Amongst the most challenging and confusing fields of endocrinology are the disorders of sex differentiation (DSD). A favorite of medical examiners, and dreaded by students, this subspecialty tests one’s grasp of clinical endocrinology in a manner that perhaps no other group of diseases can. Straddling the diverse sciences of hormone action, pituitary, adrenal, gonadal, and metabolic biology, DSD represents the epitome of classical endocrinology.

How do we, as clinical endocrinologists, view patients with DSD? Do we visualize them as scientific curiosities, meant to exercise our academic grey cells? Or biological oddities designed to interest only the molecular scientists? Or perhaps just academic entities, placed as hurdles for aspiring endocrine students? More important, however, relates to how we SHOULD BE seeing these patients. Our conscience would certainly tell us to see them simply as they are—real, suffering human beings, ridiculed by many, shunned by society, trapped within and between the narrow compartments of genotype, phenotype, and psychosocial gender that they are born with.

And, even more important is this: What explains the total silence of the endocrine community, especially in India, when it comes to public advocacy for our patients with DSD? What words do we use to describe our attitude, when athletes with DSD are subjected to ridicule and shame in the name of “endocrine” assessment? How do we defend our masterly inactivity, when purely endocrine issues are discussed in the media, and on the worldwide web, by non-endocrine professionals?

This is certainly not due to lack of precedence. The spectacular success we have achieved in patient advocacy and public health awareness, in the fields of diabetes, thyroidology, and bone health, is exemplary. Why have we not expanded this effort to include gonadal disorders or intersex conditions? Our lack of action is not due to lack of interest, either. Adrenal and gonadal diseases are frequently researched topics in endocrine academia, and case reports of rare (and not so rare) DSD are published frequently.[1,2] Polycystic ovarian syndrome and obstetric endocrine topics, such as diabetes in pregnancy, are large enough subspecialties to merit their own national and international conferences. We cannot explain our inactivity by lack of resources, either. Endocrinology is a respected specialty in India, and there is no dearth of physical or financial assets to carry out patient education and community awareness campaigns. Commitment does not seem to be a limiting factor as well. Most endocrinologists do keep themselves occupied in altruistic preventive public health campaigns, albeit at an individual or local level.

We feel we do our best possible to provide clinical and supportive care to DSD patients in our OPDs. We work hard to clinch the diagnosis and work harder to ensure an optimal life for them, within the limitations set by biology and society. Is this enough, however? In diabetology, we try to modulate the macro-environment and propagate diabetes–friendly foods, physical activity, and stress management to reduce glycemic burden. In bone health, we promote architecture designed to reduce the risk of fractures in people with osteoporosis. We speak of endocrine disruptor chemicals and try to reduce their impact on society.

However, we prefer not to speak about intersex. Why do we, as a group of committed health care professionals, remain silent when an athlete is subjected to a public discussion of her or his gender, often by media that is driven by sensationalism, rather than scientific accuracy? Why do
we not attempt to set the record straight, and explain the concepts of sex, gender, intersex, and sex determination, to fellow medical professionals and to the public? Or would we rather have the sports medicine, the gynecology, or the forensic medicine associations do this for us?

In the past few years, at least two Indian medal-winning athletes have faced public enquiry in the media, for avoidable controversies related to their gender. The cases of Pinky and Santhi are well-covered in lay media, and the details need not be repeated here. What needs to be highlighted, however, is the lack of support received by them from the endocrinologists in the country. This stands in sharp contrast to the supportive attitude exhibited by South African administrators, when their star athlete Caster Semenya was embroiled in a dispute about her gender in 2009.

Gender is not a simple issue [Table 1]. Defining gender is a complex matter, and it can be done by various means, none of which is absolutely foolproof. An individual will have a phenotypic sex, genotypic or chromosomal sex, a gender of rearing and a gender of choice. Each individual will also have a gonadal sex. While all these are usually concordant with each other, there are few persons where these biomedical attributes do not match with each other. To add to this confusion is another definition of sex, now based on hormonal levels, which has been highlighted by the International Olympics Federation (IOF) and International Amateur Athletic Association (IAAF) in recent guidelines.

The guidelines for eligibility in female athletic events are now based on a single biochemical criterion, viz. high testosterone levels, rather than a clinical syndrome or a composite clinical-biochemical-imaging definition. There is no mention of gender of rearing or choice and no specific mention of androgens other than testosterone. Chromosomal sex, used to disqualify Santhi in 2010, is not mentioned at all in the current guidelines.

Assessing the actual sex in cases of discordance is a real challenge. No single method, viz. clinical examination, karyotyping, imaging modalities or hormonal assays, can give a definitive answer. Clinical examination, for example, may miss undescended testes or may misdiagnose clitoromegaly. Unmarried women may refuse internal examination. Karyotyping may wrongly diagnose an XY individual with complete androgen insensitivity syndrome (CAIS) as male, while Barr body analysis may miss identifying girls with Turner syndrome (45XO) as female.

Hormonal assays are besought with their own limitations. The controversy relates to measurement of testosterone in women are significant enough to spawn a multitude of publications. If hyperandrogenism were to be taken as a sole criterion for sex determination, perhaps all women with polycystic ovarian syndrome would have to be classified as men!

Using gonadal and genital sex as a final decision tool is not without pitfalls, either. True hermaphrodites have ovotestes; patients with CAIS have testes but no phenotypic response to them. Women with premature ovarian failure or resistant ovary syndrome have ovaries, but non-functioning ones. If presence of genitalia were to be taken as a yardstick, how will we classify people who have undergone orchidectomy, hysterectomy, or genital mutilation?

This discussion opens up various grey zones of science and lays bare much of what we do not know with certainty. Is this the reason why we shirk our responsibility towards DSD patients in public? Is this the reason why we prefer to watch the rest of the world discussing endocrinology, while we remain silent?

There is a lot we have achieved in DSD management, and a lot we can share with others. A complete history-taking and physical examination, done with dignity and etiquette, reveals much about the sex of a particular individual. Rationally advised biochemical hormonal and imaging modalities allow us to confirm the diagnosis in virtually every case. And, as taught to us by respected teachers (Dr. AC Ammini, New Delhi), the final choice of sex of rearing lies with the patient and her/his family, not with the doctor or the media.

Most patients, with intersex, will have one of a few select adrenal or gonadal conditions [Table 2]. Others, with hyperandrogenism, but without genital ambiguity, will have PCOS, other ovarian, or adrenal abnormalities. As long as one is sure that such athletes are not using exogenous hormones or hormone-modifying medication, they should be labeled as being male or female, based upon a composite assessment of history, phenotype, and investigations. Any sex determination, solely on a single method, for example, on serum testosterone.

| Table 1: The Complex attributes of Gender |
|------------------------------------------|
| **Phenotypic Sex**                      |
| • Internal genitalia                    |
| • External genitalia                    |
| • Secondary sexual characteristics      |
| **Gonadal sex**                         |
| **Psychological sex**                   |
| • Gender of rearing                     |
| • Gender of choice                      |
| • Sexual preferences                    |
| **Genotypic/chromosomal sex**           |
| **Hormonal sex**                        |
levels, is bound to be limited in its efficacy and utility. If androgens can be used as a means of refusing permission to an athlete to participate, can other hormones not be used similarly? Will we support a call to judge eligibility for men and women based on hyperinsulinemia or on hyperparathyroidism or perhaps adrenaline levels? The current guidelines by the IOF and IAAF, therefore, need to be relooked at and revised.

This editorial does not delve into the correctness of proposed testosterone cutoffs for defining a “female.” Neither does it suggest that endocrinology, as practiced currently, has all the answers to the definition of sex and intersex.

This editorial raises its voice for Pinki, for Santhi, and for Anamika, i.e. the countless, nameless people, living with DSD, who face discrimination, especially when they achieve success on the playing field. It calls for endocrinologists to be actively involved in public awareness and patient advocacy regarding DSD. It also hopes that endocrinology will take the lead in involving stakeholders from allied disciplines such as sports administration, sports medicine, exercise physiology, gynecology, urology, and medical ethics in formulating a humane and sensitive, yet rational and scientific policy towards athletes with DSD.

The editor’s pen is a strong weapon, they say (Dr. Krishna Seshadri, Chennai). Is this pen strong enough to change societal and media attitudes towards intersex? Is it strong enough to motivate readers to speak out? We hope so. Because, as endocrinologists, we understand our responsibility towards our patients with intersex. We care.

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### Table 2: Common intersex conditions where the genotype and phenotypic sex do not correlate

| Intersex (clinical diagnosis) | Genotype | Phenotype | Testosterone levels | Psychosexual orientation |
|------------------------------|----------|-----------|---------------------|-------------------------|
| Complete androgen insensitivity | XY       | Female genitalia, amenorrhea | High | Female |
| Complete gonadal dysgenesis | XY       | Female genitalia | Low | Female |
| 5 alpha reductase deficiency | XY       | Female like genitalia at birth, masculinization at puberty | High | Usually male |
| Congenital adrenal hyperplasia | XX       | Variable masculinization of genitalia | High | Female |
| Adrenal and gonadal tumors | XX       | Hirsute with menstrual irregularities, mildly masculinized genitalia | High | Female |
| Polycystic ovarian syndrome | XX       | Hirsute with menstrual irregularities, normal female genitalia | High | Female |

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