



The anti-doping code in sport – update for 2004

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Summary

The World Anti-Doping Agency has assumed responsibility for international doping control from the International Olympic Committee. It has revised, reformed and now presented a new World Anti-Doping Code, which became globally effective in January 2004. The World Anti-Doping Code contains the List of Prohibited Substances and Prohibited Methods. This list differs from its predecessor. Caffeine has been removed from the banned list, but a new category of 'specified substances' which may produce inadvertent positive tests has been added.

Key words: doping, anabolic steroids, stimulants, caffeine.

(Aust Prescr 2004;27:84–7)

Introduction

Over recent years, the World Anti-Doping Agency (WADA)* has worked with the International Olympic Committee (through its member national organisations) to produce a new World Anti-Doping Code (WADC).¹ This replaces previous lists of prohibited substances and methods.² The new Code has a number of implications for athletes, coaches and medical practitioners. Athletes are responsible for making sure that medications they take comply with the Code.

Prohibited substances

The rationale for determining whether or not a substance should be placed on the prohibited list is based on three criteria:

- potential to enhance sport performance
- actual or potential risk to health
- violation of the spirit of sport.

If two of these criteria are met, the substance is considered for inclusion on the prohibited list (see Box 1).

Anabolic agents

Of recent notoriety is tetrahydrogestrinone, a synthetic derivative, which has produced a number of positive doping tests among sprint and power athletes. Tetrahydrogestrinone was apparently provided to athletes as a supplement, and bears

* An agency funded by the International Olympic Committee and, as at March 2004, by over 150 national governments.

a similar history in this respect to nandrolone, which has often been identified in positive urine samples.

A positive doping test for testosterone still depends upon finding a urinary testosterone/epitestosterone ratio greater than six. Should an endogenous anabolic steroid be found in such a circumstance, further investigation is obligatory in order to determine whether the ratio is due to a physiological or pathological condition.

Other anabolic agents on the prohibited list include the beta agonists clenbuterol and zeranol.

Peptide hormones

The following peptide hormones are all prohibited, as are their mimetics and releasing factors (releasing hormones):

- erythropoietin
- growth hormone (hGH and insulin-like growth factor (IGF-1))
- chorionic gonadotrophin (HCG) – prohibited in males only
- pituitary and synthetic gonadotrophins (LH) – prohibited in males only
- insulin
- corticotrophins.

Beta agonists

All beta agonists (including their D- and L- isomers) are prohibited **except**:

- formoterol
- salbutamol
- salmeterol
- terbutaline.

Box 1

Examples of prohibited substances

Stimulants (but pseudoephedrine and caffeine have been removed from the list)

Narcotics

Cannabinoids

Anabolic agents

Peptide hormones

Beta agonists

Agents with anti-oestrogenic activity

Masking agents

Glucocorticosteroids

The exempted drugs are only permitted by inhalation to prevent and/or treat asthma and exercise-induced bronchoconstriction. A medical notification is required for the athlete to compete. If the concentration of salbutamol in urine exceeds 1000 ng/mL, it will be considered an adverse analytical finding unless the athlete proves that the abnormal result was the consequence of the therapeutic use of inhaled salbutamol.

Masking agents

These agents can conceal the use of other substances and include diuretics, epitestosterone, probenecid and the plasma expanders, such as dextran and hydroxyethyl starch (see Box 2).

Glucocorticosteroids

Corticosteroids are prohibited when given orally, rectally or by intravenous or intramuscular administration. A medical notification is necessary for all topical applications, inhalational use, or intralesional or intra-articular injection.

Prohibited methods

The criteria for determining if a method of doping should be banned are the same as those for determining prohibited substances.

Enhancement of oxygen transfer

This includes blood doping and the use of products that enhance the uptake, transport and delivery of oxygen. Examples include erythropoietin, modified haemoglobin products, perfluorochemicals, and efaproxiral (RSR13).

Pharmacological, chemical and physical manipulation

These techniques are intended to alter the integrity and validity of specimens collected in doping control tests. They include catheterisation of the bladder, urine substitution and/or tampering, inhibition of renal excretion and alterations of testosterone and epitestosterone concentrations.

Gene doping

This is defined as the non-therapeutic use of genes, genetic elements and/or cells that have the capacity to enhance athletic

performance. (The Code anticipates the possible future use of genetic engineering in sport.)

Substances and methods prohibited in and out of competition

Prohibited substances include:

- anabolic agents
- peptide hormones
- beta agonists (clenbuterol, and salbutamol >1000 ng/mL in urine)
- anti-oestrogenic agents
- masking agents.

Prohibited methods include:

- enhancement of oxygen transfer
- pharmacological, chemical and physical manipulation
- gene doping.

Substances prohibited in particular sports

Under the new WADA Code, particular sports have identified particular substances they wish to prohibit only during competition periods. These substances include:

- alcohol
- beta blockers
- diuretics.

Specified substances

The prohibited list identifies substances which are particularly susceptible to unintentional violations of anti-doping rules because of their general availability in medicinal products, or because they are less likely to be successfully abused as doping agents. Consequently, a doping violation involving these specified substances **may** result in a reduced sanction (penalty) as noted in the WADA Code, provided the 'athlete can establish that the use of such a specified substance was not intended to enhance sport performance'.

Specified substances are:

- stimulants (ephedrine, L-methylamphetamine, methylephedrine)
- cannabinoids
- inhaled beta agonists (except clenbuterol)
- diuretics (except where prohibited in weight-classified sports and sports in which weight loss can enhance performance, such as ski jumping)
- glucocorticosteroids
- masking agents – probenecid
- beta blockers
- alcohol.

Box 2

Masking agents

Diuretics – promote excretion of urine

Epitestosterone – used to correct an altered testosterone/epitestosterone ratio

Probenecid – blocks excretion of anabolic agents

Plasma expanders – alter red cell parameters such as haemoglobin and haematocrit (used in the detection of erythropoietin abuse)

Caffeine

One major change from the previous regulations is the removal of caffeine from the banned list. A review of caffeine has deemed it to be performance enhancing at concentrations lower than those required to produce a positive test (urinary levels of 12 mg/L).³

As caffeine is widely available in a variety of foods and drinks it is easily used as a performance enhancing agent. Although caffeine will be monitored at competitions through urine testing, no action will be taken against athletes who show caffeine in their urine.

Medical notification

Medical notification relates to the use of substances which are not on the banned list, but are permitted for use under certain specified conditions. Notifiable substances are the beta agonists, formoterol, salbutamol, salmeterol and terbutaline, which are permitted for the treatment of asthma and exercise-induced bronchospasm.

Notification must be made by a medical practitioner on the athlete's behalf specifying the substance, the dosage, duration of treatment, and the diagnosis of asthma or exercise-induced bronchospasm. The athlete's national sporting organisation is to be notified well in advance of any competition (where the athlete may be tested by doping control). The onus is on the athlete to ensure that documentation is appropriate and timely.

Authorities should also be notified about the use of glucocorticosteroids when used by inhalation (for the treatment of asthma and/or allergic rhinitis), by injection (into joints, bursae or lesions – but not intravenously or by intramuscular injection), or as topical applications in the ear, the eye or on the skin. Notification is the responsibility of the athlete, and the sporting organisation must be notified of the details of the diagnosis, substance used, dosage, and duration of treatment.

Therapeutic use exemption

While medical notification is for substances permitted under certain conditions, therapeutic use exemption is for the therapeutic use of a substance or method which is on the prohibited list. In Australia, the Australian Sports Drug Medical Advisory Committee (ASDMAC) is the body which grants exemptions.

Should an athlete require treatment with a prohibited substance or prohibited method, a medical practitioner may apply to ASDMAC by way of its web site or by mail for a therapeutic use exemption (see Further information). The ASDMAC form specifies the relevant details which need to be provided – including athlete details, the medical condition(s) (with supporting evidence), treatment(s) being recommended (with dosages and duration of treatment) and other details as

necessary. The decision to grant an exemption depends upon:

- the capacity of the treatment (substance or method) to enhance performance 'other than that which might be anticipated by a return to a state of normal health following the treatment of a legitimate medical condition'
- the lack of reasonable therapeutic alternatives
- the risk to the health of the athlete if the substance or method were to be withheld in the course of treatment.

In addition, the need for use of the substance or method cannot be a consequence in any way of prior non-therapeutic use of any prohibited substance or method.

In medical emergencies, such as hospital admission, whereby a prohibited substance or method is used appropriately, a therapeutic use exemption can be provided after the event. An application should be made as quickly as possible.

Conclusion

At first pass the WADA Code appears complex and somewhat confusing. However, the Code attempts to limit the opportunity to cheat by specifying prohibited substances in and out of competition, while allowing for the use of substances under certain conditions (notifiable substances), the use of banned substances for therapeutic purposes, and the recognition that some substances may produce inadvertent positive dope tests while not being used for performance enhancement (specified substances). It should also be recognised that many nutritional supplements contain banned substances and extreme caution should be taken to avoid inadvertent doping.

Finally, the concerns about drugs in sport and doping are not confined to young elite athletes – similar concerns should be held for any athlete who wishes to compete at any age.

References

1. <http://www.wada-ama.org> [cited 2004 July 1]
2. Fricker PA. Drugs in sport. *Aust Prescr* 2000;23:76-8.
3. Graham TE. Caffeine and exercise: metabolism, endurance and performance. *Sports Med* 2001;31:785-807.

Further information

World Anti-Doping Agency
<http://www.wada-ama.org>

The World Anti-Doping Code
http://www.wada-ama.org/docs/web/standards_harmonization/code/code_v3.pdf

The 2004 Prohibited list
http://www.wada-ama.org/docs/web/standards_harmonization/code/list_standard_2004.pdf

Australian Sports Drug Medical Advisory Committee (ASDMAC)
– for Applications for therapeutic use exemption

PO Box 345
CURTIN ACT 2605
Fax: (02) 6206 0262
<http://www.asdmac.org.au>

Australian Sports Drug Agency (ASDA)
PO Box 345
CURTIN ACT 2605
<http://www.asda.org.au>
Phone: (02) 6206 0200
E-mail: asda@asda.org.au

Australian Sports Drug Agency (ASDA) Drugs in Sport Hotline – a confidential, free call service for athletes and their support staff that offers information on the status of Australian pharmaceutical medications and substances in sport
Phone: 1800 020 506

Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 105)

1. Caffeine is a prohibited substance in elite sports.
2. The prescription of a topical corticosteroid should be notified to an athlete's sporting organisation.

Medicinal mishap

Ibuprofen and asthma

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Case

A 17-year-old 47 kg male was admitted for an elective inguinal hernia repair. He had a past history of allergic rhinitis (no nasal polyps) and severe chronic asthma. Although he had been admitted to the intensive care unit three times previously, there had been no emergency presentations/admissions for 10 months. His asthma was well controlled with inhaled corticosteroids. The patient had no known allergies to any food or medications.

During a pre-operative consultation, the use of non-steroidal anti-inflammatory drugs (NSAIDs) for analgesia was discussed. The patient had no known prior exposure to NSAIDs or aspirin.

Surgery progressed unremarkably and postoperatively the patient was given one oral dose of 500 mg ibuprofen. Within 15 minutes he became distressed and complained of feeling 'tight' in the chest. Eight puffs of inhaled salbutamol via spacer were given immediately but the patient's respiratory symptoms continued to worsen over the next hour. He required high dependency care with nine doses of nebulised salbutamol and three doses of intravenous salbutamol, in conjunction with intravenous steroids (two doses of 8 mg dexamethasone six hourly). The patient recovered within six hours of the ibuprofen dose and was discharged home the following day after a dose of oral prednisolone (50 mg).

Comment

Aspirin-induced asthma is a distinct clinical syndrome. It is a recognised condition in adults^{1,2} but is considered rare

in children.² There are no tests to identify this syndrome in patients with asthma and the diagnosis is usually established only by observations or by direct re-challenge with aspirin.² Cross-sensitivity with other NSAIDs is possible as the syndrome is thought to be related to the inhibition of cyclo-oxygenase enzymes.^{1,2} A history of rhinitis is also consistent with the syndrome.

Our patient's asthma exacerbation was probably due to ibuprofen as the reaction occurred within 15 minutes of ingestion, symptoms peaked at 45 minutes and there were no symptoms during anaesthesia or in the immediate post-anaesthesia recovery period.

Conclusion

It is important to ask patients with asthma, or their parents, about all non-prescription medications as many people will not associate asthma with the use of aspirin or other NSAIDs, or be aware of the risk of taking these medications. Patients who are aspirin sensitive or at risk can be counselled about the risk of asthma exacerbation and the appropriate selection of analgesics. This advice becomes even more important with the recent relaxation of the scheduling of NSAIDs, increasing their availability without prescriptions.

References

1. Fahrenholz JM. Natural history and clinical features of aspirin-exacerbated respiratory disease. *Clin Rev Allergy Immunol* 2003;24:113-24.
2. Szczeklik A, Nizankowska E, Mastalerz L, Szabo Z. Analgesics and asthma. *Am J Ther* 2002;9:233-43.

Editor's note:

The Adverse Drug Reactions Advisory Committee has received three other reports of similar adverse reactions to ibuprofen in children.