



DEPARTMENT OF GLOBAL HEALTH & SOCIAL MEDICINE

Gene Transfer, Gene Enhancement & Gene Doping: Infringing on the Spirit of Sport?

Dr. Silvia Camporesi

Maine Medical Center, August 28, 2017

Doping, today: a systematic enterprise...



A question for you!

We all know it when we see it?

What actually is doping?

What is doping?



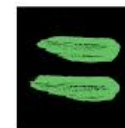
- Steroids?
- EPO?
- Human growth hormone?
- Metamphetamines?
- Hyberbaric pressure rooms?
- Lasik eye surgery?
- Vitamin supplements?
- Caffeine?
- Cannabis?

What is doping?

- Actually, according to the definition of the World Anti-Doping Agency (WADA), doping is *not* ingestion of a prohibited substance
- Doping is defined procedurally as a **rule violation** (prohibited substance ingestion is only one of the possible violations)

ARTICLE 1: DEFINITION OF DOPING

Doping is defined as the occurrence of one or more of the anti-doping rule violations set forth in Article 2.1 through Article 2.8 of the *Code*.



WORLD
ANTI-DOPING
AGENCY

play true

ARTICLE 2: ANTI-DOPING RULE VIOLATIONS

Athletes or other Persons shall be responsible for knowing what constitutes an anti-doping rule violation and the substances and methods which have been included on the Prohibited List.

The following constitute anti-doping rule violations:



- 2.1 Presence of a Prohibited Substance or its Metabolites or Markers in an Athlete's Sample.
- 2.2 Use or Attempted Use by an Athlete of a Prohibited Substance or a Prohibited Method.
- 2.3 Evading Sample Collection.
- 2.4 Filing Failures and Missed Tests.
- 2.5 Tampering or Attempted Tampering with any part of Doping Control.
- 2.6 Possession of a Prohibited Substance or a Prohibited Method.
- 2.7 Trafficking or Attempted Trafficking in any Prohibited Substance or Method.
- 2.8 Administration or Attempted Administration to any Athlete In-Competition of any Prohibited Method or Prohibited Substance
- 2.9 Complicity in an Anti-Doping Rule Violation.
- 2.10 Prohibited Association of any anti-doping rule violations

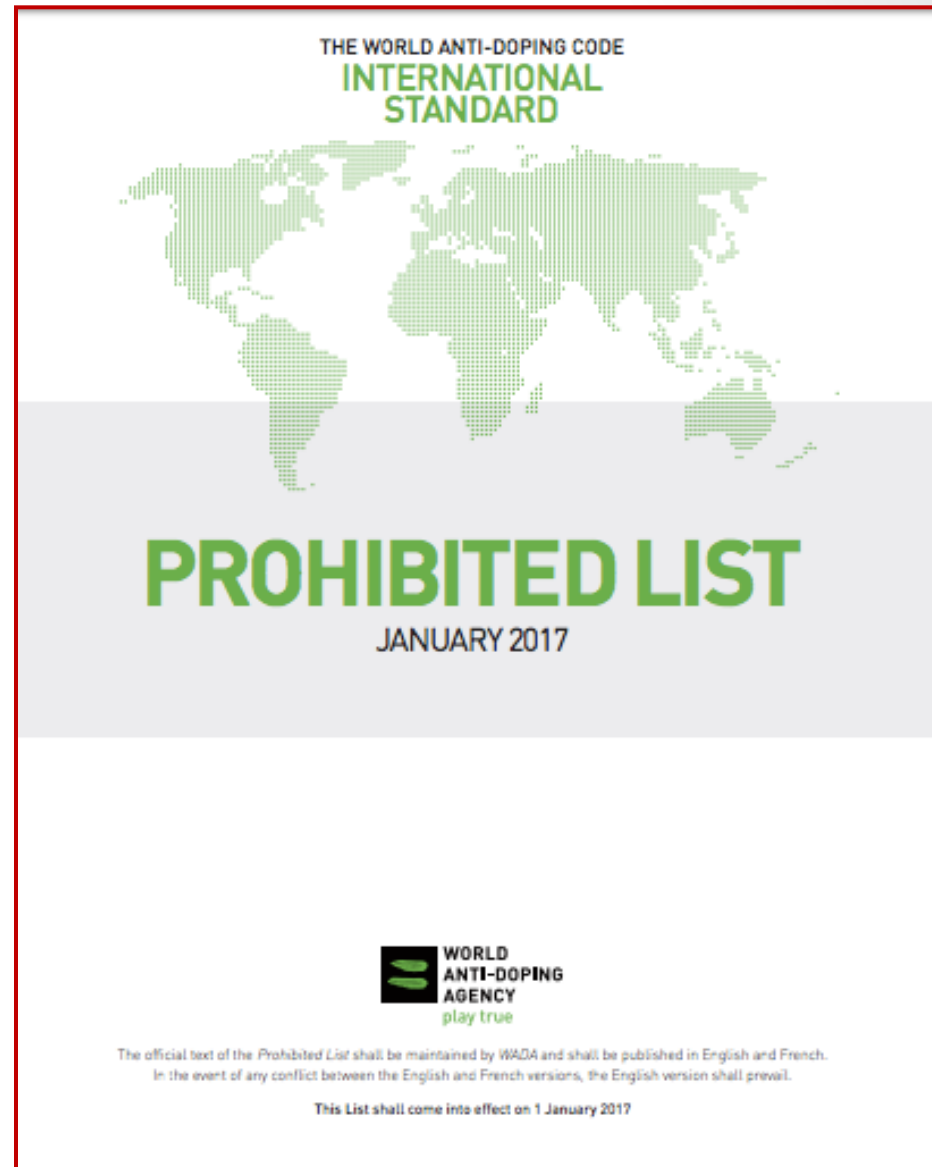
WADA's Prohibited List

Criteria for inclusion of a substance in Prohibited List
(NB: this refers to rule-violation 1.1)

1. (Potential) performance enhancement
2. (Potential) health risk
3. Violation of spirit of sport

NB: At least two (any two) of three must apply.

NB: The Code requires strict liability!



WADA on the 'Spirit of Sport'

FUNDAMENTAL RATIONALE FOR THE WORLD ANTI-DOPING CODE

Anti-doping programs seek to preserve what is intrinsically valuable about sport. This intrinsic value is often referred to as "the spirit of sport", it is the essence of Olympism; it is how we play true. The spirit of sport is the celebration of the human spirit, body and mind, and is characterized by the following values:

- Ethics, fair play and honesty
- Health
- Excellence in performance
- Character and education
- Fun and joy
- Teamwork
- Dedication and commitment
- Respect for rules and laws
- Respect for self and other *Participants*
- Courage
- Community and solidarity

Doping is fundamentally contrary to the spirit of sport.

Google 'WADA
Anti-Doping Code'

Strict liability in doping

Maria Sharapova Claims She Didn't Click The Link That Would Have Told Her Her Drug Was Banned



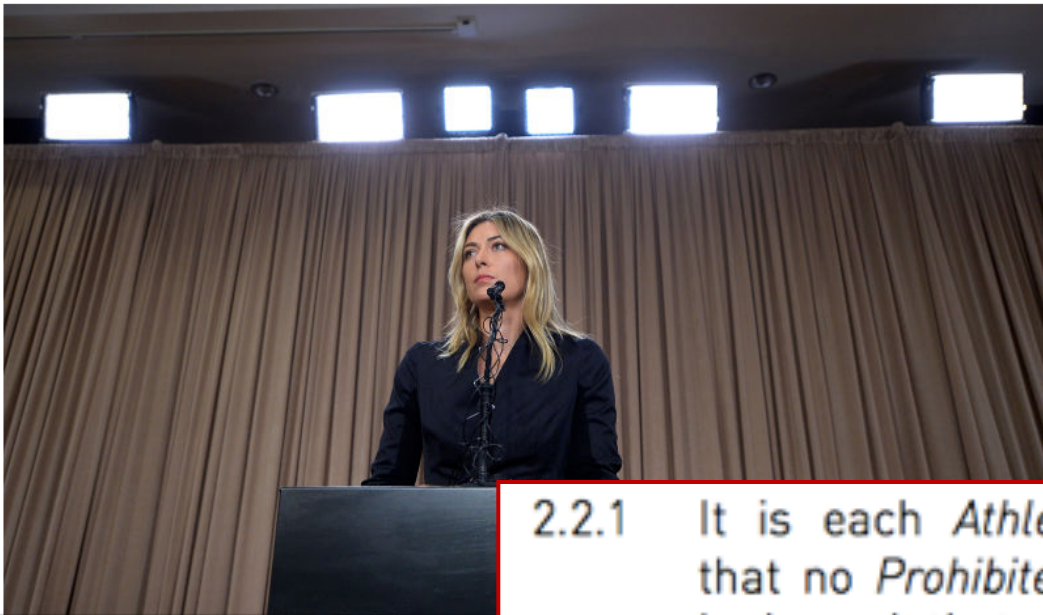
Barry Petchesky

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The 'concept of strict liability does *not* entail intentionality. A sanction is an inevitable consequence, if a doping offence has been established!

2.2.1 It is each *Athlete's* personal duty to ensure that no *Prohibited Substance* enters his or her body and that no *Prohibited Method* is *Used*. Accordingly, it is not necessary that intent, *Fault*, negligence or knowing *Use* on the *Athlete's* part be demonstrated in order to establish an anti-doping rule violation for *Use* of a *Prohibited Substance* or a *Prohibited Method*.

THE PROHIBITED LIST

The new **2017 Prohibited List** (effective 1 January 2017) can be downloaded and printed from the Resources section, or **consulted online**.



BACKGROUND INFORMATION

Since 2004, and as mandated by **World Anti-Doping Code**, WADA has published an annual List of Prohibited Substances and Methods (List). The List, which forms one of the **five International Standards**, identifies the substances and methods prohibited in- and out-of-competition, and in particular sports. The substances and methods on the List are classified by

different categories (e.g., steroids, stimulants, **gene doping**).

[https://www.wada-ama.org/sites/default/files/resources/files/2016-09-29 -
wada_prohibited_list_2017_eng_final.pdf](https://www.wada-ama.org/sites/default/files/resources/files/2016-09-29_-_wada_prohibited_list_2017_eng_final.pdf)

What is gene doping?



Brief (WADA) History of Gene Doping



- 1999: World Anti-Doping Agency (WADA) established
- March 2003: First WADA anti-doping CODE (WADC) and list of Prohibited substances released
- 2001 First working group on gene doping convened by International Olympic Committee
- **2003: Gene Doping inserted in WADA Prohibited List**
- 2004: Gene Doping “Expert Group” created with Theodore Friedmann as Chair (Director Gene Therapy Lab University of California, San Diego)

WADA Definition of Gene Doping

M3. GENE DOPING

The following, with the potential to enhance sport performance, are prohibited:

1. The transfer of polymers of nucleic acids or nucleic acid analogues;
2. The use of normal or genetically modified cells.

Gene Transfer for Athletic Enhancement: Targets

1. Growth Hormone (GH)
2. Insulin Growth Factor 1
3. Myostatin
4. Erythropoietin (EPO)
5. Vascular Endothelial Growth Factor (VEGF)
6. Endorphins

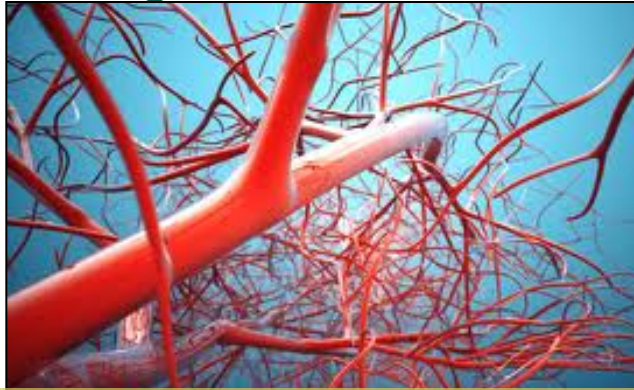


Above left, a 7-months baby with a naturally occurring mutation in myostatin gene. Above on right, transgenic mouse with the same engineered mutation.

Below, Belgian blue-cattle. Naturally-occurring mutations in myostatin gene dramatically increase muscle mass.



From bench to track & field: Gene transfer for pain in endurance events



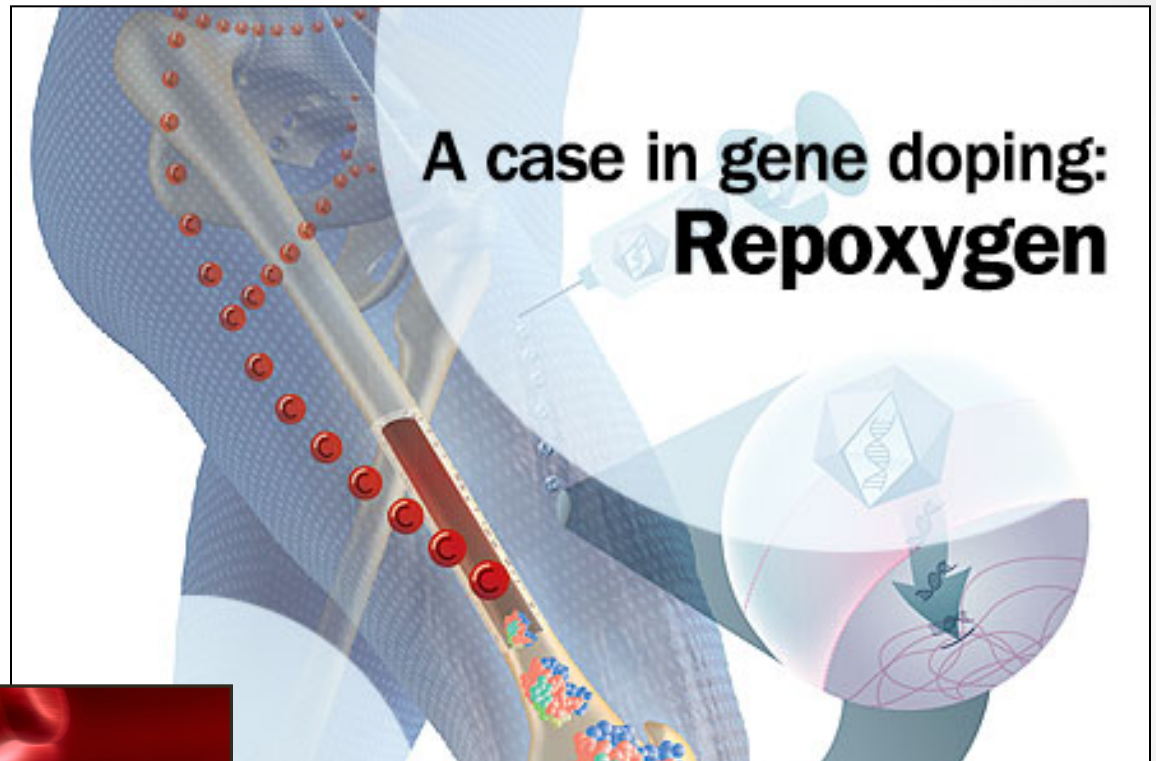
***GENE ENHANCEMENT
or GENE 'DOPING'?***



The precedent

Germany, 2006

Product of gene transfer formed by a retroviral vector carrying gene for human EPO (erythropoietin).



Was at that time in preclinical study to treat Fanconi anemia for pharmaceutical company Oxford Biomedica (UK).

What exactly is wrong with genetic enhancement?

WADA rationale for gene doping ban

“Gene doping represents a **threat to the integrity of sport** and the **health of athletes**, and as the international organization responsible for promoting, coordinating and monitoring the global fight against doping in sport in all its forms, WADA is devoting significant resources and attention to ways that will enable the detection of gene doping”

▪
(WADA Official Publication Play True 2008)



WADA finances anti-gene doping research

DEPARTMENT OF FORENSIC SCIENCE & DRUG MONITORING

ABOUT US

PEOPLE

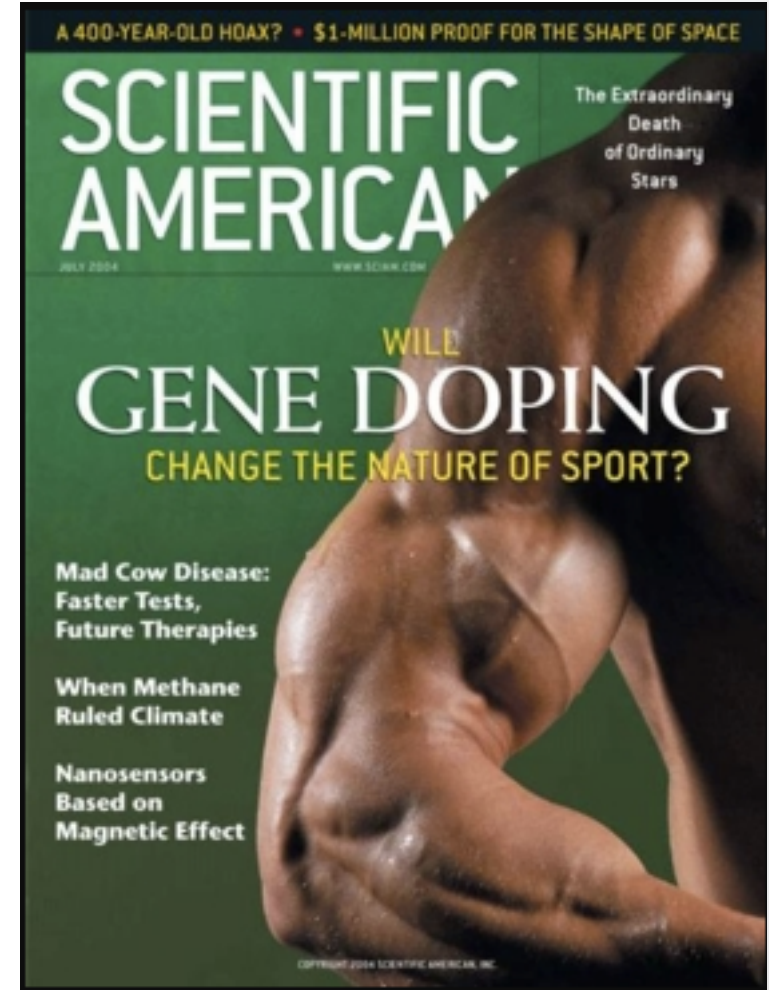
STUDY



Left, Dan Cowan, Director of *Drug Control Centre* at King's College, London, the only laboratory appointed by WADA for anti-doping control at London 2012.

Gene doping: A “bioethical” crisis of sport?

The bioethical crisis of sport is a crisis of human engineering in which our concept of human nature itself is at stake’ (John Hoberman, “Mortal Engines”).



*Genetic enhancement = unfair
advantage = Doping?*

A problem of fairness?



- “It might be argued that a genetically enhanced athlete would have an *unfair advantage* over his unenhanced competitors.
- But the fairness argument against enhancement has a *fatal flaw*... it has always been the case that some athletes are *better endowed genetically than others*, and yet we do not consider this to undermine the fairness of competitive sports.

(Michael Sandel, The Case Against Perfection, 2004)

Redressing the 'level playing field' in competition?

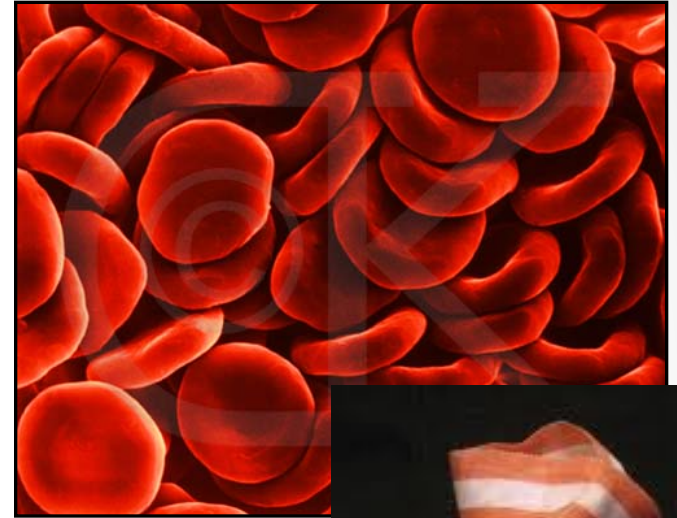


Genetic variations (1): unfair advantage?



Finnish skier Eero Mäntyranta, two gold medals at Innsbruck Winter Olympics, 1964.

Primary familial polycythemia: genetic condition causing increase in red blood cell production.



Genetic variations (2): unfair advantage?



Above: Michael Phelps: Marfan syndrome?

Left: NBA Basketball players with acromegaly

Genetic variations (3): unfair advantage?



Caster Semenya:
Hyper-androgenism.
800 m Gold medal at
Berlin World Track
Championship, 2009,
1:55.45 ;
800 m Silver medal
London Olympics
2012,
1:59.58

A problem of fairness?

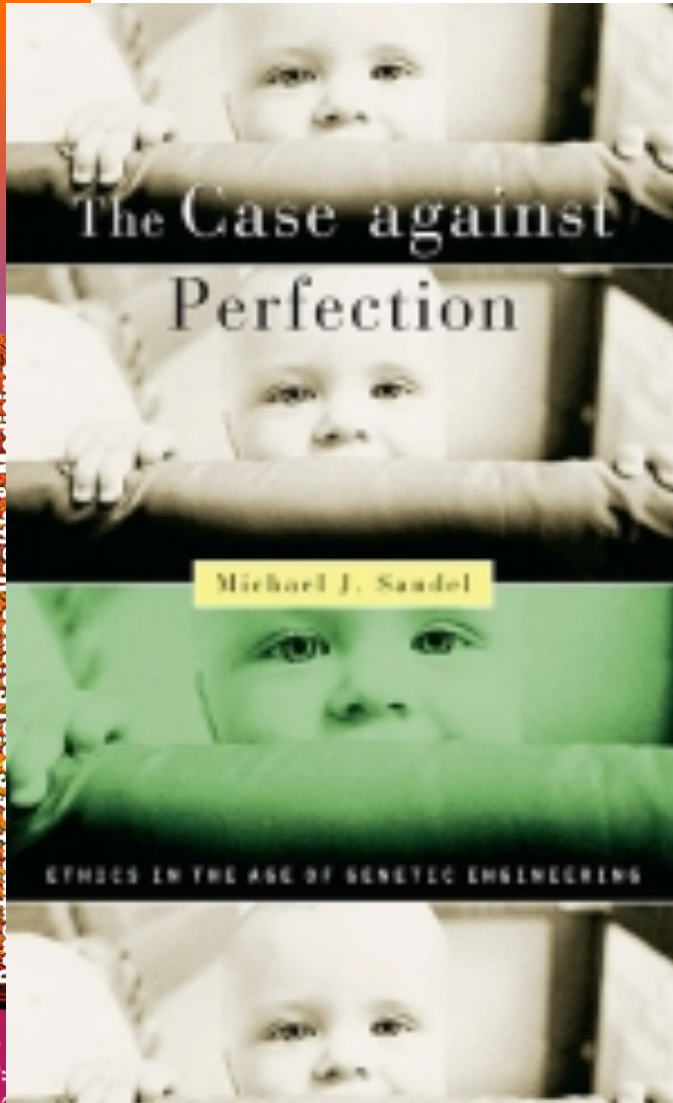


- But the fairness argument against enhancement has a fatal flaw... it has always been the case that some athletes are better endowed genetically than others, and yet we do not consider this to undermine the fairness of competitive sports.
- From the standpoint of fairness, *enhanced genetic differences would be no worse than natural ones, assuming they were safe and made available to all*".

(Michael Sandel, The Case Against Perfection, 2004)

*If it is not a problem of fairness,
then what exactly is wrong with
genetic enhancement?*

Corrupting the spirit of sport...



“The real problem with genetically altered athletes is that they corrupt athletic competition *as a human activity that honors the cultivation and display of natural talents*”.



The spirit of sport: the display of natural talents?



Le docteur Philippe TISSIÉ.
Phot. Panajou.

“Doping”, yesterday:

- For a long time, what we now consider ‘doping’ was viewed as a unremarkable way to extend the athlete’s capabilities, and sport was seen as the experimental terrain *par excellence*
- Trying to enhance one’s own athletic performance with any available means was understood as the natural human reaction to coping with fatigue: the *professional athlete* was using his own body as the *subject of experimentation*
- This identification of the athlete’s body with an experimental terrain can be dated back to 1894, when the pioneering French sports physician Philippe Tissié began to administer several types of beverages to cyclists to test their value as performance enhancers.

“Doping”, yesterday: The athletic body as a subject of self-experimentation...

1904-1920 - Performance Enhancing Drugs Used in the Modern Olympic Games

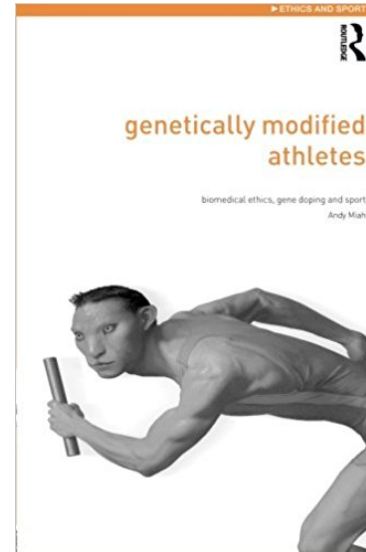
"In 1904 Olympics marathon runner, Thomas Hicks, was using a mixture of brandy and strychnine [a stimulant that is fatal in high doses] and nearly died. Mixtures of strychnine, heroin, cocaine, and caffeine were used widely by athletes and each coach or team developed its own unique secret formulae. This was common practice until heroin and cocaine became available only by prescription in the 1920s."

Right: Thomas Hicks, A Cambridge athlete, won the marathon at the 1904 Olympic games in St Louis, Missouri, with the help of **raw egg, strychnine and shots of brandy** given to him at regular intervals by his coach.



Gene Transfer to Enhance Athletic Performance = Innovation?

Gene doping: enhancing the spirit of sport?



Professor Andy Miah, Ethics of Emerging Technologies, University of Glasgow:
“Genetic enhancement should be understood as a form of *innovation in sport*, alike to ‘the development of fibreglass poles in pole vaulting, or Fosbury flop in high jump’. [...] *It allows the pursuit of excellence in sport by allowing athletes to train longer and harder*”

Strategies & Difficulties for Detection



- Viral markers expressed for a short time
- Use of non viral vectors
- Muscular biopsies not feasible as means of detection
- CRISPR Genome Editing: sequence identity

Unjustified Optimism?



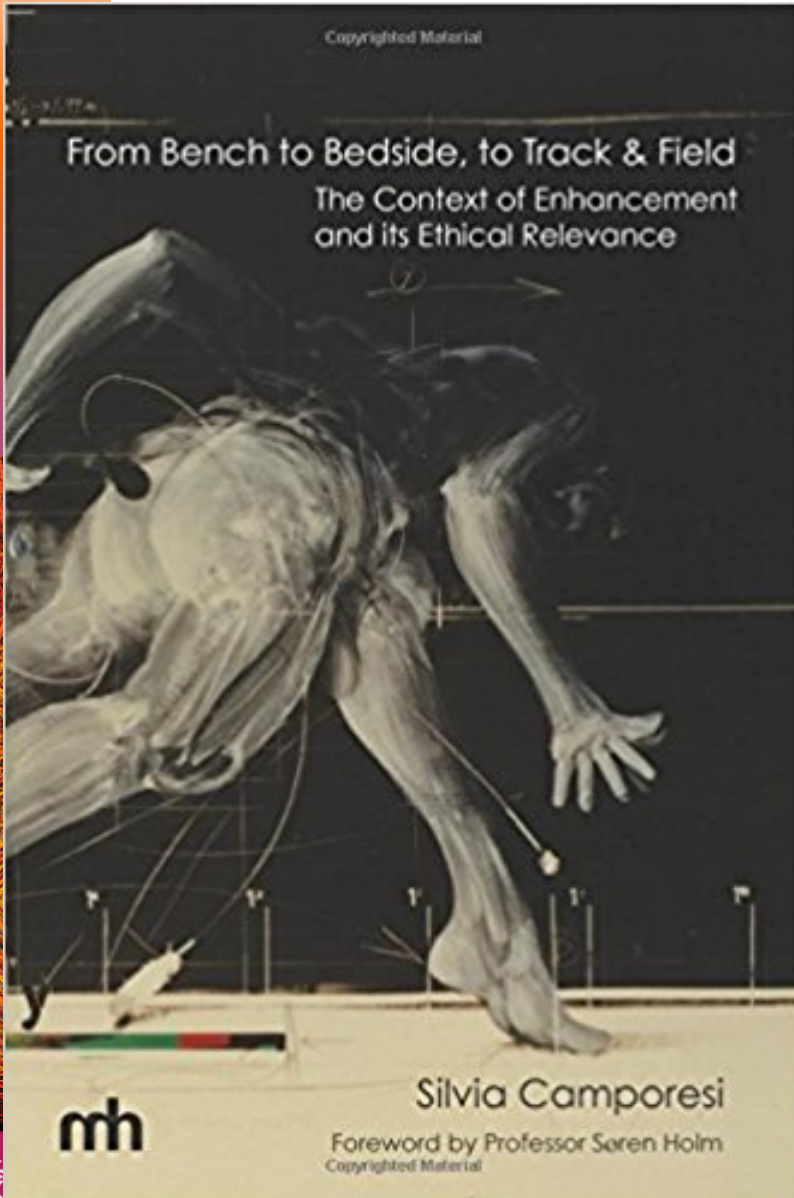
“This is a project [development of strategies for anti- gene doping] where WADA is actively involved since 2002. We are now at the point where we are quite confident it can be detected.”

(interview to ‘The Telegraph, 2009)

Above, David Howman, former President of WADA

Gene Transfer to Enhance Athletic Performance = Innovation, or Doping?

What do you think?



Thank you!

silvia.camporesi@kcl.ac.uk

[@silviacamporesi](https://twitter.com/silviacamporesi)

The solution to doping crisis: lifting the ban on doping?

Foddy and Savulescu's arguments (2004, 2010, 2016):
libertarian's perspective

1. We should give up the principle that anything that enhances performance is against the spirit of sport
2. Athletes should be allowed to take performance enhancing drugs as long as they are 'safe' (where the bar of safety "should be set at the level we allow athletes as persons to take risks")

Hence, 3. We should put 'doping under a medical context' and allow athletes to take risks compatible with other risks that we allow people to take in other realms of life

2. What would happen if doping were put under a medical context?

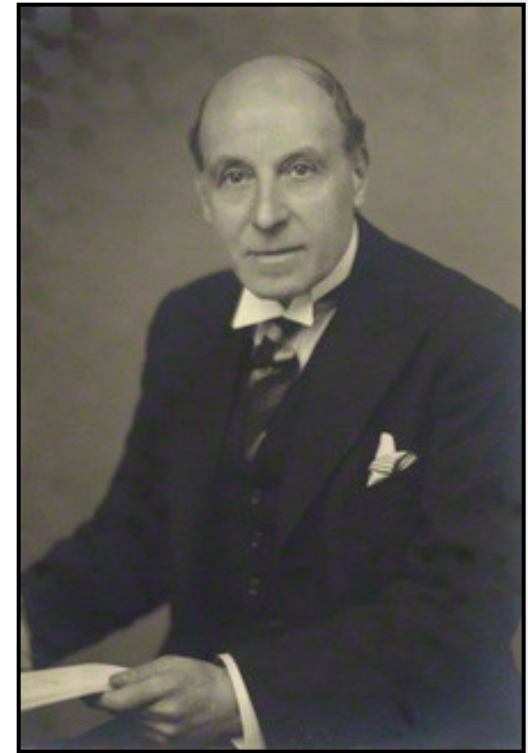
1. Athletes have strong incentives to keep doping practices secretive. Holm (2007) identifies these incentives as an instance of a 'take and hide' option that dominates other options in a Prisoner's Dilemma-style coordination game, the other options being not doping or doping and being open about it.
2. In addition, the athlete's income is controlled by his/her employer (e.g. team and, ultimately, sponsor, or federation), and the degree of control that the athlete has over the decision to play/to compete is limited (same point as Atry 2013, Camporesi and McNamee 2012).

Performance Enhancement, or Doping?

“It is not easy [...] to draw the line where **legitimate stimulation** ends and **reprehensible ‘doping’** begins; the distinction is largely a matter of opinion and of conscience”.

(Sir Adolphe Abrahams 1958)

Sir Adolphe Abrahams, an Honorary Medical Officer to the International Athletics Board and the British Olympic Team



Sir Adolphe Abrahams
by Walter Stoneman
© National Portrait
Gallery, London

Athletes: from 'amateurs' to 'freaks'



2. What would happen if doping were put under a medical context? (2)

1. Secretiveness is essential to maintain a competitive advantage and for professional athletes the option “take and hide” would be the most rational (instance of a game-theoretical problem)
2. As long as the pay-off matrix of professional sport remains unchanged, lifting the ban on doping would not lead to ‘safe doping’ under a medical context (as Savulescu/Foddy argue) but would lead to a 2-tiered system of doping
3. Holm concludes that lifting the ban on doping will lead to a two-tiered system and that the only way to curtail doping is to change the “payoff matrix” of professional sport. In this paper I reason on the basis of Holm’s premise.

How to break an unsustainable system

1. Professional sport is unsustainable
 - a. Athletes discount future health to gain a short-term competitive advantage (empirical data)
 - b. The professional sport system always requires new records (incentives doping)
 - c. Hence professional sport incentivises discounting of future health of athletes
2. How can we make professional sports sustainable?
Provided that lifting the ban on doping won't do it, what else could we do?

We need to change the financial matrix of doping in sport.