Introduction to the Doping Problem

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Doping and Society: towards the perfect human machine?

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Doping: A personal definition

- The use of pharmacological substances to artificially increase sports performance in conflict with ethical principles of sport and medicine
World Anti-Doping Program

Level 1:
- World Anti-Doping Code

International Standards

Level 2:
- List
- TUE
- Testing
- Labs

Models of Best Practice

Level 3:
- Rules and Regulations: IFs, NADOs, NOCs, EOs
- Results Management
- Education Programs
- National Anti-Doping Programs
World Anti-Doping Program

Level 1: World Anti-Doping Code

Level 2: International Standards
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Main developments of the List of Prohibited Substances and Methods

- **1968**: Stimulants and Narcotic analgesics
- **1976**: Anabolic Steroids added
- **1983**: T/E for testosterone
- **1985**: Beta-blockers and Blood doping
- **1988**: Diuretics and Peptide hormones (EPO, hGH)
- **2000**: Artificial Oxygen carriers, Plasma expanders
- **2003**: Antiestrogens, Gene Doping
- **2004**: Glucocorticoids
List of prohibited substances and methods – WADA

**PROHIBITED SUBSTANCES**
- S1. Anabolic Agents
- S2. Hormones and Related Substances
- S3. Beta-2 Agonists
- S4. Agents with anti-oestrogenic activity
- S5. Diuretics and other masking agents
- S6. Stimulants
- S7. Narcotics
- S8. Cannabinoids
- S9. Glucocorticosteroids

**PROHIBITED METHODS**
- M1. Enhancement of oxygen transfer
- M2. Chemical and physical manipulation
- M3. Gene Doping

**SUBSTANCES PROHIBITED IN PARTICULAR SPORTS**
- P1. Alcohol
- P2. Beta-blockers
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Abbreviated Therapeutic Use Exemptions
ATUE

Please complete all sections in capital letters or typing.

beta-2 agonists by inhalation  glucocorticosteroids by  non-systemic routes *

* All routes other than orally, rectally, intravenously and intramuscularly. Dermatological glucocorticosteroids do not require any TUE

1. Athlete Information

Surname:  Given Names:  
Female  Male  
Date of Birth (d/m/y):  

Address:  

City:  Country  Postcode:  

Tel.:  E-mail:  
(with international code)

Sports:  Discipline/Position:  

International or National Sporting Organization:  

2. Medical information

Diagnosis:  

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N.B. Any ATUE may be reviewed at any time, by the ADO and/or WADA

3. Medical practitioner’s and athlete’s declaration

I certify that the above-mentioned treatment is medically appropriate and that the use of alternative medications not on the Prohibited List would be unsatisfactory for this condition.

Name:  

Medical Speciality:  

Address:  

Tel.:  Fax:  

E-mail:  

Signature of Medical Practitioner:  Date:  

I certify that the information under 1. is accurate and that I am requesting approval to use a Substance or Method from the WADA Prohibited List. I authorize the release of personal medical information to the Anti-Doping Organization (ADO) as well as to WADA staff, to the WADA TUEC (Therapeutic Use Exemption Committee) and to other ADO under the provisions of the Code. I understand that if I ever wish to revoke the right of these organizations to obtain my health information on my behalf, I must notify my medical practitioner and my ADO in writing of that fact.

Athlete’s signature:  Date:  

Parent’s/Guardian’s signature:  Date:  

(if the athlete is a minor or has a disability preventing him/her to sign this form, a parent or guardian shall sign on the form on behalf of the athlete)

Incomplete Applications will be returned and need to be resubmitted.

Please submit the completed form to the ADO and keep a copy for your records.
Type of samples

INTERNATIONAL STANDARD FOR TESTING

Annex C – Collection of urine samples
Annex D – Collection of blood samples
Análisis de la muestra

1. El deportista deposita la muestra de orina en un frasco homologado
2. El deportista rellena un formulario y la muestra se distribuye en dos frascos. Uno rojo (A) y otro azul (B) y se envían al laboratorio
3. Sólo se analiza la muestra roja (A). La azul (B) sólo se desprenderá en presencia del deportista y si hay positivo
4. Ya en el laboratorio antidepaje se desprende la caja con las muestras
5. Personal cualificado desprecinta la muestra roja (A)
6. La muestra azul (B) se congela, ya que sólo se utilizará si es preciso el contraanálisis
7. Los refrigeradores con las muestras azules (B) se guardan a buen roceado
8. Los analistas inician el proceso para limpiar y purificar la orina
9. Diversas dosis de orina se distribuyen en varias probetas para asegurar el proceso analítico
10. El doctor Segura y su ayudante, Rosa Ventura, verifican el proceso final del control antiadipaje
Antidoping control – Analytical strategy

- Reception
- Distribution
- Screening
- Negative result
- Adverse finding
- Results report

- Counter analysis
- Distribution
- Confirmation
- Result
- Results report
QUALITY ASSURANCE

☑ ISO 17025 ACCREDITATION: General requirements for the competence of testing and calibration laboratories

☑ (IOC) WADA ACCREDITATION
Accredited antidoping laboratories
Recent new analytical challenges ...
'Scientific Analysis of Essential and Toxic Elements Impacting the Quality of Life'

Designer drugs

 Bayer Ariba Laboratory Co-operative

High-Tech Nutritional Assessment
Mimetics and analogues according to the WADA Prohibited List

• ANALOGUE
  – An analogues is defined as a substance derived from the modification or alteration of the chemical structura of another substance while retaining a similar pharmacological effect

• MIMETIC
  – A mimetic is defined as a substances with pharmacological effect similar to that of another substance, regardless of the fact that it has a different chemical structure
... and other non analytical challenges
Detection of doping substances

• Difficulties with substances identical to endogenous ones

• Analytical aspects

• Criteria to distinguish from an abnormal natural concentration
  *Indirect markers
  *Direct markers
WADA supported areas of Research

• Compounds and/or methods enhancing oxygen delivery (e.g., autologous blood transfusion)
• Compounds and or methods enhancing growth (IGF-1, insulin)
• Gene and cellular technologies applied to sports (GH, IGF-1, EPO, myostatin, vectors, non-invasive imaging)
• Other projects related to the Prohibited List
Monitoring Gene Therapy by External Imaging of mRNA: Pilot Study on Murine Erythropoietin

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Abstract: Gene therapy is anticipated as being an important medical development. Essential to its effectiveness is the appropriate activity (protein expression) in the expected target cells. A noninvasive diagnostic procedure of successful gene expression will be of paramount importance to validate its use or its misuse (eg, sports gene doping). Externally detectable labeled oligonucleotide hybridizing with the messenger RNA generated by the transferred gene has been proposed as a possibility to monitor successful gene therapy. The authors selected the erythropoietin gene (Epo) for a pilot study on erythropoietin protein expression in mouse muscle. Oligonucleotides of peptide nucleic acid (PNA) type capable of antisense binding to unique murine Epo-mRNA sequences were synthesized by solid phase methods, and elongated at the N-terminus with the HIV Tat (48–60) cell penetrating peptide. They were labeled with fluorescence and radioactive tags to verify penetration and longer half-life properties in Epo gene transfected C2C12 mouse muscle cells as compared with corresponding wild-type cells. Downregulation of newly expressed erythropoietin protein in such cells additionally confirmed the penetration and hybridizing properties of the selected labeled oligonucleotide. ¹²³I-labeled Tat-PNAs were intravenously injected into mice that had previously received the Epo gene into the right tibialis muscle by DNA electrottransfer. Preferential accumulation of radioactivity in the transferred limb as compared with the contralateral limb was ascertained, especially for ¹²³I-Tat-CTA CGT AGA CCA CT (labeled Tat-PNA 1). This study provides experimental data to support the potential use of external noninvasive image detection to monitor gene therapy. The extension of the approach to more sensitive methods for whole-body external detection such as positron emission tomography appears feasible.

Key Words: gene therapy, gene doping, gene expression, detection, peptide nucleic acid, antisense

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