Too fast to be female?
Unravelling the controversy over androgens in female elite athletes

ABSTRACT

Told through the example of South African middle-distance runner Caster Semenya, this discussion starter examines the controversial area of gender in sport from a scientific viewpoint. Women have been segregated from men in most sporting disciplines for as long as they have been permitted to compete, but seated in a society only just beginning to delineate the concepts of sex and gender identity, consensus needs to be reached on how or if we should categorise elite athletes, whilst upholding the integrity and fairness of competitive sport. The parameters used to sort athletes into today’s binary gender categories have recently come under scrutiny in the cases of athletes with Differences of Sex Development (DSD). Semenya has elevated serum testosterone and her eligibility to continue competing and winning with females has now been brought into contention by the IAAF resulting in a legal battle. However, the scientific evidence on which the IAAF ruling is based is far from robust. Athletics, a sport tainted by a history of doping with anabolic steroids, is fighting to maintain values of fairness by aiming to govern the levels endogenous steroids permitted in competition. Semenya’s is a pertinent example of a wider issue which is of interest from a scientific, ethical, political, legal and social standpoint because of the complexity of hormone systems and the fact that circulating levels of hormone do not necessarily equate with actions of those hormones. With confusing mainstream media coverage lacking consensus, the scientific community deserve clarity on the issue to allow us to engage in meaningful discussion and contribute to the debate.
INTRODUCTION

As the president of the International Association of Athletics Federations (IAAF) Lord Sebastian Coe put it: “It’s pretty straightforward. Athletics has two classifications; it has age and gender.” (1) However, far from straightforward is the matter of how we define these currently binary male/female categories in sport. In light of the new competition eligibility regulations released by the IAAF in April 2018, focused on regulating the levels of testosterone in female athletes with differences of sex development (DSD) that are permitted to compete, (2) the topic is more controversial than ever. This discussion takes place in the context of a progressive society with an increasing acceptance for values of feminism and gender-equality, which is only beginning to understand the complexities of gender as a fluid concept.

For the purposes of this article:
• ‘Sex’ – the biological classification largely considered binary in terms of male/female as comprised of chromosomal, phenotypic and hormonal components
• ‘Gender’ – one’s own identity in relation to masculinity and femininity, self-defined and nuanced within social and cultural influences

It is indisputable that taking performance-enhancing anabolic steroids in sport is immoral and considered ‘doping’, but how do we manage and classify athletes, specifically females, who synthesise an excess of these steroids naturally? The issue of gender and sport has generated significant public attention, and although caught up in legal battles themselves, the individual athletes it affects the most have become involuntary figureheads of mainstream media campaigns surrounding the issue. Whilst those in media and sport are quick to discuss the topic through the stories of these athletes, largely left out of the debate has been the scientific community, who could be instrumental in providing the biomedical expertise and objective oversight that this dispute necessitates.

A QUESTION OF SEX (3)

Women have been segregated from men in all competitive sports since their inclusion has been permitted, with a few notable exceptions including equestrian and mixed pair events. Differences in human physiology based on sex, which give men a physical advantage in many competitive sports, forms the basis of this segregation. However, with any categorisation, a sorting process must occur. Physical examinations were relied upon in the 1960s to prevent men competing as women; these were later replaced by buccal smears to identify sex chromosomes – but the smears were considered unreliable, so the IAAF abandoned them in 1991. Genetic testing is also inherently flawed in some DSD athletes, since XY individuals can develop female characteristics due to androgen insensitivity and conversely, XX individuals can develop male characteristics due to hyperandrogenism for a number of reasons – congenital adrenal hyperplasia, for example, where there is an excess of androgen because of a genetic biochemical aberration in steroid hormone.

Currently, there are no IAAF rules to endorse standard sex testing, since men attempting to compete as women would presumably be identified in anti-doping urine tests. However, any athlete can be asked in front of a medical panel including an endocrinologist, a psychologist and a gynaecologist should their sex be challenged. Since androgens are responsible for the development of many of the advantage-conferring male characteristics in either sex, testosterone is the IAAF’s chosen route on which to base their regulation. Such a binary classification system inevitably runs into trouble when it invites a global population which doesn’t fit neatly into two categories to compete. Does such a system become discriminatory when it doesn’t include transgender and intersex members of society, or subjects them to rigorous medical testing that other athletes would not be subject to?

THE NEW REGULATIONS

Summarised in Box 1 are the current IAAF regulations as released in April 2018 and refined in 2019, stating that DSD female athletes are only permitted to compete in competitive sport with medical intervention. It is important to understand the historical context which shaped these regulations. First mention of ‘Hyperandrogenism Regulations’ by the IAAF was in May 2011 following the emergence of Caster Semenya at the 2009 Athletics world championships in Berlin, winning the 800m gold at the age of 18. (4) The regulations stated that any athlete, female in law, with hyperandrogenism would only be permitted to compete if their testosterone was below the ‘male range’ defined as <10 nmol/L or within the ‘male range’ and have an “androgen resistance such that she derives no competitive advantage”. (5)

2015 saw the landmark case of Dutee Chand, a hyperandrogenic female Indian athlete who was one of the first from her country to reach a global sprinting final in 2013, get caught in a legal dispute against the IAAF and her home institution of the Athletics Federation of India who demanded she take a gender test after her elevated serum testosterone was discovered. (6) Chand won her appeal on the grounds of the IAAF providing the panel with insufficient scientific evidence to support their 2011 hyperandrogenism regulations – specifically the exact degree of advantage which testosterone gave hyperandrogenic female athletes. The Court of Arbitration for Sport therefore suspended the ‘Hyperandrogenism Regulations’ for a period of two years during which the IAAF was expected to provide written evidence to support them, leaving Chand free to resume competing. “I am who I am” she stated at the time. (6,7)

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During that two years (which was eventually extended to three) the IAAF commissioned two scientific papers to provide a foundation for their revised and most recent regulations on DSD athletes as summarised below. (8,9) The integrity of this research has since been scrutinised by experts. (4) The regulations propose potentially effective methods to reduce testosterone to below the 5nmol/L limits as oral contraceptives, GNRH agonists (akin to those used to treat prostate cancer) and even gonadectomy. (8) However, it advocates the use of oral contraceptives which “are generally milder and have less significant side effects”. (7) Combined oral contraceptives reduce both ovarian and adrenal endogenous androgen production. (10) It justifies the ruling as risk-acceptable due to the fact testosterone reduction is the clinical standard of care for these 46 XY DSD conditions.

**SEMENTYA’S STORY**

Mokgadi Caster Semenya became known on the global athletics stage at the Berlin World Championships in 2009. But instead of being known for her outstanding success of an 800m gold at the age of 18, the South African’s achievement soon became overshadowed by becoming the unwilling face of the dispute over hyperandrogenous female athlete. Her gender began to be scrutinised by the world, and Semenya stated that she was facing “relentless public scrutiny”. (7,11) The greatest backlash, however, came from her fellow competitors: “These kinds of people should not run with us” said Italian athlete Elisa Cusma. (12) “Just look at her…” said Russian fifth place finisher Mariya Savinova, who ironically later had her London 2012 gold removed for illegal doping, whilst Semenya’s silver medal was subsequently upgraded. (13,14)

Figure 2 details a timeline of Semenya’s milestones over the last decade; she has been in a battle with the authorities ever since being questioned about her gender in 2009. Semenya is a cisgender woman, a female by law and assigned at birth. Her medical records are rightly confidential, however, there has been significant media speculation over what may have caused her to have an ‘androgenous physical appearance’. Given that the DSD regulations have been applied to her, it has been assumed that she is 46XY with DSD. (2,6,7)

One can often empathise with Semenya once understanding her legal battle against the IAAF over her right to race; almost half of her time since its beginning has been spent taking testosterone-suppressing medication. (7) There was no established clinical protocol at the time to lower testosterone to <5 nmol/L in an a 46XY DSD athlete, therefore Semenya’s treatment has been somewhat experimental. The ASA contended she did not give informed consent for the participation in the IAAF research. (7) She suffered a range of side effects including weight gain, nausea, fevers and constant abdominal pain (some of this would be attributable to withdrawal from testosterone), which affected her mental and physical commitment to training. (7) On the other side of the case, the IAAF claim that the DSD regulations are “to give female athletes the same opportunities to excel and profit from the sport as male athletes” claiming they “do not involve any judgement on or questioning of an individual’s sex or gender identity.” (7)

**Box 1**

Summary of the current IAAF regulations for eligibility for DSD athletes refined in 2019. (8)

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**Figure 1**

Summary of the normal physiological pathway of androgen synthesis, blue text represents enzymes
Masculinisation of females can arise from the delivery of ‘male’ doses of testosterone (or a synthetic analogue) orally, trans-dermally, or intramuscularly as demonstrated by the historical example of Andreas Krieger (previously European shot-put champion Heidi) in the East German doping scandal of the 80s. (6) Testosterone is a potent androgen transported freely in the blood or bound to sex hormone binding globulin (SHBG), and contributes to the development of male secondary sexual characteristics. (16) Its relevant qualities here are derived from its anabolic action on skeletal muscle, increase in circulating haemoglobin, and inhibition of adipogenesis explaining its exogenous use as a performance-enhancing drug – it has received extensive press coverage in doping scandals. (16) For an outline of the cellular effects of testosterone, see figure 3.

After the Chand ruling, the main paper released by the IAAF was published in the British Journal of Sports Medicine, which we shall refer to as BG17. (17) A second paper was published a year later in response to criticism (BHKE18), which acknowledged methodological changes which led to changes in calculated performance differences compared to BG17. (4,18) The research found that based on 21 athletic events, female athletes with higher serum free testosterone performed significantly better (p<0.05) in 400m (2.73% margin), 400m hurdles (2.78%), 800m (4.53%), hammer throw (4.53%) and pole vault (2.94%). (17) Chand’s sprinting distances did not feature in the testosterone performance-enhancing events, hence why the DSD regulations focus on middle distance events. Interestingly, of the aforementioned events which did show testosterone-related performance differences, higher testosterone conferred the smallest advantage in Semenya’s event (800m). Despite having shown a significant testosterone-related performance difference in both the hammer throw and pole vault, the IAAF has decided to feature neither of these field events in their DSD regulations. Semenya commented “it feels like this new rule was created because of me”. (7)

This work was conducted by those with a conflict of interest and has been methodologically criticised, with many academics arguing that it is inherently flawed. (19–21) Given its importance, it is imperative that this research is held to high bioethical standards, and the only way to do this is by the involvement of the scientific community. Professor Roger Pielke Jr. of the University of Colorado and director of its sports governance centre, who also acted as an

Figure 2
Timeline of key events in Caster Semenya’s running career and dealings with the IAAF, adapted from (7,15).

Figure 3
Schematic diagram detailing the anabolic mechanisms by which androgens increase muscle mass. AR = androgen receptor (16).
expert witness for Semenya in her CAS case against the IAAF, responded to a question about the integrity of the research: “We wouldn’t want tobacco companies doing research on health effects of cigarettes. This is the same.” Professor Pielke wrote a thought-provoking piece for Nature on the topic, explaining how the IAAF have violated the principles of the Helsinki declaration in their research process, highlighting the risks of implementing sports policy sanctioning ‘unproven interventions’. (22)

Further, the ‘cut-off’ testosterone level chosen by the IAAF is arbitrary. We have no substantial evidence on the effects of testosterone suppression in this DSD group as interventional placebo-controlled studies aren’t practically or ethically feasible. 5 nmol/L was lowered (after the original 10 nmol/L before the Chand ruling) based on the data from Handelsman e. 2018. (23) which actually used performance data from Semenya herself and other athletes who underwent testosterone suppression before the Chand ruling. The paper derived a bimodal distribution of testosterone concentrations in healthy men (7.7-29.4 nmol/L) and healthy pre-menopausal women (0-1.68 nmol/L) and by making an allowance for women with PCOS and mild hyperandrogenism, decided the cut-off should be 5 nmol/L. Based on healthy subjects from the general population, this data may not be directly applicable to elite athletes or those with DSD, and these ranges are not consistent with a more recent review. (24) It is very difficult to ascertain an absolute threshold for a measurement that displays natural variation in the population, and evidence on DSD athletes is extremely limited. However, it is vital that the IAAF is completely informed before sanctioning medical interventions and enforcing bans on athletes in order maintain testosterone below an arbitrary level.

**DISCUSSION**

Success in elite sport is a product of a range of environmental and genetic factors, and testosterone is a significant but by no means the only influence on this. By following the precedent set by the DSD regulations, do we need to look at other sports and correct other physiological advantages? It would certainly be ethically controversial to approach a successful swimmer and impose a medical intervention to suppress their elevated haemoglobin. Sport can never truly be ‘fair’, it relies on natural and environmental advantages to separate those who emerge victorious. If we continue to correct for biological advantage, could we eventually homogenise the field?

It is thought provoking to ask: if Semenya hadn’t been so successful in her sport, would the new DSD regulations and the controversy surrounding the entire issue exist? We may question whether the regulations are discriminatory based on appearance: not all females get tested so it relies on singling out athletes who have a phenotypically ‘male’ appearance. One of the reasons these regulations are so controversial is the fact testosterone are seen to have a fair advantage, whereas female athletes’ testosterone-conferring advantage is seen as needing intervention.

The World Medical Association (a partner organisation to the WHO and Global Health Workforce Alliance) displayed ethical concerns, stating: “Medical treatment for the sole purpose of altering the performance in sport is not permissible.” (22) Are the IAAF displaying double standards by banning the use of performance-enhancing drugs whilst condoning the use of performance-diminishing ones? No treatment comes without side effects, and we need to weigh up the benefits of protecting the female sporting category against the risks of physical side effects of testosterone withdrawal and potential thromboembolic events in the case of oral contraceptives, in addition to the psychological distress of subjecting them to intimate examinations and gender verification proceedings. (7) It is important to remember that running for these women is not only a passion, but their means of making a living – the judiciary panels owe them a wholly informed decision.

At the core of this debate is what it means to be female. The more this is discussed it emerges that this definition may not be the same in every context. Sex is a combination of genetic, hormonal, psychological and physical components, and what it means to be female in sport may be different to what it means in law, or genetics, for example. As a society we are discovering that what makes the topic of sex and gender so interesting is how it is not binary as traditionally thought. No Y chromosome per se gives you the advantage to win a race. Perhaps the Paralympics are ahead of able-bodied sport in the way that they allow multiple sub-categories within genders and event types, to reflect the diversity of society.

What is non-negotiable in this debate is that these athletes deserve to be treated with sensitivity and respect. We cannot influence individual cases if we are not professionally involved, but we can hold the organisations in charge to the bioethical standards that we expect in all medical research and care, to ensure fairness in the treatment of future athletes. This is clearly a challenging issue that would benefit from the sporting, legal, and medical communities working together to provide the expertise required to reach the best possible outcome. No matter what our opinion as healthcare professionals, the discussion can benefit from further input. Amidst the controversy, much can be learnt from Semenya’s case: an athlete who simply wants to run “free of drugs, free of speculation and free of judgement”. (7)

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