

Drugs, sex, and enhancement: Threats to sports integrity at the Olympics

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BACKGROUND

The Olympic Games represents a majestic sporting showcase on a uniquely global scale. The Paris 2024 Olympics could mark the start of a new era for the Olympic Movement. This viewpoint focuses on three existential threats to modern Olympic Games: doping, gender issues, and enhancement, while cut-ting-edge research and science need to be at the heart of a concerted reaction to restore integrity of competition and protect the concept of "true" sport. Performance enhancement in the context of sport denotes or relates to a drug or other substance or method used with the prospect of improving an athlete's performance; specifically, substances and methods that enhance any number of components of physical and mental performance, such as agility, speed, strength, power, endurance, and competition preparation and execution.

ANTI-DOPING CHALLENGES

The World Anti-Doping Agency (WADA) was established in 1999 to harmonize doping control and provide educational strategies to avoid doping. However, some 20 years later, the prevalence of doping in sport has not substantially abated. While the true prevalence of doping in sport is impossible to accurately determine, it is substantially higher than the adverse analytical findings reported. For example, the figures for adverse analytical findings have varied between 1.1% (2008) and 1.6% (2016), while a recent large systematic review of 175 studies published between 1975 and 2019 reported doping prevalence rates in competitive sport ranging from 0% to 73% for doping behavior, with most falling under 5%.¹ It is important, therefore, that new methods are developed with greater sensitivity and specificity to detect blood doping—a method of choice by those wishing to cheat and gain a significant performance advantage (Figure 1).

Despite a number of positive developments in anti-doping, the last major development aimed at providing a step change in blood doping detection was the Athlete Biological Passport (ABP) and implemented in 2009. While urine testing is the main method of detecting recombinant human erythropoietin (rHuEpo), its relatively short window of detection (less than 24 h in some cases) renders this method ineffective for blood doping detection. The hematological module of the ABP uses Bayesian inference techniques and longitudinal measurements of blood parameters. Despite its appeal, the ABP has important limitations due to the simplicity of metrics and its impact by confounding factors such as hydration status and the natural hematological response to altitude training that complicate interpretation of ABP profiles. The ABP is also unable to effectively detect administration of micro-doses of rHuEpo, given the relatively small fluctuations in hematological parameters.² Therefore, there is an urgent need for a paradigm shift away from "in sport, the cheats are usually a step ahead" to "in sport, the testers need to be a few steps ahead."

A potential game changer that has, until now, not been used substantially in the anti-doping field is "omics" technologies: genome, transcriptome, proteome, and metabolome. In a series of closely interconnected studies conducted in our laboratory and funded by WADA and the International Olympic Committee (IOC) using "omics" from microarrays to RNA sequencing technology, we successfully identified, replicated, and validated the blood "molecular signature" of rHuEpo administration,³ indicating that "omics" technologies can improve current anti-doping methods such as the ABP. The results we have generated to date,



Figure 1. Joint efforts from athletes, scientists, and cutting-edge research for the integrity of Olympic sports replicated by others, confirm that it is only a matter of when rather than if "omics" methods will revolutionize anti-doping.

GENDER ISSUES: INTEGRATION OF INTERSEX AND TRANSGENDER ATHLETES INTO ELITE SPORT

Sport is historically designated by binary categorization of male and female that conflicts with the science of sex and modern society. This frequently overlooked fact, appreciated since antiquity, has come to the fore more recently with attempts to include transgender athletes and athletes with differences in sex development (DSD) into elite sports.⁴ The issue is that the performanceenhancing effect of testosterone, which is widely accepted in the literature, and the exposure to higher concentrations of testosterone in trans women and DSD women athletes is expected to provide a competitive performance advantage. This expectation has led to an ever-increasing number of international federations (IFs) banning participation of trans female athletes in elite sports, and the same expected for DSD athletes. While these policy rules and their backing assumptions to primarily ban these athletes from competing may, in time, be proven correct, until data from longitudinal transgender and DSD athlete case comparison studies that control for variations in hormonal exposure and involve numerous indices of performance become available, there is just as much circumstantial evidence to support the policy to ban these athletes than there is to oppose it. The International Federation of Sports Medicine (FIMS) published its position with the European Federation of Sports Medicine Associations on the IOC framework on fairness, inclusion, and non-discrimination based on gender identity and sex variations, highlighting the need for innovative longitudinal research studies with specific athlete populations to generate physiological and sport performance knowledge and more reliable biomarkers for a fairer classification of athletes. The statement highlighted the fact that serum testosterone can be a valuable marker to regulate the inclusion of transgender athletes and DSD athletes into the elite female category but has limitations due to the multifactorial nature of sports performance. This led the authors of the joint position to conclude that longitudinal and sport-specific gender affirmation hormone therapy studies are needed to enhance our knowledge of impact of testosterone on performance and identify biomarkers of testosterone sensitivity/responsiveness, including molecular tools to determine the functional status of androgen receptors. Subsequently, the IOC published its position after consulting with many stakeholders, including FIMS. In general, it re-affirmed the position of FIMS but, also, importantly, assigned to individual IFs the responsibility to establish their own rules to ensure equitable and fair competition. How this complex situation resolves will depend on the outcomes of research studies using appropriate experimental designs and state-of-the-art technologies that remain to be commissioned and how individual IFs prioritize fairness, safety, and inclusion in sport. There is also the need to consider the ever-changing legal landscape, where more and more countries are supporting the right to self-identify. Policy makers must also consider the Olympic Charter, which clearly stipulates that "The enjoyment of the rights and freedoms set forth in this Olympic Charter shall be secured without discrimination of any kind, such as race, colour, sex, sexual orientation, language, religion, political or other opinion, national or social origin, property, birth or other status."

ENHANCED GAMES

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The Enhanced Games is a planned annual international event involving five sports (track and field, swimming, gymnastics, weightlifting, and combat sports), masterminded by Aron D'Souza, an Australian businessman, where athletes will not be tested by WADA. The premise of the Enhanced Games is to safeguard athlete health while upholding the principle of personal choice to use any enhancements. Despite much opposition, the inaugural event is destined to happen in 2025. The primary concern, especially of the sports medicine community,⁵ is the health hazards of drug use in young aspiring athletes, who could be exploited in the quest for fame and fortune and the allure of the Enhanced Games. Although the Enhanced Games plan to conduct medical screening capable of discovering possible health risks for competitors, it is obvious that medical screening is insufficient to detect the side effects of many banned substances and methods. Many health side effects of banned substances and methods can be expected only after several years of use and not even with a most comprehensive medical assess-

ment after only short-term use; for example, psychiatric disorders induced by anabolic-androgenic steroids or the risk of hepatocellular carcinoma.

Despite what one may think about the Enhanced Games, ironically, its launch may help detect those who cheat by better understanding the methods used to dope. Due to the secrecy of the drug culture in sport, there is limited knowledge about sophisticated doping practices. A particular difficulty in anti-doping science is the inaccessibility to samples from doped athletes to allow new testing to be developed, improved, and perfected. With this in mind, the Enhanced Games could bring doping into focus, where it can be properly studied, but this would involve an uncomfortable evolution of anti-doping science so ethical research could be conducted during doping associated with the Enhanced Games to allow anti-doping science to better understand the life cycle of different substances and/or methods and their effects on elite performance and health. This partnership of convenience between the Enhanced Games and anti-doping organizations could result in smarter, more effective ways to detect drug use in sport while at the same time informing athletes about the true adverse health effects of drug use.

PROTECTING THE CONCEPT OF "TRUE" SPORT

In this viewpoint, we highlight three major threats to the future of the Olympics, but we also highlight solutions that are firmly based on science, experimentation, innovation, and application of cutting-edge technologies. Common to the doping and gender issues we address, it is the real or perceived unfairness that underpins both of these existential threats for Olympic sport, but also limited consensus on what constitutes "fairness." Part of the confusion is due to the use of terms to set the rules of sport, such as "the spirit of sport," that have no universal meaning. For example, WADA states that anti-doping policies have been developed to protect certain values in sport. The World Anti-Doping Code 2021 states that "The spirit of sport is the celebration of human spirit, body and mind. It is the essence of Olympism and is reflected in values we find in and through sport, including: Health; Ethics; fair play and honesty; Athletes' rights as set forth in the Code; 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. The spirit of sport is expressed in how we play true. Doping is fundamentally contrary to the spirit of sport." But such descriptions can only serve their purpose if these terms mean the same thing to different societies and people, which clearly is not the case. For example, the Enhanced Games use the same term, "spirit of sport," very differently. The only way forward is for each sport to decide what constitutes the "true" essence of their sport and prioritize its main constituents, such as inclusion, safety, and fairness. Such a decision-making process to achieve meaningful competition is already being explored in the integration of trans women into elite competition. Once there is consensus, it is essential that all stakeholders who participate in that sport must agree to play by the rules, and these rules need to be enforceable so that everyone has a chance to succeed, albeit not an equal chance. This decision-making approach and a concerted effort involving cutting-edge research and scientific data are urgently needed and represent the best response to the three major threats to integrity of competition we will witness in Paris in 2024.

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