

REPORT ON SPORT CLASSIFICATION REGULATIONS FOR ATHLETES WITH DIFFERENCES IN SEXUAL DEVELOPMENT

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Introduction

On 23 April, 2018, the International Association of Athletics Federations (IAAF) published the following: ELIGIBILITY REGULATIONS FOR FEMALE CLASSIFICATION (ATHLETES WITH DIFFERENCES OF SEX DEVELOPMENT) (1) that was scheduled to come into force on 1 November, 2018, but this was suspended on the basis of the appeal made by the female athlete, Caster Semenya, before the Court of Arbitration for Sport (CAS) and conditional upon its final ruling.

These regulations were drawn up as a consequence of the debate which arose due to the sports results of women athletes who had achieved very significant advantages over their opponents. All this was particularly significant in the case of the South African athlete mentioned above. This female athlete won the women's 800m trial in the 2009 World Championship in Berlin with a time of 1:55.45 min, while the athlete coming in second took 1: 57.90: a difference of 2.45 seconds i.e. a distance of more than 16 meters (Figure 1). In this 800m trial Semenya won the final of the Olympic Games in Rio de Janeiro 2016 and was World Champion in Berlin in 2009 and in London in 2017. Her best time was 1:54.25 and she also won international competitions between 400m and 1500m. However, it should be borne in mind that she was also defeated on the track in the 800m women's race in the London Olympics in 2012 and the 2011 Daegu World Championship, both times by an athlete who was subsequently stripped of both gold medals for having used doping and who was suspended for that reason for 4 years. Both medals were then also awarded to Caster Semenya.

The case of Semenya has been giving rise to speculations in the media, like she had used doping substances, or that she was in fact a man.

As a result of all this, Semenya has undergone a number of different medical and genetic studies, some of whose results seem unfortunately to have been leaked to the media. In the case of other studies, numerous speculations have been reported. What seems clear is that the athlete suffers from androgenism and that

she has a blood testosterone level higher than the reference values for women of her characteristics.

Before moving forward, it must be considered that other elite athletes have also been subjected to intense media exposure for the same reasons: their physical appearance and exceptional sports performance. The perception that several of them are competing or have competed at the highest level in the 800m trial, like the holder herself of the world record for that distance (1: 53.28 since 1983) seems very strange.

Back in 2010, Semanya underwent a thorough examination by a group of specialists who determined that she should compete as a woman and without any limitation. However, her exceptional performance and its media impact led the IAAF to look for a method to avoid such major differences between competitors, to the point of producing the regulations of 2018, already cited (1).



Figure 1.- Arrival of the women's 800m final of the World Athletics Championships, Berlin 2009.

As a result of all the above, this report aims to analyse the regulations that the IAAF intends to impose in order to reduce the differences in performance in women's athletics, from the points of view of Sports Ethics and especially of Medicine.

Physiological aspects

It is undeniably clear that men have significant advantages in muscle size, strength and power, compared with women. Table 1, produced by the authors, shows the percentage differences between men and women, in some of the world records in athletics. To this end, only trials where women and men competed under equal conditions (ruling out obstacle races, which have different height, and throwing with different weights) have been considered. In order to compare these differences in jumps and races, the records of female athletes have been expressed by transforming the record time into the race speed (metres per second⁻¹).

Table 1.- Analysis of the percentage differences between men and women for some world records in athletics.

TRIAL	WORLD RÉCORD MALE	SPEED (msec-1) or DISTANCE (m)	WORLD RECORD FEMALE	SPEED (mseg-1) o DISTANCE (m)	DIFFERENCE (%)
100m	9,58	10,44	10,49	9,53	8,7
200m	19,19	10,42	21,34	9,37	10,1
400m	43,03	9,30	47,60	8,40	9,6
800m	1:40,91	7,93	1:53,28	7,08	10,7
1500m	3:26:00	7,28	3:50,07	6,52	10,5
5000m	12:37,35	6,60	14:11,15	5,87	11,0
10000mm	26:17,53	6,34	29:17,46	5,69	10,2
Marathon	2:01,39	5,75	2:15,25	5,17	10,2
20km walk	1:16,36	4,35	1:24,38	3,94	9,5
Relay 4x100	36,84	10,86	40,82	9,80	9,8
Relay 4x400	2:54,29	9,17	3:15,17	8,19	10,7
Long jump	8,95	8,95	7,52	7,52	16,0
Triple jump	18,29	18,29	15,50	15,50	15,3
High jump	2,45	2,45	2,09	2,09	14,7
Pole vault	6,16	6,16	5,06	5,06	17,9

Generally, this difference is quantified as a 10-12% advantage for men (1). This is attributed to man's higher testosterone levels from puberty, among other possible causes. The cellular and molecular mechanisms of the advantage that a higher rate of testosterone provides are clearly described (2).

In Table 1 it can be seen how, in race trials, the advantage of male athletes would be between 8.7% and 11.0%, however specifically in the distances between 400m and one mile (including the 4x400m relay) they do not seem to have a wider difference (between 9.6 and 10.7%) than the rest of the distances. In addition, it can be seen how, in the case of jumps, where rapid use of muscle strength is of major importance, the differences are greater (advantages for male athletes are between 14.7% and 17.9%). Although this cannot be compared, one could venture that it is very possible that in throwing that difference would be even greater.

Gender and sport. Classification and verification systems

Sport-based classification, separated by gender, in practically all sports and sports specialties, is something totally accepted today. The almost insurmountable differences in performance between women and men is the clear reason for this separation.

To maintain this separation and avoid the pitfalls in gender classification, in 1950 the IAAF set down a regulation including physical medical examinations, regulations that, in the long run, were extended to other sports. Back in 1950, an athlete was prevented from continuing her sports career due to refusing to undergo one of these medical examinations. The standards developed further and in 1966 Barr's chromatin began to be studied in female athletes who wanted to participate in female trials, using the karyotype in a saliva sample as an initial test. If in this test some Y chromosome was detected, medical examinations were carried out, including the morphological verification of external genitalia.

Although these physical explorations ended up being considered degrading and were happily repealed in all sports. In the early 1990s the use of the Polymerase Chain Reaction (PCR) technique was advocated for the extension and examination of DNA strands, as a method which was more objective and scientific.

Finally, in 2011 the IAAF set down two different regulations, one for people with sex reassignment (3), and another for female athletes with hyperandrogenism (4). However, in 2015, a female Indian athlete brought an appeal to the CAS regarding her suspension due to a diagnosis of hyperandrogenism, after a process described by her, as "horrible and humiliating". The athlete obtained a favourable ruling, since the CAS finally accepted that there was not enough evidence of the advantage that a higher level of testosterone could produce in female athletes (5). Thus, the IAAF regulation on hyperandrogenism was repealed.

As can be seen, this is a recurrent issue, which appears to be harming a number of women athletes, until institutions are persuaded that the matter should be left off the agenda. Now, in 2018 and 2019, we are once again in the worst possible position as regards the rights of certain athletes

Sexual differentiation

Biological gender is a general term that includes different aspects of chromosomal, gonadal, hormonal and phenotypic sex, each of which is fixed in an individual. Generally, all these classifications of gender are aligned in a conventional binary: male and female. However, it must be considered that there are congenital conditions that cause misalignment and atypical development of the chromosomal, gonadal and / or anatomical genders. As a medical description of these conditions, terms such as "disorders or anomalies of sexual development (6, 7) and later "intersexual states" or "intersex" began to be used. The term "anomalies of sexual differentiation" was introduced in 2006 (6), however all of these have been widely contested in the scientific literature (6, 8, 9, 10).

Currently they are classified as "differences in sexual development" or DSD, although later the term "variations in sexual development" (VSD) was proposed (10).

As will be seen later, DSD may involve ambiguity of external genitalia and various combinations of chromosomal genotypes and sexual phenotypes other than XX-woman and XY-man (7, 11). In the administrative field, there are a number of national systems that recognize legal genders which are different from "man" and "woman", such as "intersex", "X" or "other".

Different institutions with powers in the field of the protection of human rights attempt to avoid harmful practices and discrimination against people with these conditions. In 2015, the United Nations High Commissioner launched a campaign for the free equality of rights of people classified as "intersex" (12). Equally, in 2015 the Council of Europe made a statement asking member states for a non-binary gender classification and to seriously consider the implications of a new and better classification of "intersex" individuals (13). In 2016, numerous Committees and U.N. subcommittees (Against Torture, of the Rights of the Child, of the Rights of Persons with Disabilities), together with the Council of Europe and the Human Rights Commissions of Africa and the Americas, launched a document calling for an end to the violent and harmful medical practices on "intersex" children and adults (14).

We should not forget that disclosing information about the medical history of any patient can lead to very serious consequences (15). Furthermore, in these sensitive cases public knowledge of this protected data will have irreparable consequences for the normal physical development of young people and the psychosocial sphere of all those affected (16, 17), as established by the World Health Organization (18).

Regarding the embryological aspect of foetal sexual differentiation, it should be observed that this encompasses a series of processes whose determination and regulation involve numerous genes, proteins and hormones. Starting from a first

stage of gonadal and genital development (6 weeks post-fertilization), which is common to both sexes, it is in the period of differentiation when these conditions may occur and have been given the controversial classifications previously identified. These comprise a broad spectrum of discrepancies between chromosomal, gonadal and phenotypic (genital) criteria that define sexual differentiation and are now considered "Differences in Sexual Development (DSD)". Their classification can be seen in Table 2 (19).

As regards the involvement of testosterone, it should be remembered that the majority of women (including elite athletes) have circulating blood testosterone levels (0.12-1.79 nmol.L⁻¹) which are lower than those of post-pubertal males ((7.7-29.4 nmol.L⁻¹). It is accepted that, in the absence of DSD or tumour, no woman should have serum testosterone levels equal to or greater than 5 nmol.L⁻¹ (20).

Table 2. Classification of Differences in Sexual Development (DSD) (19).

Chromosome changes	47,XXY: Klinefelter syndrome and variants 45,X0 and mosaics 45,X0 / 46,XX: Turner syndrome and variants 45,X0 / 46,XY: Mixed gonadal dysgenesis 46,XX / 46,XY: ovotesticular ADS/DSD, 47,XYY chimerism	
Karyotype 46,XY Anomalies in gonadal development	Gonadal dysgenesis 46,XY (complete or partial) (SRY, SOX9, NR5A1, WT1, DHH, etc.) ovotesticular 46,XY Testicular regression syndrome (includes anorchy and testicular leakage syndrome) Changes in androgen synthesis	

<p>Anomalies in genital development due to changes in hormonal synthesis or action</p>	<p>Mutations in the LH receptor (plasia or aplasia of Leydig cells; LHCGR) Smith-Lemli-Opitz syndrome (deficit in 7-dehydrocholesterol reductase: DHCR7) Defects in the synthesis of testosterone Congenital lipoid suprarenal hyperplasia (StAR) Deficiency in cholesterol desmolase (CYP11A1) Deficiency in 3_-hydroxysteroid dehydrogenase (HDS3B2) Deficiency in 17_-hydroxylase / 17-20 lyase (CYP17A1) Deficiency P450 oxidoreductase (POR) Deficiency in cytochrome b5 (CYB5) Deficiency in 17_-hydroxysteroid dehydrogenase (HDS17B3) Deficiency in 5_-reductase type 2 (SRD5A2) Changes in the action of androgens Insensitivity to androgens (AR; total or partial = CAIS or PAIS) Drugs and environmental modulators Changes in the synthesis or action of the antimullerian hormone Persistent Mullerian duct syndrome (AMH / AMHR2)</p>
<p>Others</p>	<p>Malformation syndromes with changes in male genital development (e.g.: cloacal anomalies, Aarskog syndrome, Robinow syndrome, etc.) Severe early-onset intrauterine growth restriction Isolated hypospadias (CXorf6 or MAMLD1) Congenital hypogonadotropic hypogonadism Cryptorchidism (INSL3, RXFP2 [o INSL3R or GREAT])</p>
<p>Karyotype 46,XX Anomalies in gonadal development</p>	<p>Gonadal dysgenesis 46,XX Ovotesticular 46,XX Testicular 46,XX ADS/DSD (SRY, dup SOX9, RSPO1) or male 46,XX Foetal production Deficiency in 21-hydroxylase (CPY21A2) Deficiency in 11_-hydroxylase (CYP11B1) P450 oxidoreductase deficiency (POR) Deficiency in cytochrome b5 (CYB5) Deficiency in 3_-hydroxysteroid dehydrogenase (HSD3B2) Mutations of the glucocorticoid receptor (NR3C1) Fetoplacental production Deficiency in placental and foetal aromatase (CYP19A1) P450 oxidoreductase deficiency (POR) Foetal or placental tumours that produce androgens Maternal production Androgenic drugs Maternal virilising tumours (e.g. luteomas, Krukenberg tumour)</p>
<p>Others</p>	<p>Malformation syndromes Hypoplasia/agenesis of Mullerian structures (Rokitansky-Hauser syndrome type I and type II - MURCS) Uterine anomalies (e.g. MODY 5) Vaginal atresia Adhesions of vaginal labia</p>

People with DSD may have very high levels of natural testosterone that may be similar to, or higher than, normal male values (20). There is a broad medical and scientific consensus that, if these people are sensitive to androgens, i.e. if they have normo-functioning androgen receptors, and record such high levels of natural testosterone, their muscle mass, strength and haemoglobin level may also be much higher and, therefore, significantly improve their sports potential (21-35). It can be considered that an increase of blood testosterone rate in women between 0.9 and 7.3 nmol.L⁻¹ produces an increase in muscle mass of 4% and in muscle strength of 12-26%. The increase in testosterone to levels of: 5, 7, 10 and 19 nmol.L⁻¹, increases the amount of haemoglobin by 6.5%, 7.8%, 8.9% and 11%, respectively.

It is therefore estimated that the ergogenic advantage of testosterone levels in the male range instead of the female range is over 9% (21). All this indicates that, for the most part, the competitive advantages of men are attributable to the action of male sex hormones, in such a way that the increase in testosterone in women from the range of female values to the male range would cause this increase in muscle mass, strength and the rate of haemoglobin.

The ergogenic power of testosterone and that of all its derivatives and other substances with similar chemical structure or biological effects, is manifested by its inclusion in the World Anti-Doping Agency's (WADA) List of Prohibited Substances and Methods (36). These substances are prohibited at all times (in and out of competition) and in all sports, as Non-Specific Substances in Category S1: Anabolic Agents. These are included in that list since it has existed, and their use is considered to be a case of utmost seriousness.

However, from the legal point of view, the CAS ruling of 2015 should be recalled, (5) stating that there is not enough evidence of the advantage that a higher rate of testosterone may give to female athletes.

For its part, the IAAF has compiled observational data on the effects of artificial suppression of high testosterone levels on athletes with DSD, depending on

whether or not their testosterone levels are suppressed. The suppression of circulating testosterone levels in the case of three female athletes with DSD from between 21 and 25 nmol.L⁻¹ down to a rate below 2 nmol.L⁻¹ led to a decrease in their performance on average of 5.7%, as can be observed in Figure 3 (21, 37).

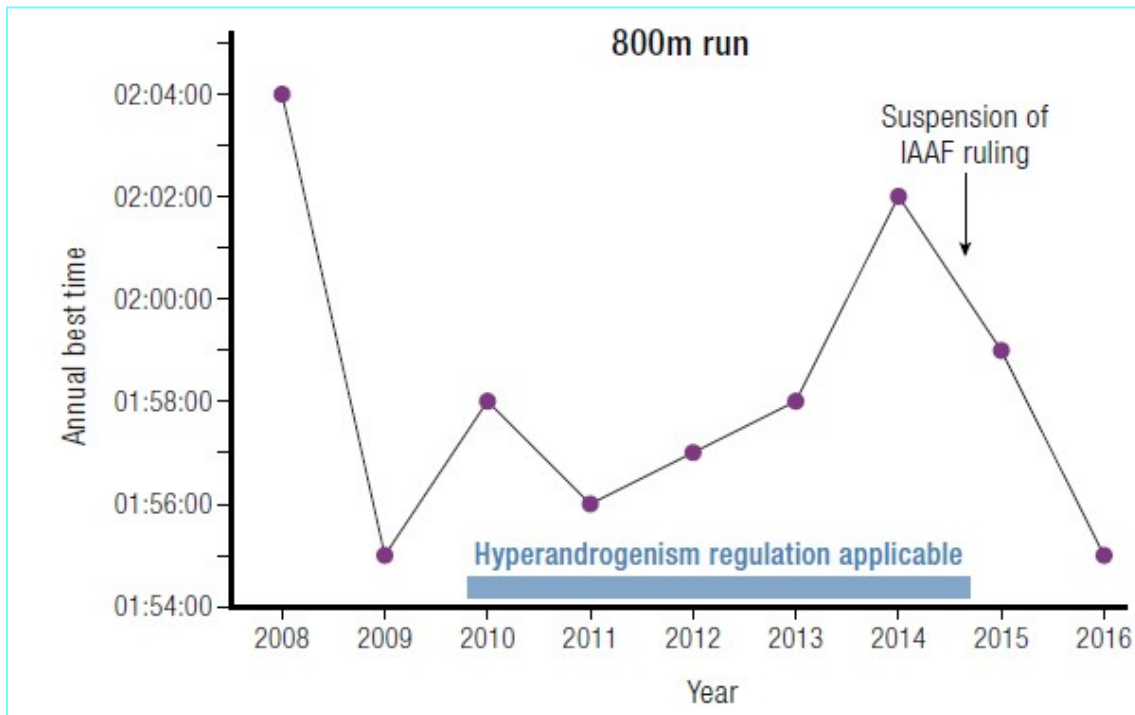


Figure 3. Best annual times in the 800m for an elite female athlete with DSD between 2008 and 2016, with control of her testosterone rate between 2010 and 2014 (21).

This study shows that athletes with DSD with circulating testosterone levels in the normal male range have a significant competitive advantage over athletes with testosterone levels in the normal female range, and for the IAAF this would justify forcing these athletes with DSD to reduce testosterone levels to the normal female range to continue competing in the female category.

Application of the IAAF regulations (1).

- Sphere

The IAAF data would indicate that the advantages of some athletes with DSD have had a significant effect on mid-distance track events, so it is inferred from this that the rule only applies to events from 400m to a mile (which the regulations term "Restricted Events"). In international competition and outdoor track events, these events are: 400m., 400m hurdles, 800m, 1500m and one mile, alone or as part of a relay race or a combined trial.

The special eligibility requirements described apply only to "Relevant Athletes" in the female classification in a Restricted Event in International Competition.

The regulations describe as "Relevant Athlete" those who meet the following three criteria:

- Women with one of the following DSDs:
 - o Deficiency of 5 α -reductase type 2.
 - o Partial androgen insensitivity syndrome (PAIS). or Deficiency of 17 β -hydroxysteroid dehydrogenase type 3) or Congenital adrenal hyperplasia or Deficiency of 3 β -hydroxysteroid dehydrogenase.
- Ovotesticular DSD, or Another genetic disorder with impaired gonadal steroidogenesis.
- Has circulating blood testosterone levels of ≥ 5 nmol.L⁻¹.
- Has sufficient sensitivity to androgens so that these testosterone levels have an androgenizing effect.

- Conditions for eligibility:
 - Being recognized by law as a woman or as intersexual (or equivalent).
 - Reducing the rate of circulating blood testosterone to below 5nmol.L^{-1} for a continuous period of at least 6 months, using, for example, contraceptives.
 - Maintaining the circulating blood testosterone level below 5nmol.L^{-1} continuously (in or outside competition) for as long as wished to maintain eligibility to compete in the female classification in Restricted Events in international competition (or setting a world record in a Restricted Event in a competition that is not an international contest).

- Taking part without suppressing high levels of testosterone:

The regulations allow women athletes who do not want to follow the above guidelines to participate in the following circumstances:

- In the female classification:
 - In any competition that is not an international competition.
 - In international competitions: in any discipline other than track events of between 400m and one mile.

- In the men's classification: In any competition at any level, in any discipline, without restriction.

- In any 'intersex' classification (or similar) that the organizer of the event can offer in any competition at any level, in any discipline, without restriction

- Reasons given by the IAAF for implementing this rule.

The arguments expressed by the IAAF in the text (1), are as follows:

- To guarantee fair and valid competition in athletics within categories that create a level playing field and to guarantee that success is determined by talent, dedication, hard work, other values and characteristics that sport embodies and celebrates.
- To benefit a broad class of female athletes.
- To encourage athletes to achieve the great commitment and sacrifice required to excel in sport, and thus inspire new generations to take up sport and to aspire to the same excellence. It does not wish to risk discouraging those aspirations by having conditions of unfair competition, which would deny female athletes a fair chance of succeeding.
- Because of the significant advantages in size, strength and power that men generally possess over women from puberty, largely due to much higher levels of circulating testosterone in males, and the impact these advantages may have on sport performance, it is generally accepted that competition between male and female athletes would not be fair and would risk discouraging women from participating in sport. Therefore, in addition to the separate competition categories based on age, the IAAF has also created separate competition categories for male and female athletes.

Sports ethics arguments against the IAAF regulations

We must begin with the very concept of competitive sport as a human activity based on inequality between people. Competition attempts to measure precisely that inequality that is what gives rise to the victory of some over others. Setting down rules that try to eliminate or reduce this inequality would transform athletic competition into something else.

Sports performance is an extremely complex phenotypic trait that in turn is influenced, although not determined, by many other traits, such as the distribution

of muscle fibre type, aerobic power and capacity, strength and anaerobic capacity, and the ability to train physical skills (38). Although the extrinsic determinants of human athletic performance, such as training, nutrition, living conditions, etc., have an undoubted and significant impact on sports performance, the importance of extrinsic determinants must not be trivialized, among these the genetic ones. It is clear that it is impossible to establish a single formula for anyone to become a sports champion and that quantifying the contribution of each of these determinants continues to be a challenge to research in sports science (39-42).

However, certain people who have not undergone scheduled training is already able to demonstrate extraordinarily high levels of physical performance. Some people also show a better response to training and improve their performance much more than others. when following the same working programme (40, 41).

The fact that genetics is a very significant intrinsic factor in athletic performance is shown by the analysis of athlete rankings (year 2018 on 17 December) where it can be seen that, in the 1500m, 14 of the 15 best all-time records were set by athletes born on the African continent, and that the first 7 athletes in this trial in 2018 were born in Ethiopia, while only one thrower with one of the top 60 world times (15 in each of the weight-lifting, discus, hammer and javelin trials) was born in Africa, and only 4 in total (7%) had a phenotype for that continent.

The IAAF intends to delimit a group of Restricted Events (400m to one mile) to apply this regulation, without stating any objective reason why this is done in these trials and not in other events. It should be borne in mind that, as has already been explained, there is no evidence that high testosterone levels in women may be more advantageous in these trials than in others, and it has already been seen that in the jump disciplines this advantage may be greater. In this way the IAAF would be legislating in violation of the principle of generality by derogating *a la carte* and committing injustice towards a very specific population, almost singling out specific female athletes.

In addition, it seems essential to consider that the artificial reduction of the advantage that nature has granted to certain women in the form of higher blood testosterone levels, could be somewhat random, since there is no evidence of a direct relationship between the reduction in the rate of testosterone in female athletes, hyperandrogenism and the impact on sports performance. Consequently, with the same decrease in blood testosterone, even taking this at the same level, this could affect the running speed to a different extent in one female athlete from another.

And what happens in men who have circulating testosterone levels higher than the reference values? In the 80s, the genetic basis of Polycystic Ovarian Syndrome began to be studied (43), a basis that has become much better known over the last decades (44-45). Today, numerous studies are advancing in the description of a genetic load similar to the cases of female hyperandrogenism with Polycystic Ovarian Syndrome and various types of male hyperandrogenism (46-50). Why should not men who could obtain good results in those Restricted events or any other trial have applied to them regulations similar to those that the IAAF wants to apply to women?

We cannot conclude without taking into account the efforts that the governments of the world and the sports movement have been making to eradicate the scourge of doping. As the World Anti-Doping Code says in justifying this effort in its Fundamentals: *"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, the pursuit of human excellence through the dedicated perfection of each person's natural talents. It is how we play true. The spirit of sport is the celebration of the human spirit, body and mind, and is reflected in values we find in and through sport, ..."*

As can be seen, natural talent is the excellence that is sought to be preserved, so how can this fight be justified, if when these natural talents appear, the attempt is to eliminate them in an artificial way? That way we cannot defend fair play (51).

Medical ethics arguments against the IAAF regulations

If sports ethics arguments against these regulations seem overwhelming evidence, medical arguments that are very clear and concise seem much more important - and any medical professional will undoubtedly understand these.

The rules of Medicine prohibit the use of medication that is not destined to treat a disease or pathology. Moreover, medications must be used following the established indications and not for any other purposes. The use of medication outside these circumstances is contrary to medical practice and is therefore an offence on the part of the prescribing physician (52).

These regulations, which aim to reduce performance in people who have innate qualities of genetic origin and have not been obtained by illegal means, would undoubtedly apply in these cases, and doctors who prescribe treatments for this purpose could clearly be committing an offence.

But above all, it should be noted that in the mind of every doctor, in their relationship with their patients, the side effects, contraindications and risks that prescribed medication could have should take pride of place. It should not be forgotten that the drugs that affect the hormonal sphere of individuals involve significant health risks, risks that are accentuated exponentially if these drugs are used beyond their medical indications (53).

Finally, it is necessary to add the problem that arises in cases like these with respect to the protection of data and even individuals' rights. We are seeing women who, as a result of wanting to exercise their right to practice sports, find themselves involved in the maximum possible circulation internationally of their tests results, examinations and medical diagnoses, to then be exhibited in the media at the same level as cheating athletes who use doping to excel in sports.

Conclusion

Faced with these regulations that clearly fly in the face of unquestionable evidence from the point of view of sportsmanship, against the oath of medical practice, and even against the rights of individuals, we can only demand their immediate repeal.

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