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·*Review*·

Olympic sports and transsexuals

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Abstract

Sex segregation in competitive sports is regarded as fair. Before puberty boys and girls do not differ in height, muscle and bone mass. Testosterone (T) exposure during puberty leads to an ultimate average greater height in men of 12–15 cm, longer and larger bones and muscle mass and strength and higher hemoglobin levels. Postpubertal androgen ablation reverses, at least in part, previous anabolic effects of T on muscle, bone mineral density and hemoglobin but the long bones remain longer and wider. T administration dose dependently increases muscle mass and maximal voluntary strength. Therefore, exogenous androgens, being performance enhancing drugs, are banned for all athletes. An issue is the participation in competitive sports of people with errors of sexual differentiation and particularly transsexuals who have been sex-reassigned. In view of the effects of T, a clear demarcation is whether sex reassignment has taken place before or after hormonal puberty. Pubertal effects of T are in part reversible but there is no reliable evidence as to its completeness. The International Olympic Committee (IOC) has taken an inevitably arbitrary decision with regard to participation of sex-reassigned transsexuals in elite sports: sex reassignment must have taken place at least two years earlier, hormone treatment must be appropriate for the reassigned sex and the reassigned sex must be legally recognized. The IOC policy is not binding for other organizations. *(Asian J Androl 2008 May; 10: 427–432)*

Keywords: sports; sex difference; gender; testosterone; muscle

1 Introduction

There is wide agreement that sex segregation in competitive sports is defensible and fair. As adult men have inherent performance advantages over women due to their average greater height and muscle mass and power, sex specific competitions provide women with a countervailing advantage.

This difference is largely based on correspondingly different exposures to androgens from the onset of puberty. Before puberty boys and girls do not differ in height, muscle and bone mass [1] though girls have more truncal fat. Testosterone (T) exposure during puberty leads to an ultimate average greater height in men of 12–15 cm, larger and longer bones and muscle mass and strength and higher hemoglobin levels. Clinical and experimental studies show that androgen deprivation reverses, at least in part, previous anabolic effects of T on muscle, bone and hemoglobin [2]. But the pubertal effects of T producing a greater length, diameter and thickness of bones in men, is not reversed upon androgen ablation. T administration dose dependently increases muscle mass and maximal voluntary strength but not fatigability or specific tension [3].

So, to overcome the physical disadvantages, sex specific competitions for women are allowed and there is therefore a legitimate need to establish the sex of people who engage in competitive sports. The question is: can this be done in a way that is scientifically well founded and is fair to those who wish to engage in competition.

In the vast majority of sports people's determination of sex is not an issue. They will have a history of having been born and grown up unambiguously as male or female. The problems arise in those for whom this has

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not been the case.

Genotyping (determination of Barr bodies in buccal smears) has been the established means of determining sex for competition in sports. The results were unsatisfactory and as a result this criterion has been dropped since the year 2000 [4]. Chromosomal sex, when taken as the sole criterion for the purpose of ensuring fair competition in sports, is, indeed, not a particularly adequate indicator. In humans, there is no solid evidence that the pattern of sex chromosome has a direct effect on muscle mass and strength. Rather, the influence is indirect through determination of the nature of the embryonic gonadal anlagen (testis or ovary) and their hormonal products (T and estradiol and their quantitative relationship). Also other criteria (the nature of the gonad, sex hormones and genitalia) do not provide workable criteria to determine sex and gender of human beings. The implication is that in humans, manhood and womanhood cannot be assessed by laboratory techniques alone but require additionally a self-description of one's gender identity/role. In sports, previous and present exposure to androgens is a reasonable criterion for reducing unfair competition. In a series of studies Bhasin and coworkers [5] have demonstrated that there is a positive correlation between blood T concentrations and leg press strength, thigh and quadriceps muscle volume, and levels of hemoglobin and insulin-like growth factor-1 (IGF-1), and that the anabolic response to T can largely be predicted by the dose administered [6]. This dose-response curve between T and muscle properties goes linearly beyond the physiological range but does not seem to apply to bones mass/strength.

2 People with disorders of sexual differentiation and sports

Some children are born with ambiguous genitalia, a perplexing discovery for parents. A child born with ambiguous genitalia constitutes a psychosocial emergency in which sex assignment must take place without much delay, rather over days than over weeks. A socio-cultural given of the human condition is an absolute dichotomy between male and female with regard to sex. In cases of genital ambiguity, modern techniques such as karyotyping, molecular biology, and imaging techniques allow a rather precise diagnosis of the condition, but decisions regarding sex assignment are still based on very limited empiric data [7].

The widely adopted policy nowadays is to arrive at a prognosis on the "optimal sex" for the newborn, the elements of which are an overall sex-appropriate appearance with stable gender identity, good sexual function (preferably combined with reproductive function if attainable), minimal medical procedures, and a reasonably happy life given the limitations [7]. To those without experience in this area this policy might seem erratic, but the outcome studies show that this is an acceptable practice for patients, though there should be room for later sex reassignment if the subject experiences the assigned sex as incongruous [8, 9]. The implication of contemporary medical practice is that, ultimately, there is no single solid biological criterion for the determination of sex for the purpose of sex assignment of children with genital ambiguity. When a criterion is needed for sex for a specific purpose, the optimal solution seems to be to adopt a criterion that serves best the purpose for which it is needed. In sports, previous and present exposure to androgens is a reasonable criterion for reducing unfair competition. Nowadays most intersexed subjects are identified early in life, if not immediately postnatally. Usually, before they engage in sports, they have received long-term endocrine treatment, the nature of which being determined by their sex of assignment. This is consistent with the International Olympic Committee's (IOC) policy on gender verification requiring a two-year period of stable gender re-assigment.

3 Transsexualism

Transsexualism is the condition in which a person with apparently normal somatic sexual differentiation has the unshakeable conviction that he or she is actually a member of the other sex. This conviction is accompanied by the irresistible urge to live in the gender experienced as self, which requires hormonal, anatomical, legal, and psychosocial adaptations. Psychological assessment may conclude that sex reassignment will bring relief to an individual suffering from gender dysphoria–the extreme feeling often described as being "trapped in the wrong body"–and may result in an indication for hormone and surgical treatment of transsexuals.

Increasingly, countries are offering transsexuals who have undergone sex reassignment procedures, the possibility to change their legal sex to allow them to take part in public life, with the same rights as anyone born into that sex. The practical implementation of this policy may involve complex and difficult decisions. As with other intersexed individuals, the medical and legal system is being called upon to humanely provide a safe space for these people to function as men or women with as little needless hindrance as possible, yet consistent with the gender bipolarity of modern human society.

The acquisition of the secondary sex characteristics of the other gender, to the fullest extent possible, is fundamental to sex reassignment for the transsexual patient. Obviously, acquisition of these secondary sex characteristics is contingent on sex steroids. At least in the rat, no essential difference in sensitivity to the bio-

logical action of sex steroids on the basis of genetic configurations or gonadal status has been demonstrated [10]. The typical transsexual requesting treatment is a young to middle-aged and usually healthy person.

4 Physical changes following administration of cross-sex hormones postpubertally

Since 1975, the gender clinic of the Vrije Universiteit in Amsterdam, the Netherlands, has provided sex reassignment treatment to more than 3 000 transgendered people.

The physical changes resulting from cross-sex hormone administration have been reported [11–13]. The standard hormone treatment before sex reassignment surgery in male-to-female transsexuals (M2F) is combination of anti-androgen with estrogens. In Europe, the most widely-used drug is cyproterone acetate (usually 50 mg twice daily), a progestational compound with anti-androgenic properties. If not available, medroxyprogesterone acetate, 5 to 10 mg/day, is a less effective alternative. Long-acting gonadotrophin-releasing hormone agonists (GnRH), injected monthly, also inhibit gonadotropin secretion [14]. Finasteride (5 mg/day), a 5α-reductase inhibitor, might also be considered. The latter drug but none of those mentioned previously are banned by the IOC. Sex reassignment surgery including gonadectomy, usually takes place following two years of cross-sex hormones. Then anti-androgen treatment in M2F transsexuals is usually stopped, while estrogen treatment continues.

Female-to-male transsexuals (F2M) receive treatment with T. The most commonly used preparations are T esters, an injectable administered intramuscularly in doses of 200 to 250 mg every two weeks. In some countries, parenteral T undecanoate (1 000 mg) is available, and injections may be spaced at 10–12 weeks [15, 16]. After ovariectomy, androgen treatment in F2M subjects is continued at a dosage level as administered to hypogonadal men. In this regard the situation of F2M (and intersexed individuals assigned to the male sex) is comparable to the situation of agonadal/hypogonadal men receiving T replacement and would require approval for all elite competitive athletes.

While principally administration of exogenous T is prohibited for participants in competitive sports, it is the policy now to allow medically indicated T replacement in men provided T blood levels have not exceeded and do not exceed those that naturally occur in men with normal testicular hormone production. This goal is difficult to attain with the traditional T esters whose pharmacokinetic profile is characterized by peaks and troughs of circulating levels of T [17]. Use of implantable or transdermal depot preparations may be more compliant with this idealized requirement.

5 Physical changes in transsexuals following cross-sex hormone treatment postpubertally

Androgen deprivation in M2F and androgen administration to F2M have consistent effects on the following variables: plasma T levels, muscle mass measured with MRI at the level of the thigh, levels of haemoglobin and IGF-1 [18–20] (Table 1). The results of androgen deprivation plus estrogen treatment in M2F are compared to the findings in F2M before T administration, and vice versa the results of T administration in F2M are compared to the findings in M2F before androgen deprivation plus estrogen administration (Table 2).

Androgen deprivation plus estrogen administration of M2F decreased plasma T to castrate levels and reduced muscle area significantly after one year of treatment, with no further reduction after three years of hormones. Hemoglobin levels decreased significantly and values after one and three years hormone administration were not different, and the latter were not different from values in F2M before T administration. After one year of cross-sex hormones values of plasma IGF-1 fell significantly to levels lower than in F2M before T administration.

In F2M T administration increased plasma T levels to values above the reference range for eugonadal men (12–28 nmol/L). After 1-year muscle area, levels of hemoglobin and IGF-1 were in the same range as in M2F before cross-sex hormones, with no further increases in

Table 1. Changes in plasma testosterone (T) and associated changes in biological variables. All values are means ± SD. $^{*}P < 0.05$, baseline *vs.* 1 year (Mann-Whitney test), no significant difference between 1 and 3 years. IGF-1, insulin-like growth factor-1. Reproduced with permission from Gooren *et al*. [20]. © 2004 by Society of the European Journal of Endocrinology.

	Male-to-female transsexuals (n = 19)			Female-to-male transsexuals (n = 17)		
	Baseline	1 year	3 years	Baseline	1 year	3 years
Plasma T (nmol/L)	21.5 ± 5.8	1.0 ± 0.0*	0.9 ± 0.1	1.6 ± 0.6	30.8 ± 11.4	30.0 ± 13.0
Muscle area (cm^2)	306.9 ± 46.5	277.8 ± 37.0*	271.0 ± 39.0	238.8 ± 33.1	285.3 ± 35.6*	280 ± 39*
Hemoglobin (mmol/L)	9.3 ± 0.7	8.0 ± 0.7*	8.1 ± 0.6	8.2 ± 0.7	9.4 ± 0.8*	9.3 ± 0.9
IGF-1	38.0 ± 10.0	14.0 ± 8.0*		26.0 ± 12.0	36.0 ± 14.0*	

muscle area and hemoglobin levels after 3 years of T administration.

In spite of the of the cross-sex hormone induced reduction, mean muscle area in M2F after 1 year of hormones remained significantly greater than in F2M before T treatment. Before cross-sex hormone administration to M2F and F2M there was a large overlap in muscle area between the two but means were significantly different (Figure 1). This overlap was almost complete when androgen deprived M2F were compared to non-treated F2M, although means remained significantly different (Figure 1).

Our data allow the following conclusions: androgen deprivation in M2F reduces levels of hemoglobin and IGF-1 to female levels. The reduction in muscle area is significant but mean muscle area remains significantly higher than in females but showing an almost complete overlap. M2F were on average 12 cm taller than F2M. When androgen deprived M2F were compared to pre-treatment F2M in a linear regression model, height was a strong predictor of muscle area (α = 2.29; P = 0.001). After correction for the effect of gender, the relation between height and muscle area remained significant (α = 1.63; P = 0.036). The reduction in variables three years after start of cross-sex hormones was not greater than after one year.

T administration in F2M inducing plasma levels of T above the references range for eugonadal men increased muscle area, levels of hemoglobin and IGF-1 to levels of men. The increases after three years of T administration

Table 2. Effects of testosterone (T) administration/deprivation on anthropometric variables. All values are mean ± SD and 95% confidence interval (CI) of the difference of the mean. $^*P < 0.5$, *vs.* baseline (Mann-Whitney test). Reproduced with permission from Gooren *et al.* [20]. © 2004 by Society of the European Journal of Endocrinology.

	46,XY before T deprivation *vs.* 46,XX after T treatment			46,XY after T deprivation *vs.* 46,XX before T treatment		
	46,XY (n = 19)	46,XX (n = 17)	95% CI of the difference	46,XY (n = 19)	46,XX (n = 17)	95% CI of the difference
Height (cm)	177.8 ± 7.9	167.1 ± 7.8	5.4–16.0*	177.8 ± 7.9	167.1 ± 7.8	5.8–16.0*
Body weight (kg)	66.1 ± 11.7	63.4 ± 11.4	25.1–10.4	69.9 ± 11.3	60.7 ± 11.8	1.4–16.8*
Body mass index (kg/m^2)	20.8 ± 2.6	22.6 ± 3.0	23.7–0.1	22.0 ± 2.7	21.7 ± 3.5	21.7–2.4
Muscle area (cm^2)	306.9 ± 46.5	285.3 ± 35.6	26.4–49.5	277.8 ± 37.0	238.8 ± 33.1	15.1–62.9*
Serum T (nmol/L)	21.5 ± 5.8	30.8 ± 11.4	215.7–3.0*	1.0 ± 0.0	1.6 ± 0.6	20.9–0.3*

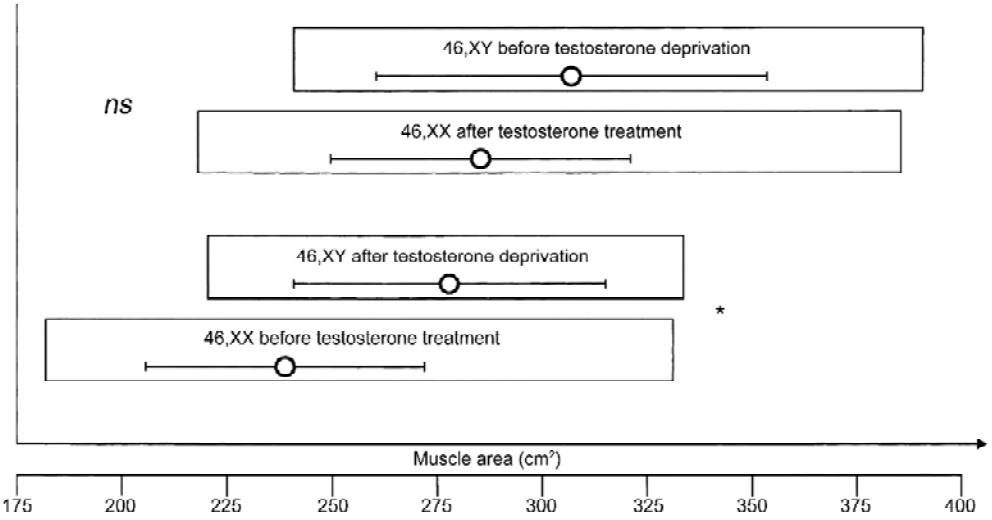

Figure 1. Relative changes in muscle mass after 12-month cross-sex hormonal treatment in 19 male-to-female and 17 female-to-male transsexual subjects. The means of 46,XY before testosterone (T) deprivation and 46,XX before T treatment differ with statistical significance. Beams represent range of all subjects. $^*P < 0.05$, Mann-Whitney test asymp. sig. (two-tailed). ns: not statistically significant. Mean in cm^2 with SD (whiskers). Reproduced with permission from Gooren *et al.* [20]. © 2004 by Society of the European Journal of Endocrinology.

were not greater than after one year.

We observed an overlap in muscle area between non-treated M2F and F2M (Figure 1). Upon androgen deprivation of M2F the overlap in muscle area with untreated F2M was almost complete (Figure 1) though the mean of the muscle area in androgen-deprived M2F remained above the mean in untreated F2M, but height was a strong predictor of muscle mass in both groups.

In the case of transsexuals, the further question arises whether an individual who has undergone normal physical pubertal and post-pubertal development in one sex, with prolonged exposure to sex appropriate levels of sex steroids before surgical sex reassignment, can fairly compete as a member of the other sex. In terms of actual androgen hormone levels, M2F transsexuals after surgical sex reassignment, have no competitive advantage over other women, but the effects of prior androgen exposure on muscle mass and strength do carry over for a certain time period, making this a relevant consideration. The fairness of this is subjective and controversial.

6 Prepubertal administration of cross-sex hormones

The above refers to transsexuals who have undergone sex reassignment postpubertally. Adult transsexuals often recall that their gender dysphoria started early in life, well before puberty. Children with gender identity problems increasingly come to the attention of the psychomedical care system. From follow-up studies in cohorts of juvenile transsexuals who have undergone sex-reassignment treatment, it appears that that they benefit from somatic treatment [21]. If, in an expert's opinion, a child's cross-sex gender identity will not change during long-term follow-up the individual may be spared the torment of (full) pubescent development of the "wrong" secondary sex characteristics. Depot forms of LHRH antagonists/agonists, following the regimen in children with precocious puberty, can be used when clear signs of sexual maturation are evident in order to delay pubertal development until an age that a balanced and responsible decision can be made to transition to the other sex [21]. These juvenile transsexuals have never been exposed to the sex hormones of their natal genetic sex and their participation in competitive sports is therefore as much an issue as non-transsexuals who need sex hormone replacement. Such policies are potentially controversial and are not yet widely adopted.

There will always be an element of arbitrariness in the drawing of competitive lines. Different individuals are born with and develop postnatallly different potentials. The caprices of genetics and postnatal development will make any form of competition intrinsically unfair at some level. In the studies of Bhasin and coworkers changes in muscle size correlated with T dose and concentration [5, 6]. These correlations were established in groups of men receiving graded doses of T. There was, however, considerable heterogeneity in response to T administration within each group receiving the same amount of T. These individual differences in response to androgen administration might reflect differences in activity level, T metabolism, nutrition, or polymorphisms in androgen receptor, myostatin, 5α-reductase, or other muscle growth regulators. The length of CAG tract was, however, only a weak predictor of change in thigh muscle volume and lean body mass [6].

7 IOC

The IOC approved the expert panel's recommendation that postpubertal transsexual individuals, both M2F and F2M, be eligible to compete under the following criteria [22, 23]:

- Surgical anatomical changes completed, including external genitalia changes and gonadectomy;
- Legal recognition of their assigned sex has been conferred by appropriate official authorities;
- Hormonal therapy appropriate for assigned sex has been administered in a verifiable manner and for a sufficient length of time to reduce to a minimum gender-related advantages in sport competitions.

Based on the scientific data available, the expert panel recommended that eligibility should begin no sooner than 2 years after gonadectomy. Although these criteria have been widely disseminated in the lay and sports press, not often appreciated is the fact that the recommendations included the caveat that every individual would be assessed on a case-by-case basis, in confidence and that, in the event that the gender of a competing athlete was questioned, the medical delegate or equivalent of the relevant sporting body would have authority to take all appropriate measures to ascertain the gender of that competitor. The following are criteria put in place after genetic-based laboratory screening of female athletes was discontinued by the IOC in the year 2000 [4]. The IOC rules, referred to as the Stockholm consensus are spelled out on the website: http://www.olympic.org/uk/organisation/commissions/medical/full_story_uk.asp?id=841. Other websites providing information are: http://www.uksport.gov.uk/assets/File/Generic_Tem-plate_Documents/Standards_in_Sport/transsexuals.pdf. and http://www.ausport.gov.au/women/fstrans.asp.

The recommendations are applicable only to elite competition in events sanctioned by the IOC and, while not formally binding on other international sports governing bodies, most tend to follow IOC guidelines for elite sport at international and national level. The further local application to the entire panoply of sporting events

may be more flexible.

8 Summary and conclusions

Until 2000 the genetic criterion of sex applied in competitive sports and precluded the participation of sex reassigned transsexuals as well as other intersexed individuals. While this criterion has been dropped, it is still regarded as fair, given the physical characteristics of the two sexes, that members of the same sex compete with each other, except for types of competitive sports where the physical differences between men and women offer no advantage or disadvantage. Presently, greater weight is given to the essence of the differences in physical properties between men and women, which is previous and present exposure to the anabolic effects of androgens. Upon cessation of the exposure to androgens, these effects are largely reversible but is not completely understood whether this reversibility is truly complete in M2F transsexuals. F2M transsexuals, similar to hypogonadal men, use T preparation. While their physical properties in the reassigned state do not offer an obvious advantage over men, there is a potential of overdosing T. The criterion adopted by the IOC, that in cases of transsexuals a time span of two years must have been passed, may be an acceptable compromise where definitive policy could become intractably difficult.

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