Editorial

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Disorders of sex development

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Disorders of sex development (DSD) pose a considerable challenge for those affected, their families and care takers but also for medical professionals who attempt to and by their profession and ethical standards do provide advice, medical services and care for the affected people. Both at an individual and a community and societal basis there is a lot of controversy and most importantly uncertainty and the feeling of insecurity and sometimes even guilt. Some of the people affected will in adulthood not agree with and not adjust to the gender identity that they had to assume during their childhood: Adults who feel that they may have been treated wrongly as children, sometimes embark on what they might view as a revenge path and rarely but decisively and visibly speak up against what they might feel are medical practices or opinions that are and/or have been wrong and even false. Sometimes they do forget that history is also a history of medicine and medicine does have history. In other words, what might have been viewed as being correct medical practice 30 years ago might now been viewed as being harmful, obsolete or even neglectful. This does not mean that physicians treating patients in a certain way 30 years ago did this to cause harm and therefore their doing should not be considered malpractice. In addition and importantly, medicine does not live a life outside society. In other words, what might be considered correct, ethical and right in one society and in one culture might be viewed conspicuously and as false and wrong in another culture and in other circumstances. It is our duty to discuss medical practice openly and install transparency, listen to everyone and find the ideal ways to cope with nature's challenges and our own fallacies.

In this issue of the *Journal of Pediatric Endocrinology and Metabolism*, we wish to share with our readers and the learned societies two important reports on DSD in children, one from South Africa and one from Thailand. Ganie et al. describe the prevalence, clinical characteristics and etiological diagnosis in 416 children with DSD who presented to a tertiary referral center in South Africa over a period of 20 years from January 1995 to December 2014. They state in their article that DSD is not an uncommon diagnosis in African patients in sub-Saharan Africa. They also conclude from their data that the most common etiological diagnosis – based on the current classification [Lawson Wilkins Paediatric Endocrine Society (LWPES) and European Society for Paediatric Endocrinology (ESPE)] definitions – in children with DSD in their African region was 46,XY DSD and biochemical variation in androgen synthesis and action, followed by ovotesticular DSD. Congenital adrenal hyperplasia (CAH) was only the third most common entity in their case series. There was a significant relation ($p < 0.001$) between the age of presentation and etiological diagnosis [1].

In the other related paper presented in this issue of our journal, Ittiwut et al. from Bangkok, Thailand, conducted a cross-sectional study in 46,XY DSD with normal or increased testosterone production ($n = 43$) as evaluated by human chorionic gonadotropin (HcG) stimulation test or clinical features consistent with 5α-reductase deficiency or partial androgen insensitivity (PAIS). Abnormalities of dihydrotestosterone conversion (5α-reductase deficiency: OMIM 607306) or actions of androgens (partial androgen insensitivity syndrome: PAIS: OMIM 312300) during the 8th–12th weeks of gestation cause varying degrees of undervirilized external genitalia in 46,XY DSD with increased testosterone production. Therefore, the objective of their study was to determine clinical and genetic characteristics of patients with 46,XY DSD in their country. PCR-sequencing of the entire coding regions of the *SRD5A2* and *AR* genes was performed. Molecular modeling analysis of the androgen receptor-ligand binding domain (AR-LBD) of a novel mutation was then carried out. In their case series mutations were found in seven patients (16.3%); five (11.6%) and two (4.7%) patients had mutations in *SRD5A2* and *AR*, respectively. Two novel mutations, *SRD5A2* c.383A>G (p.Y128C) and *AR* c.2176C>T (p.R726C), were identified. In summary, the molecular causes of 46,XY disorders of sex development are multifold and variable. Not all underlying genetic variations and mechanisms of DSD have been elucidated as yet and causes and consequences have to be viewed individually and on a case-by-case basis [2].

Many of DSD patients are infertile or remain childless and this issue might add to impaired quality of life and worries and psychological distress in patients with DSD. We have therefore decided to add in this issue of *JPEM* a paper that describes the knowledge and training of pediatric

endocrinologists from the USA in respect to infertility and sexual dysfunction in general. As the authors state and rightly so, infertility and sexual dysfunction can result from a large number of different conditions and treatments and can profoundly impact on quality of life. According to Nahata et al., the American Academy of Pediatrics (AAP) has recommended that these patients and their families should consult "fertility specialists" for counseling, but it remained unclear who these specialists were. Therefore, in their study, they tried to assess whether or not pediatric subspecialists who manage hypogonadism and/or genitourinary conditions felt adequately trained to provide fertility and sexual function counseling. An online survey was distributed to members of the Pediatric Endocrine Society (PES), the Society for Pediatric Urology (SPU) and the North American Society for Pediatric and Adolescent Gynecology (NASPAG). All health care providers reported whether or not they felt adequately trained in these areas. Two hundred and eighty-four surveys were completed by endocrinologists, 124 surveys by urologists and 41 surveys by gynecologists. The majority of the respondents (79%) worked at academic centers; 34% of providers had been practicing for >20 years. Comfort level was variable and lowest in young males. Ninety-one percent of pediatric endocrinologists reported routinely seeing patients at risk for infertility, but only 36% felt adequately trained in fertility, and 25% felt adequately trained in sexual function. The authors conclude that their results suggest that pediatric endocrinologists, who frequently manage male and female hypogonadism, feel insecure and not well trained in this area of medicine and that they should receive formal training in these areas. It is hypothesized that optimizing counseling would help prevent missed opportunities for fertility preservation and alleviate distress among patients and families [3].

In conclusion, issues of DSD touch upon emotional dimensions, psychological, biological, genetic and medical issues. They depend upon and relate to society, history and culture. Problems arising from dealing and coping with DSD can only be solved by seeking consent between individuals and exerting the utmost respect for one another and each human being. There is no and will not be a single recipe that can help in each individual situation. This notion might be hard to accept by some but might serve as a guideline in difficult situations where decisions need to be arrived at. However, the fact that in principle the interest, view, self-determination and own will of the affected individual is the lead, the principle and the major path along which any decision is allowed to be arrived at should be clear. In addition, training pediatric endocrinologists needs to include training of understanding and coping with issues of DSD, sexuality and fertility.

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