is conflicting data about whether the use of prohormones generally leads to positive results from urinary drug screening tests,<sup>18-20</sup> which means that none of the anabolic steroid prohormones can be considered “safe” for athletes who are subject to

testing, yet certain individuals may still test negative for anabolic steroids after taking low doses of prohormones. Over recent years, many athletes who have tested positive for low levels of the anabolic steroid nandrolone have claimed that they took only apparently “legal” supplements. Several studies from overseas have suggested that up to 10%–15% of supplements may contain contaminated substances.<sup>18,21</sup> Clearly, there are problems with the supplement industry worldwide, and solutions must include self-regulation of manufacturing processes to ensure uncontaminated and accurately labelled products, appropriate government regulations, and product testing and certification programs for athletes.

Another confusion about prohormone supplements lies with their ability to enhance sports performance in young adults with normal endogenous production of steroids. The present consensus from acute and chronic studies of prohormone supplementation is that there is little evidence of improved muscle size or strength above the gains achieved through resistance training.<sup>14</sup> Although it is tempting to say that these products “don’t work”, the treatment doses used in studies are conservative in comparison to the doses recommended and used by some athletes.<sup>22</sup>

### Testing for “social” drugs that are not performance-enhancing

Major controversy also surrounds testing for illegal drugs that do not enhance performance, but which athletes may take for social (or recreational) purposes. The banning of stimulants, such as cocaine, when competing is universally accepted. The dilemma lies in whether stimulant drugs should be tested out-of-competition (where presumably they convey no performance advantage) and whether drugs such as marijuana, which are illegal but unlikely to confer any performance advantage, should be tested for and potentially lead to disqualification. The argument offered by WADA is that these drugs affect the health of the athlete, and that taking of drugs inappropriately is against the spirit of sport.

It may be considered an invasion of privacy to test for non-performance-enhancing drugs outside periods of athletic competition. However, it is hard to argue in defence of athletes who choose to break not only antidoping, but also criminal laws by using illicit social drugs. It may be more appropriate that these athletes receive counselling, and perhaps shorter suspensions, than other athletes found using drugs that would confer an unfair performance advantage.

### Conclusion

Doping authorities are further ahead than they have ever been, but awareness that doping is prevalent in sport is also greater than it has ever been. With current antidoping policies, authorities greatly decrease the widespread use of dangerous substances in sport. However the difficulties with enforcing prohibitions lead to many areas of controversy. It is planned that subtle ongoing changes will be made to the WADA Code, making it necessary for all medical practitioners who treat athletes to know how to check up-to-date lists of legal drugs and substances.

### Competing interests

Susan White is a member of the Australian Sports Drug Medical Advisory Committee (ASDMAC). Peter Fricker was a member of ASDMAC while writing this article, but has since resigned after accepting the position of Director of the Australian Institute of Sport.

### References

- 1 Yesalis C, Bahrke M. Anabolic-androgenic steroids and related substances. *Curr Sports Med Rep* 2002; 1: 246-252.
- 2 Videman T, Lereim I, Hemmingsson P. Changes in hemoglobin values in elite cross-country skiers from 1987–1999. *Scand J Med Sci Sports* 2000; 10: 98-102.
- 3 Stray-Gundersen J, Videman T, Penttila I, Lereim I. Abnormal hematologic profiles in elite cross-country skiers: blood doping or? *Clin J Sport Med* 2003; 13: 132-137.
- 4 Savulescu J, Foddy B, Clayton M. Why we should allow performance enhancing drugs in sport. *Br J Sports Med* 2004; 38: 666-670.
- 5 World Anti-Doping Agency. Comment on para 10.5. WADA Anti-doping code, 2005. Available at: <http://www.wada-ama.org/en/> (accessed Jan 2006).
- 6 National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra: NHMRC, 1999. Available at: <http://www.nhmrc.gov.au/publications/synopses/cp30syn.htm> (accessed Jan 2006).
- 7 van Baak M, de Hon O, Hartgens F, Kuipers H. Inhaled salbutamol and endurance cycling performance in non-asthmatic athletes. *Int J Sports Med* 2004; 25: 533-538.
- 8 Kaufman K. Modafinil in sports: ethical considerations. *Br J Sports Med* 2005; 39: 241-244.
- 9 Hodges A, Lynn B, Bula J, Donaldson M, et al. Effects of pseudoephedrine on maximal cycling power and submaximal cycling efficiency. *Med Sci Sports Exerc* 2003; 35: 1316-1319.
- 10 Magkos F, Kavouras S. Caffeine and ephedrine: physiological, metabolic and performance-enhancing effects. *Sports Med* 2004; 34: 871-889.
- 11 Orchard J. Is it safe to use local anaesthetic painkilling injections in professional football? *Sports Med* 2004; 34: 209-219.
- 12 Conway A, Handelsman D, Lording D. Use, misuse and abuse of androgens. *Med J Aust* 2000; 172: 220-224.
- 13 Corrigan B. Attention deficit hyperactivity disorder in sport: a review. *Int J Sports Med* 2003; 24: 535-540.
- 14 Burke L. Sports supplements and sports foods. In: Hargreaves M, Hawley J, editors. *Physiological bases of sports performance*. Sydney: McGraw Hill, 2003.
- 15 van Loon L, Oosterlaar A, Hartgens F, et al. Effects of creatine loading and prolonged creatine supplementation on body composition, fuel selection, sprint and endurance performance in humans. *Clin Sci (Lond)* 2003; 104: 153-162.
- 16 Requena B, Zabala M, Padial P, Feriche B. Sodium bicarbonate and sodium citrate: ergogenic aids? *J Strength Cond Res* 2005; 19: 213-224.
- 17 Blue JG, Lombardo JA. Steroids and steroid-like compounds. *Clin Sports Med* 1999; 18: 667-689.
- 18 Geyer H, Parr MK, Mareck U, et al. Analysis of non-hormonal nutritional supplements for anabolic androgenic steroids — results of the international IOC study. *Int J Sports Med* 2004; 25: 124-129.
- 19 Bosy T, Moore K, Polkis A. The effect of oral dehydroepiandrosterone (DHEA) on the urine testosterone/epitestosterone (T/E) ratio in human male volunteers. *J Anal Toxicol* 1998; 22: 455-459.
- 20 Uralets VP, Gillette PA. Over-the-counter anabolic steroids 4-androsten-3,17-dione; 4-androsten-3beta,17beta-diol; and 19-nor-4-androsten-3,17-dione: excretion studies in men. *J Analyt Toxicol* 1999; 23: 357-366.
- 21 Geyer H, Bredehoft M, Mareck U, et al. High doses of the anabolic steroid metandienone found in dietary supplements. *Eur J Sport Sci* 2003; 3: 1-5.
- 22 Yesalis C. Medical, legal, and societal implications of androstenedione. *JAMA* 1999; 281: 2043-2044.

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