Intersex

Introduction

Terminology

"Intersex" (from Latin, literal translation "between the sexes") is a term grounded in the binary system of sex underlying mammalian (including human) reproduction. In medicine the term is colloquially applied to individuals with significant variations in the reproductive tract. Some variations, often labeled "genital ambiguity," preclude the simple recognition of somatic sex as male or female and require a comprehensive physical, endocrine, and genetic work-up, before a sex/gender can be "assigned." In recent years "intersex" has also become an identity label adopted by some individuals with intersex conditions and a subset of (non-intersex) individuals with a non-binary gender identity (Tamar-Mattis et al., 2018). However, in this chapter, the term "intersex" refers to congenital physical manifestations only.

At a 2005 international consensus conference on intersex management, conditions of somatic intersexuality were subsumed under a new standard medical term, "Disorders of Sex Development" (DSD), defined as "congenital conditions in which development of chromosomal, gonadal, or anatomical sex is atypical" (Hughes, Houk, Ahmed, Lee, & LWPES/ESPE Consensus Group, 2006). DSD covers a much wider range of conditions than those included in traditional intersexuality and comprises conditions such as Turner's syndrome and Klinefelter syndrome, which are much more prevalent. In addition, many affected individuals dislike the term "disorder," viewing it as inherently stigmatizing (Carpenter, 2018; Griffiths, 2018; Johnson et al., 2017; Lin-Su, Lekarev, Poppas, & Vogiatzi, 2015; Lundberg, Hegarty, & Roen, 2018; Tiryaki et al., 2018). Clinicians also vary in their acceptance of the term (Miller et al., 2018). The wide-spread alternative reading of DSD as "Differences in Sex Development" can be seen as less pathologizing, but is semantically unsatisfactory, as this term does not distinguish the typical genital differences between males and females from atypical sexual differentiation. Other recent attempts to come up with less obviously stigmatizing terms such as "Conditions Affecting Reproductive Development" (CARD; Delimata et al., 2018) are identical to DSD in their intended coverage and are not specific to intersexuality. Given these definitional issues, in this chapter we are using the term "physical intersexuality" for purposes of descriptive clarity and historical continuity. This choice is not meant to indicate an intention on our part to take sides in the ongoing discussion regarding the concept of sex/gender as a bipolar system or as a continuum, which may vary with considerations of context and utility (Meyer-Bahlburg, 2019). In 21st century societies the concepts of sex and gender are in a process of evolution.

Incidence

The incidence of intersex conditions depends on the definition used. Obvious genital atypicality ("ambiguous genitalia") occurs with an estimated frequency ranging from approximately 1:2000 – 1:4500 people (Hughes, Nihoul-Fékété, Thomas, & Cohen-Kettenis, 2007). The most inclusive definitions of DSD estimate an incidence of up to 1.7% (Blackless et al., 2000). Although these numbers are high in aggregate, the individual conditions associated with the intersex variations tend to be much rarer. For instance, androgen insensitivity syndrome (AIS) occurs in approximately 1 in 100,000 46,XY births (Mendoza & Motos, 2013), and classic congenital adrenal hyperplasia (CAH) in approximately 1 in 15,000 46,XX births (Therrell, 2001). Incidence figures for individual syndromes may vary dramatically between countries and ethnic groups.

Presentation

The presentation of individuals with intersex traits varies widely. Physical intersexuality can be recognized during prenatal ultrasound imaging, although most patients will be identified during genital examinations at birth. Within the first weeks of life, such children will undergo extensive medical diagnostic procedures. Taking into consideration the specific medical diagnosis, physical and hormonal findings, and information from long-term follow-up studies about gender outcome, joint decision-making between the health-care team and the parents leads to the newborn being assigned to a male or female sex/gender. Some individuals with physical intersexuality come to the attention of specialists only around the age of puberty when they are evaluated for primary amenorrhea.

Health professionals (HPs) assisting patients with both gender identity exploration and physical intersexuality need to be aware that the medical context in which such patients have grown up is typically very different from that of people without physical intersexuality. There are many different syndromes of physical intersexuality, and each syndrome can vary in its degree of severity. Thus, hormonal and surgical treatment approaches vary accordingly, and this needs to be taken into consideration in the planning of treatment in the minority of cases who develop gender dysphoria.

Some physical manifestations of intersexuality may require early urgent intervention, as in cases of urinary obstruction or of adrenal crisis in CAH. Most physical variations among individuals with intersexuality neither impair function, at least in the early years, nor risk safety for the individual. Yet, the psychosocial stigma associated with atypical genital appearance often motivates early “normalizing” genital surgery long before the patient reaches the age of consent. This approach is highly controversial, because it conflicts with ethical principles supporting patient autonomy (Belmont Report, 1979; Carpenter, 2021; Kon, 2015). In addition, among the manifestations without immediate safety concerns, some individuals, when older, may opt for a range of medical interventions to optimize function and appearance. The specifics of medical treatments are far beyond the scope of what can be addressed in this chapter, and the interested reader should consult the respective endocrine and surgical literature.

Some conditions of physical intersexuality are associated with a greater variability in long-term gender-identity outcome than others (Dessens, Slijper, & Drop, 2005). For instance, the incidence of a non-cisgender gender identity in 46,XX individuals with CAH assigned female may be as high as 5-10%, compared with 0.6% in the general population (Furtado et al., 2012). The substantial biological component underlying gender identity is a critical factor that must be considered when offering psychosocial, medical, and surgical interventions for individuals with conditions of physical intersexuality.

There is also ample evidence that people with physical intersexuality and their families may experience psychosocial distress (de Vries et al., 2019; Rosenwohl-Mack et al., 2020; Wolfe-Christensen et al., 2017)), in part related to psychosocial stigma (Meyer-Bahlburg, Khuri, Reyes-Portillo, & New, 2017a; Meyer-Bahlburg, Reyes-Portillo, Khuri, Ehrhardt, & New, 2017b; Meyer-Bahlburg, Khuri, Reyes-Portillo, Ehrhardt, & New, 2018).

Rationale for Addition to the SOC

Since 1980, the American psychiatric nomenclature recognized individuals with physical intersexuality who meet the criteria for gender-identity variants; however their diagnostic categorization changed with successive DSM editions. For instance, in DSM-III (American

Psychiatric Association, 1980), the Axis-I category of “transsexualism” could not be applied to such individuals in adulthood, but such children were labeled “gender identity disorder of childhood,” with the medical intersex condition to be specified in Axis III. In DSM-IV-TR (American Psychiatric Association, 2000), individuals with physical intersexuality were excluded from the Axis-I category of “gender identity disorder” regardless of age and, instead, grouped with other conditions under the category “gender identity disorder not otherwise specified.” In DSM-5 (American Psychiatric Association, 2013), which moved away from the multiaxial system, “gender identity disorder” was re-defined as “gender dysphoria” and applied regardless of age and physical intersex status, but individuals with physical intersexuality received the added specification “with a disorder of sex development” (Zucker et al., 2013). The forthcoming text revision of DSM-5 will keep the term gender dysphoria, but will refer in the text to the recent change of the International Classification of Diseases [ICD-11], i.e., the move of “gender incongruence” from the chapter “Mental, Behavioral or Neurodevelopmental Disorders” to a new chapter “Conditions Related to Sexual Health” (J. Drescher, personal communication, May 14, 2021).

Given this background, the decision was made to include a chapter on the clinical approach to individuals with both gender-identity variants and physical intersexuality in SOC-7, which will also be continued in SOC-8. A separate chapter is devoted to such individuals because they differ from those without physical intersexuality in phenomenological presentation, life trajectories, epidemiology, etiology, and stigma risks. In addition, this chapter provides recommendations on the general clinical approach to the management of individuals with physical intersexuality regardless of the specific gender-identity outcome.

The following statements are based on a thorough review of the pertinent available literature and a favorable risk-benefit ratio by clinical judgment.

Summary of Recommendations

Statement 1: We suggest that a multidisciplinary team, knowledgeable in diversity of gender identity and expression as well as in physical intersexuality, provide care to patients with physical intersexuality and their families.

Statement 2: We recommend that health professionals providing care for transgender youth and adults seek training and education in the aspects of intersex care relevant to their professional discipline.

Statement 3: We suggest that health professionals educate and counsel families of children with physical intersexuality from the time of diagnosis onward about their child’s specific intersex condition and its psychosocial implications.

Statement 4: We suggest that both providers and parents engage children/individuals with physical intersexuality in ongoing, developmentally appropriate communications about their intersex condition and its psychosocial implications.

Statement 5: We suggest that health professionals and parents support children/individuals with physical intersexuality in exploring their gender identity throughout their life.

Statement 6: We suggest that health professionals promote well-being and minimize the potential stigma of having an intersex condition by working collaboratively with both medical and non-medical individuals/organizations.

Statement 7: We suggest that health professionals refer patients with physical intersexuality and their families to mental-health providers as well as peer and other psychosocial supports as indicated.

Statement 8: We recommend that health professionals counsel patients with physical intersexuality and their families about puberty suppression and/or hormone treatment options within the context of the patient's gender identity, age and unique medical circumstances.

Statement 9: We suggest that health professionals counsel parents and patients with physical intersexuality (if cognitively sufficiently developed) to delay gender-confirming genital surgery, gonadal surgery, or both, when feasible, so as to optimize the child's self-determination and ability to participate in the decision based on informed consent.

Statement 10: We suggest that only surgeons experienced in intersex genital or gonadal surgery operate on patients with physical intersexuality.

Statement 11: We recommend that health professionals who are prescribing or referring patients for hormonal therapies/surgeries counsel individuals with physical intersexuality and fertility potential and their families about a) known effects of hormonal therapies/surgery on future fertility; b) potential effects of therapies that are not well studied and are of unknown reversibility; c) fertility preservation options; and d) psychosocial implications of infertility.

Statement 12: We suggest that health professionals caring for patients with physical intersexuality and congenital infertility introduce them and their families, early and gradually, to the various alternative options of parenthood.

Statement 1:
We suggest that a multidisciplinary team, knowledgeable in diversity of gender identity and expression as well as in physical intersexuality, provide care to patients with physical intersexuality and their families.

Physical intersexuality, a subtype of DSD, is a complex congenital condition that requires the involvement of experts from various medical and behavioral disciplines (Hughes et al., 2006). Team composition and function can vary depending on team location, local resources, diagnosis, and the needs of the individual with physical intersexuality and her/his family. The ideal team includes pediatric subspecialists in endocrinology, surgery and/or urology, psychology/psychiatry, gynecology, genetics, and, if available, personnel trained in social work, nursing, and medical ethics (Lee, Houk, Ahmed & Hughes, 2006). The structure of the team can be in line with 1) the traditional multidisciplinary medical model, 2) the interdisciplinary or interprofessional model, or 3) the transdisciplinary model. Although these structures can appear similar, they are in fact very different and can exert varying influences on how the team functions (Sandberg & Mazur, 2014). The 2006 Consensus Statement makes no decision about which model is best—multidisciplinary, interdisciplinary, or transdisciplinary—and only states that the models "imply different degrees of collaboration and professional autonomy" (Lee et al., 2016). Since the publication of the Consensus Statement in 2006, such teams have been

created both in Europe and in the United States. A listing of teams in the United States can be found on the DSD-Translational Network (DSD-TRN) website. There are also teams in a number of European countries (Thyen et al., 2018*).* While there are barriers to the creation of teams as noted by Sandberg and Mazur (2014), interdisciplinary teams help address a number of problems that have undermined the successful care of individuals with a diagnosis of physical intersexuality and their families, such as the scattered nature of services, the limited or absent communication between professionals, and the resulting fragmented nature of the explanations patients receive that cause more confusion than clarity.

Most individuals born with physical intersexuality will be identified at birth or shortly thereafter, while others will be identified at later times in the life cycle, for example at puberty (see Brain et al., 2010, Table 1). When this happens the team approach will be modified based on the diagnosis, and the age of the person. In some circumstances, the composition of the team can be expanded to include other specialists as needed.

It has been reported that children seen by an interdisciplinary team were significantly more likely to receive nearly the full range of services rather than only those services offered by a single provider (Crerand et al., 2019). Parents who received such care positively endorsed psychosocial services and the team approach and reported receiving more information than those who did not interact with such a team (Crerand et al., 2019).

Statement 2:
We recommend that health professionals providing care for transgender youth and adults seek training and education in the aspects of intersex care relevant to their professional discipline.

Results from interviews with medical trainees (Zelin et al., 2018; Liang, Gardner, Walker & Safer, 2017) and from programmatic self-audits and surveys (DeVita, Bishop & Plankey, 2018; Khalili, Leung, & Diamant, 2015) suggest that medical training programs are not adequately preparing practitioners to provide competent care to individuals presenting with gender dysphoria and intersexuality. Professional and stakeholder attendees of intersex-specific events have identified ongoing education and collaboration as an important professional development need (Mazur, Cohen-Kettenis, Meyer, Meyer-Bahlburg, & Zucker, 2007; Bertalan et al., 2018). This may be especially true for adult-care providers who may have less clinical guidance or support in assisting those individuals who are transitioning from pediatric to adult care (Crouch & Creighton, 2014).

However, there are few guidelines for training or assessing practitioner competency in managing these topics, and those that are available primarily apply to mental health professionals (MHPs) (ALGBTIC LGBQQIA Competencies Taskforce et al., 2013; Hollenbach, Eckstrand, Dreger, & AAMC Advisory Committee SOGI & SD, 2014).

For HPs wanting to improve their competency, seeking consultation from experts may be an option when formal education or empirical guidelines are otherwise unavailable. Given the relative widespread adoption of multidisciplinary expert teams in the treatment of intersexuality (Pasterski, Prentice & Hughes, 2010), individuals serving on these teams are well positioned to consult with and educate other health care staff who may not have received adequate training (Hughes et al., 2006). Therefore, it is recommended that the training of other professionals be a central component of team development (Auchus et al., 2010) and that members of multidisciplinary teams receive training specific to team-based work, including strategies for

engaging in interprofessional learning (Bisbey, Reyes, Traylor, & Salas, 2019; Interprofessional Education Collaborative Expert Panel, 2011).

Statement 3:
We suggest that health professionals educate and counsel families of children with intersexuality from the time of diagnosis onward about the child's specific intersex condition and its psychosocial implications.

Full disclosure of medical information to families of children with intersex conditions through education and counseling should begin at the time of diagnosis and should be consistent with guidance from multiple international consensus guidelines. The practice of disclosure seeks to enable more fully informed decision-making about care. Additionally, while shame and stigma surrounding physical intersexuality is associated with poorer psychosocial outcomes, open and proactive communication of health information has been proposed as a strategy to reduce those risks (de Vries et al., 2019). Depending on the person's diagnosis and developmental stage, intersex conditions may differentially impact individuals and their health care needs. Intersex-health-related communication must therefore be continuous and tailored to the individual. Research on decision-making in intersex care suggests that families are influenced by how clinical teams communicate (Timmermans et al., 2018). In keeping with the SOC, we encourage providers to adopt normalizing, affirming language and attitudes across education and counseling functions. For example, describing genital atypia as a "variation" or "difference" is more affirming than using the terms "birth defect" or "abnormality."

All HPs involved in a patient's care can provide essential education and information to families. In interdisciplinary teams, the type of education may align with an HP's area of expertise, for example a surgeon educating the patient on their anatomy, an endocrinologist teaching the specifics of hormonal development, or an MHP conveying the spectrums of gender and sexual identity. Other HPs may need to provide comprehensive education. Families should receive information that is pertinent to the patient's specific intersex variation, when known. All HPs can supplement this information with patient-centered resources available from support groups. People with physical intersexuality have also been hired as team members to provide education using their lived experience.

Consensus guidelines also recommend that families be offered ongoing peer and professional psychosocial support (Hughes et al., 2006) that may involve counseling with a focus on problem-solving and anticipatory guidance (Hughes et al., 2006). For example, families may seek guidance in educating other people – siblings, extended family, and caregivers – about the specific intersex condition of an individual. Other families may need support or mental-health care to manage the stress of intersex treatment. Adolescents may benefit from guidance on how to disclose information to peers as well as from support when navigating dating and sex. Providing counsel may also involve guiding families and individuals of all ages through a shared decision-making process around medical or surgical care. Providers may employ decision aids to support this process (Sandberg et al., 2019; Weidler, Baratz, Muscarella, Hernandez, & van Leeuwen, 2019).

Statement 4:
We suggest that both providers and parents engage children/individuals with intersexuality in ongoing, developmentally appropriate communications about their intersex condition and its psychosocial implications.

Communicating health information is a multi-directional process that includes the transfer of information from providers to patients, from parents to patients, as well as from patients back to their providers (Weidler & Peterson, 2019). While much emphasis has been placed on communicating to parents around issues of diagnosis and surgical decision-making, youth with DSD have reported barriers to engaging with healthcare providers and may not always turn to their parents for support (Callens, Kreukels, & van de Grift, 2021). To prepare individuals to be fully engaged and autonomous in their treatment, it is critical that both providers and parents communicate continuously with children/individuals.

Providers must set an expectation as soon as possible for ongoing, open communication between all parties, especially since parents may experience distress due to the uncertainty associated with DSD and may seek quick fixes (Roberts et al., 2020, Crissman et al., 2011). Models of shared decision-making as well as related decisional tools have been developed to support ongoing communication between healthcare providers and families/individuals (Weidler et al., 2019; Sandberg et al., 2019; Siminoff & Sandberg, 2015; Karkazis, Tamar-Mattis, & Kon, 2010). In addition to setting an expectation for dialogue, providers can also set the tone of communication. Providers can help parents and individuals tolerate diagnostic uncertainty while simultaneously providing education on anatomic variations, modeling openness to gender and sexual identity, and welcoming the child's/individual's questions. As they age, children/individuals may have questions or need age-appropriate information on issues of sex, menstruation, fertility, the need for hormone treatment (adrenal/sex), bone health, and cancer risk.

Parents also play a critical role in educating their children and may be the first people to disclose health information to their child (Callens et al., 2021). As part of expectation-setting around communication, providers should prepare parents to educate their child and members of their support system about the intersex diagnosis and treatment history. Some parents report difficulties in knowing how much to disclose to others as well as to their own children (Danon & Kramer, 2017; Crissman et al., 2011). The stress parents experience while raising children with an intersex condition is increased when parents adopt an approach that minimizes disclosure/discussion of their child's diagnosis (Crissman et al., 2011). The level of stress also varies by developmental stage, with parents of adolescents reporting higher rates of stress (Hullman, Fedele, Wolfe-Christensen, Mullins, & Wisniewski, 2011). Therefore, HPs should assist parents in developing strategies specific to their child's developmental stage that address their psychosocial or cultural concerns and values (Weidler & Peterson, 2019; Danon & Kramer, 2017). Finally, broader research on sexuality and gender variance has found that – counter to the associations between shame/stigma and negative health outcomes – supportive family behaviors (including talking with children about their identity and connecting them with peers) predicted greater self-esteem and better health outcomes in individuals (Ryan, Russell, Huebner, Diaz, & Sanchez, 2010).

Statement 5:

We suggest that health professionals and parents should support children/individuals with intersexuality in exploring their gender identity throughout their life.

Psychological, social, and cultural constructs all intersect with biological factors to form an individual's gender identity. As a group, individuals with physical intersexuality show increased rates of gender nonconforming behavior, gender-questioning, and cross-gender wishes in childhood, dependent in part on the discrepancy between the prenatal sex-hormonal milieu, in

which the fetal brain has differentiated, and the sex assigned at birth (Callens et al., 2016; Hines, Constantinescu, & Spencer, 2015; Meyer-Bahlburg et al., 2016; Pasterski et al., 2015). Gender identity problems are observed at different rates in individuals with physical intersexuality (de Vries, Doreleijers, & Cohen-Kettenis, 2007). More recently, some individuals have been documented to develop a non-binary identity, at least privately (Kreukels et al., 2018). Although the majority of people with physical intersexuality may not experience gender dysphoria or wishes for gender transition, they may still have feelings of uncertainty and unanswered questions regarding their gender (Kreukels et al., 2018). Questions about gender identity may arise from such factors as genital appearance, pubertal development, and knowledge of items such as the diagnostic term of the medical condition, gonadal status, sex chromosome status, and history of genital surgery. Therefore, HPs need to be accessible for clients to discuss such questions and feelings, openly converse about gender diversity, and adopt a less binary approach to gender. HPs are advised to guide parents as well in supporting their children in exploring gender.

Furthermore, such support should not be confined to the childhood years. Rather, individuals should be given the opportunity to explore their gender identity throughout their lifetime, because different phases may come with new questions regarding gender (for example, puberty/adolescence, childbearing age). Children in general may have questions regarding their gender identity at salient points during their maturation and evolution. When faced with additional stressors, for example, genital ambiguity, genital examinations and procedures, as well as the intersectionality of cultural bias and influences, individuals with physical intersexuality may need support and should be encouraged to seek educated professional assistance and guidance when needed. Also, HPs should inquire regularly to determine if their clients with physical intersexuality are in need of such support.

When people experience gender incongruence, gender-affirming interventions may be considered. Procedures that should be applied in such interventions are described in other chapters.

Statement 6:

We suggest that health professionals promote well-being and minimize the potential stigma of having an intersex condition by working collaboratively with both medical and non-medical individuals/organizations.

Individuals with physical intersexuality are reported to experience stigma, feelings of shame, guilt, anger, sadness and depression (Carroll, Graff, Wicks, & Thomas, 2020; Joseph et al., 2017, Schützmann, Brinkmann, Schacht, & Richter-Appelt, 2009). Higher levels of psychological problems are observed in this population than in the general population (Liao & Simmonds, 2013; de Vries et al., 2019). In addition, parental fear of stigmatization still plays an important role in clinical decision-making (Fleming, Kanfl & van Riper, 2017; Rolston, Gardner, Vilain, & Sandberg, 2015; Timmermans et al., 2019).

Thyen, Richter-Appelt, Wiesemann, Holterhus and Hiort (2005) found that repeated genital examinations appear to be correlated with shame, fear and pain and may increase the likelihood of developing post-traumatic stress disorder (PTSD) later in life (Alexander et al., 1997; Money & Lamacz, 1987). Exposure to repeated genital examinations, fear of medical interventions, parental and physician secrecy about being intersex, ultimately undermines the self-empowerment and self-esteem of the person with intersexuality (Meyer-Bahlburg et al., 2018; Thyen et al., 2005; Tishelman, Shumer, & Nahata, 2017; van de Grift, Cohen-Kettenis, de Vries,

& Kreukels, on behalf of dsd-LIFE, 2018). For recommendations on how to conduct genital examinations to minimize adverse psychological side effects please see Tishelman et al. (2017).

There is an active movement within the intersex community to alleviate stigma, and return human rights and dignity to intersex people, rather than viewing them as medical anomalies and curiosities (Yogyakarta Principles, 2007, 2017). Chase (2003) summarizes the major reasons for the intersex advocacy movement and outlines how stigma and emotional trauma are the outcome of ignorance and the perceived need for secrecy. Public awareness of intersex conditions is infrequent, and images and histories of individuals with intersexuality are still presented as ”abnormalities of nature”. We, therefore, advise HPs to actively educate their colleagues, intersex patients, their families, and communities, raise public awareness, and increase knowledge about physical intersexuality. Societal awareness and knowledge regarding intersexuality may help reduce discrimination and stigmatization. Tools and education/information materials may also help individuals with physical intersexuality disclose their condition, if desired (Ernst et al., 2016).

HPs should be able to recognize and address stigmatization in their clients (see Meyer-Bahlburg et al., 2017a, 2017b, 2018) and should encourage people with physical intersexuality of various ages to connect via support groups. There is a need for developing specific techniques/methods for assisting clients to cope with stigma related to intersex.

Statement 7:
We suggest that health professionals refer patients with intersexuality and their families to mental-health providers as well as peer and other psychosocial supports as indicated.

For almost all parents, the birth of a child with somatic intersexuality is entirely unexpected and comes as a shock. Their inability to respond immediately to the ubiquitous question, “Is your baby a boy or a girl?”, their lack of knowledge about the child’s condition, the uncertainty regarding the child’s future, and the pervasive intersex stigma are likely to cause distress, sometimes to the level of PTSD, and may lead to prolonged anxiety and depression (Pasterski, Mastroyannopoulou, Wright, Zucker, & Hughes, 2014; Roberts et al., 2020; Wisniewski & Sandberg, 2015). This situation may affect parental care and long-term outcome of their child with physical intersexuality (Schweizer, Brunner, Gedrose, Handford, & Richter-Appelt, 2017). As these children grow up, they are also at risk of experiencing intersex stigma in its three major forms (enacted, anticipated, internalized) in all spheres of life (Meyer-Bahlburg et al., 2017a, 2017b, 2018), along with other potential difficulties such as body-image problems, gender-atypical behavior, gender-identity questioning. Many may face the additional challenge presented by the awareness of the incongruence between their assigned gender and biological characteristics such as sexual karyotype, gonads, past and/or current sex-hormonal milieu, and reproductive-tract configuration. This situation may also adversely affect patients’ mental health (Godfrey, 2021; Meyer-Bahlburg, in press). As intersex conditions are rare, parents of such children and later the patients themselves may experience their situation as unique and very difficult for others to understand.

Thus, based on clinical experience, there is a consensus among PHs who are experienced in intersex care, that social support is a crucial component of intersex care, not only through professional support by MPHs (Pasterski et al., 2010), but also, importantly, through support groups of individuals with intersex conditions (Baratz, Sharp, & Sandberg, 2014; Cull & Simmonds, 2010; Hughes et al., 2006; Lampalzer, Briken, & Schweizer, 2021). A detailed

international listing of DSD and intersex peer support and advocacy groups with their websites has been provided by Lee et al. (2016). Given the heterogeneity of intersex conditions and treatment regimens, a patient may find it most helpful to associate with a support group that include members with the same or similar condition as that of the patient. It is important that HPs specializing on intersex care also collaborate closely with such support groups so that occasional differences in opinions regarding specific aspects of care can be resolved through detailed discussions. Close contacts between HPs and support groups also facilitate community-based participatory research that benefits both sides.

Statement 8:

We recommend that health professionals counsel patients with intersexuality and their families about puberty suppression and/or hormone treatment options within the context of the patient's gender identity, age and unique medical circumstances.

While the majority of people with intersexuality have a gender identity in line with their XX or XY karyotype, there is sufficient heterogeneity that HPs should be able to provide customized approaches. For example, among XX individuals with virilizing CAH, a larger than expected minority have a male gender identity (Dessens et al., 2005). Among XY individuals with partial androgen insensitivity syndrome, gender identity can vary significantly (Babu & Shah, 2021). Furthermore, among XY individuals with 5α-reductase-2 (5α-RD-2) deficiency and with 17beta-hydroxysteroid dehydrogenase-3 deficiency who are assigned the female sex at birth, a large fraction (56–63% and 39–64%, respectively) change from a typical female gender role to a typical male gender role as they age (Cohen-Kettenis, 2005).

One of the most fraught issues for a child with intersexuality, particularly when associated with noticeable genital ambiguity, is sex assignment, and, from the parents' perspective, the gender of rearing (Fisher et al., 2016). For many years, it was believed that sex assignment had to be made as quickly as a thorough diagnostic evaluation would permit (Houk & Lee, 2010; Yang, Baskin, & Disandro, 2010). For instance, a female sex assignment was traditionally recommended for 46,XX newborns with CAH and a male sex assignment for those with 46,XY 5α-RD-2 deficiency. However, this approach did not consider the patient's potential gender identity or the patient's participation in the decision-making process.

People with intersexuality have a wide range of medical options open to them depending on their gender identity and its alignment with anatomy. Options include puberty-suppression medication, hormone treatment, and surgeries all customized to the unique circumstances of the patient (Weinand & Safer, 2015; Safer & Tangpricha, 2019a) (see Adolescent Medicine and Hormone Therapy chapters). Specifically, when functional gonads are present, puberty may be temporarily suspended by using gonadotropin-releasing hormone analogues (GnRHas). Such intervention can facilitate the necessary passage of time needed by the patient to explore gender identity and to actively participate in sex designation, especially for conditions in which sex role change is common (i.e., in 5α-RD-2 deficiency; Cocchetti et al., 2020; Fisher et al., 2016).

HPs can counsel patients and their families directly if the providers have sufficient expertise and can leverage expertise needed to determine both a course of treatment appropriate for the patient and the logistics involved in implementing the chosen therapeutic option.

Statement 9:

We suggest that health professionals counsel parents and patients with intersexuality (when cognitively sufficiently developed) to delay gender-confirming genital surgery, gonadal surgery, or both, so as to optimize the child's self-determination and ability to participate in the decision based on informed consent.

International human rights organizations have increasingly expressed their concerns that surgeries performed before a child can participate meaningfully in decision-making may endanger the child's human rights to autonomy, self-determination, and an open future (e.g., Human Rights Watch, 2017). Numerous medical and patient advocacy organizations, as well as several countries, have joined these international human rights groups in recommending the delay of surgery when medically feasible (Dalke et al., 2020; National Academies of Sciences, Engineering, and Medicine, 2020).

However, it is important to note that some anatomic variations, such as obstruction of urinary flow or exposure of pelvic organs, pose an imminent risk to physical health (Mouriquand et al., 2016). Others, such as menstrual obstruction or long-term malignancy risk in undescended testes, have eventual physical consequences. A third group of variations, i.e., variations in the appearance of external genitals or vaginal depth, pose no immediate or long-term physical risk. The above recommendation addresses only those anatomic variations that, if left untreated, have no immediate adverse physical consequences and where delaying surgical treatment poses no physical health risk.

Non-urgent surgical care for patients with these variations is complex and often contested, particularly when a patient is an infant or a young child and cannot yet participate in the decision-making process. Older people with intersexuality have reported psychosocial and sexual health problems, including depression, anxiety, and sexual and social stigma (Rosenwohl-Mack et al., 2020; de Vries et al., 2019). Some studies have suggested that patients with a specific variation (e.g., 46,XX CAH) agree with surgery being performed before adolescence (Bennecke et al., 2021). Recent studies suggest that some adolescents and adults are satisfied with the appearance and function of the genitals after childhood surgery (Rapp et al., 2020). A child's genital difference can also become a source of stress for parents, and there is research that reports a correlation of surgery to create binary genitals with a limited amount of reduction in parental distress (Wolfe-Christensen et al., 2017), although a minority of parents may report decisional regret (Ellens et al., 2017). Consequently, some organizations recommend that surgery be offered to very young children (American Urological Association, 2019; Pediatric Endocrine Society, 2020).

Nonetheless, long-term outcomes studies are limited, and most studies reporting positive outcomes lack a non-surgical comparison group (Dalke, Baratz, & Greenberg, 2020; National Academies of Sciences, Engineering, and Medicine, 2020). There is also no evidence that surgery protects children with intersex conditions from stigma (Roen, 2019). Adults with intersexuality do experience stigma, depression, and anxiety related to their genitalia, but can also experience stigma whether or not they have surgery (Ediati et al., 2017; Meyer-Bahlburg et al., 2017a, 2017b, 2018). There is also evidence that surgeries may lead to significant cosmetic, urinary, and sexual complications extending into adulthood (Gong & Cheng, 2017; National Academies of Sciences, Engineering, and Medicine, 2020). Recent studies suggest that some groups of patients may have particularly negative experiences with gonadectomy, though this risk has to be weighed against that of gonadal malignancy (Duranteau et al., 2020; Rapp et al., 2020). People with intersex conditions are also far more likely than the general population to be gender diverse or have gender dysphoria (Almasri et al., 2018; Pasterski et al., 2015). Genital

surgeries may therefore irreversibly reinforce a binary sex assignment that a child may not identify with in the future.

However, it is very important to note the division within the medical field regarding its management guidelines for early genital surgery, and also the authors of this chapter did not reach a consensus. Some intersex specialists consider it inappropriate and potentially harmful to insist on a universal deferral of early genital surgery for genital variations without immediate medical risks. Multiple reasons supporting this view include: 1) intersex conditions are highly heterogeneous with respect to type and severity as well as associated gonadal structure, function, and malignancy risk; 2) societies and families vary tremendously in gender ideologies and intersex-stigma potential; 3) early surgery may present certain technical advantages; and 4) most importantly, ten published surveys of clinic patients with intersexuality (most of whom had previously undergone genital surgery) show that the majority endorse surgery before the age of consent, overwhelmingly so in the case of patients with 46,XX CAH and less strongly in patients with XY intersex conditions (Meyer-Bahlburg, under review). Under these circumstances, a syndrome- and syndrome-severity-specific, individualized approach to decisions regarding genital surgery and its timing is called for, an approach that has been adopted adopted by medical societies whose members include primary intersex specialists (Bangalore Krishna et al., 2021; Pediatric Endocrine Society, 2020; Speiser et al., 2018; Stark, Shoag, & Poppas, 2019) and by certain support organizations of patients/families with 46,XX CAH (CARES Foundation; Krege et al., 2019, Appendix). To withhold information about such conflicting guidelines from patients and families would appear to violate informed-consent regulations.

Statement 10:
We suggest that only surgeons experienced in intersex genital or gonadal surgery operate on patients with intersexuality.

Intersex conditions are rare, and intersex genital and gonadal anatomy is heterogeneous. Surgeries have been associated with a risk of significant long-term complications (e.g., National Academies of Sciences, Engineering, and Medicine, 2020), and most surgical training programs do not prepare trainees to provide this specialized care (Grimstad, Kremen, Streed, & Dalke, 2021). In recognition of the complexity of surgical care across the lifespan, standards produced by expert and international consensus recommend that this care be provided by an interdisciplinary teams of experts (Krege et al, 2019; Lee et al., 2016; Pediatric Endocrine Society, 2020). Therefore, we advise that surgical care be limited to intersex-specialized, interdisciplinary settings that include experienced surgeons.

Statement 11:
We recommend that health professionals who are prescribing or referring for hormonal therapies/surgeries counsel individuals with intersexuality and fertility potential and their families about a) known effects of hormonal therapies/surgery on future fertility; b) potential effects of therapies that are not well studied and are of unknown reversibility; c) fertility preservation options; and d) psychosocial implications of infertility.

Patients with certain intersex conditions may have reproductively functional genitalia but experience infertility due to gonad development. Others may have functioning gonads with viable germ cells but an inability to achieve natural fertility secondary to incongruent internal or external genitalia (van Batavia & Kolon, 2016). Pubertal suppression, hormone treatment with sex steroid hormones, and gender-affirmation surgeries may all have an adverse impact on

future fertility. The potential consequences of the treatment and fertility preservation options should therefore be reviewed and discussed.

Individuals with functioning testes should be advised that prolonged treatment with estrogen and suppression of testosterone, as studied in people with transgenderism without physical intersexuality, may cause testicular atrophy and a reduction in sperm count (Mattawanon, Spencer, Schirmer, & Tangpricha, 2018). Although interruption of such cross-sex hormone treatment may improve sperm quality, a complete reversal of semen impairment cannot be guaranteed (Sermondade et al., 2021). The principal fertility preservation option for individuals with functioning testes is cryopreservation of sperm collected through masturbation or vibratory stimulation (de Roo, Tilleman, T'Sjoen, & de Sutter, 2016). Although there are no data for success in humans, there is a proposal to offer direct testicular extraction and cryopreservation of immature testicular tissue to adolescents who have not yet undergone spermarche (Mattawanon et al., 2018).

Individuals with functioning ovaries should be advised that testosterone therapy usually results in cessation of both menses and ovulation, often within a few months of initiating therapy. There are major gaps in knowledge regarding the potential effects of testosterone on oocytes and subsequent fertility. In transgender people, one study reported that testosterone treatment may be associated with the development of polycystic ovarian morphology (Grynberg et al., 2010). However, other researchers have not found evidence of polycystic ovarian syndrome (PCOS) among transgender men receiving gender-affirming hormone therapy, based on metabolic (Chan, Liang, Jolly, Weinand, & Safer, 2018) or histologic parameters (de Roo et al., 2017). Individuals with an intact uterus and functioning ovaries may regain their fertility potential if testosterone therapy is discontinued.

Fertility preservation options in post-pubertal people with physical intersexuality and functioning ovaries include hormonal stimulation for mature oocyte cryopreservation or ovarian tissue cryopreservation. Alternatively, stimulated oocyte extraction has been reported even for a patient continuing testosterone therapy (Safer & Tangpricha, 2019b). Similarly, oocyte cryopreservation after ovarian stimulation has been reported in a transgender boy on GnRHa therapy (Rothenberg, Witchel, & Menke, 2019). It should be noted that ovarian stimulation, temporary cessation of GnRHa, testosterone treatment, or both, and gynecological procedures, all can be psychologically distressing to individuals, with the stress reaction being influenced by mental health, gender identity, and other medical experience. Applicability of certain interventions may depend on the support of others including potential partners.

Statement 12:

We suggest that health professionals caring for patients with intersexuality and congenital infertility should introduce them and their families, early and gradually, to the various alternative options of parenthood.

For people with intersex characteristics, the likelihood of infertility may be recognized in infancy, childhood, adolescence as well as in adulthood, without first engaging in attempts to conceive. For many individuals, a diagnosis of infertility accompanies the intersex diagnosis (Jones, 2020). For some patients, assisted heterologous fertilization (e.g., oocyte or sperm donation) may be an option.

Multiple adoption pathways exist. Some may require commitment and a considerable investment of time. Individuals who are either not interested in engaging in the efforts to achieve

fertility previously described or for whom fertility is not possible, can benefit from early exposure to the options available for adoption and alternative parenthood. While uterus transplantation has had preliminary success in people with Mullerian agenesis (Richards et al., 2021), there is no protocol to date that avoids exposure of the developing fetus to the risks associated with the medications used to avoid transplant rejection.

References:

Alexander, T. (1997). The medical management of intersexed children: an analogue for childhood sexual abuse. Retrieved from Intersex Society of North America: www.isna.org/library/analog.ht

ALGBTIC LGBQQIA Competencies Taskforce, Harper, A., Finnerty, P., Martinez, M., Brace, A., Crethar, H. C., … Hammer, T. R.. (2013). Association for Lesbian, Gay, Bisexual, and Transgender Issues in Counseling Competencies for Counseling with Lesbian, Gay, Bisexual, Queer, Questioning, Intersex, and Ally Individuals. Journal of LGBT Issues in Counseling, 7(1), 2–43. https://doi.org/10.1080/15538605.2013.755444

Almasri, J., Zaiem, F., Rodriguez-Gutierrez, R., Tamhane, S. U., Iqbal, A. M., Prokop, L. J., . Murad, M. (2018). Genital reconstructive surgery in females with congenital adrenal hyperplasia: A systematic review and meta-analysis. Journal of Clinical Endocrinology and Metabolism, 103(11), 4089-4096. doi:10.1210/jc.2018-01863

American Psychiatric Association. (1980). Diagnostic and statistical manual of mental disorders C(3rd ed., DSM-III). Washington, DC: Author.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (4th ed., text rev., DSM-IV-TR). Washington, DC: Author.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed., DSM-5). Washington, DC: Author.

American Urological Association (AUA) Board of Directors. (2019). Pediatric decision making and differences of sex development: A Societies for Pediatric Urology and American Urological Association joint position statement." Available at https://www.auanet.org/guidelines/guidelines/joint-statement-on-dsd. Accessed July 15, 2021

Auchus, R. J., Witchel, S. F., Leight, K. R., Aisenberg, J., Azziz, R., Bachega, T. A., Baker, L. A., … Zuckerman, A. E. (2010). Guidelines for the development of comprehensive care centers for congenital adrenal hyperplasia: Guidance from the CARES Foundation Initiative. International Journal of Pediatric Endocrinology, 2010, 1–17. https://doi.org/10.1155/2010/275213

Babu, R., & Shah, U. (2021). Gender identity disorder (GID) in adolescents and adults with differences of sex development (DSD): A systematic review and meta-analysis. Journal of Pediatric Urology, 17(1), 39-47.

Bangalore Krishna, K. , Kogan, B. A., Mazur, T., Hoebeke, P., Bogaert, G., & Lee, P. A. (2021). Individualized care for patient with intersex (differences of sex development): part 4/5. Considering the Ifs, Whens, and Whats regarding sexual-reproductive system surgery. Journal of Pediatric Urology, 17(3), 338-345. https://doi.org/10.1016/j.jpurol.2021.02.011.

Baratz, A. B., Sharp, M. K., & Sandberg, D. E. (2014). Disorders of sex development peer support. Endocrine Development, 27, 99-112.

Belmont Report (1979). Available from: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont/html.

Bennecke, F., Bernstein, S., Lee, P., van de Grift, T. C., Nordenskjöld, A., Rapp, M., …on behalf of the dsd-LIFE Group. (2021). Early genital surgery in disorders / differences of sex development (DSD). Patients' perspectives. Archives of Sexual Behavior, 50, 913-923.

Bertalan, R., Lucas-Herald, A., Kolesinska, Z., Berra, M., Cools, M., Balsamo, A., & Hiort, O. (2018). Evaluation of DSD training schools organized by cost action BM1303 "DSDnet." Orphanet Journal of Rare Diseases, 13(1). https://doi.org/10.1186/s13023-018-0967-3

Bisbey, T. M., Reyes, D. L., Traylor, A. M., & Salas, E. (2019). Teams of psychologists helping teams: The evolution of the science of team training. American Psychologist, 74(3), 278–289. https://doi.org/10.1037/amp0000419

Blackless, M., Charuvastra, A., Derryck, A., Fausto-Sterling, A., Lauzanne, K., & Lee, E. (2000). How sexually dimorphic are we? Review and synthesis. American Journal of Human Biology, 12(2), 151-166.

Brain, C. E., Creighton, S. M., Mushtaq, I., Carmichael, P. A., Barnicoat, A., Honour, J. W., … Achermann, J. C. (2010). Holistic management of DSD. Best Practice & Research. Clinical Endocrinology & Metabolism, 24(2), 335–354. https://doi.org/10.1016/j.beem.2010.01.006

Callens, N., Kreukels, B. P. C., & van de Grift, T. C. (2021). Young Voices: Sexual Health and Transition Care Needs in Adolescents with Intersex/Differences of Sex Development—A Pilot Study. Journal of Pediatric and Adolescent Gynecology, 34(2). https://doi.org/10.1016/j.jpag.2020.11.001

Callens, N., Van Kuyk, M., van Kuppenveld, J.H., Drop, S.L., Cohen-Kettenis, P.T., Dessens, A.B.; Dutch Study Group on DSD, (2016). Recalled and current gender role behavior, gender identity and sexual orientation in adults with Disorders/Differences of Sex Development. Godfrey, L. M. (2021). Mental health outcomes among individuals with 46,XY disorders of sex development: A systematic review. Journal of Health Psychology, 26(1), 40-59.

CARES Foundation. (2020). Statement on Surgery. https://www.caresfoudation.org/treatment/surgery.pdf

Carpenter, M. (2018). Intersex variations, human rights, and the International Classification of Diseases. Health and Human Rights Journal, 20(2), 205-214.

Carpenter, M. (2021). Intersex human rights, sexual orientation, gender identity, sex characteristics and the Yogyakarta principles plus 10. Culture, Health & Sexuality 23(4): 516-532.

Carroll, L., Graff, C., Wicks, M., & Thomas, A. D. (2020). Living with an invisible illness: a qualitative study exploring the lived experiences of female children with congenital adrenal hyperplasia. Quality of Life Research, 29(3), 673-681

Chan, K. J., Liang, J. J., Jolly, D., Weinand, J. D., & Safer, J. D. (2018). Exogenous testosterone does not induce or exacerbate the metabolic features associated with PCOS among transgender men. Endocrine Practice, 24(6):565-572.

Chase, C. (2003). What is the agenda of the intersex patient advocacy movement? The Endocrinologist, 240-2.

Cocchetti, C., Ristori, J., Mazzoli, F., Prunas, A., Bertelloni, S., Magini, A., ... Fisher, A.D. (2020). 5alpha-Reductase-2 deficiency: is gender assignment recommended in infancy? Two case-reports and review of the literature. Journal of Endocrinology Investigation, 43(8):1131-1136.

Cohen-Kettenis, P.T. (2005) Gender change in 46, XY persons with 5alfa-reductase-2 deficiency and 17alpha-hydroxysteroid dehydrogenase-3 deficiency. Archives of Sexual Behavior, 34:399–410

Crerand, C. E., Kapa, H. M., Litteral, J. L., Nahata, L., Combs, B., Indyk, J. A., … Hansen-Moore, J. (2019). Parent perceptions of psychosocial care for children with differences of sex development. Journal of Pediatric Urology, 15(5), 522e1-522e8. https://doi.org/10.1016/j.jpurol.2019.06.024.

Crissman, H. P., Warner, L., Gardner, M., Carr, M., Schast, A., Quittner, A. L. … Sandberg, D. E. (2011). Children with disorders of sex development: A qualitative study of early parental experience. International Journal of Pediatric Endocrinology, 1(10), 1-11.

Crouch, N. S., & Creighton, S. M. (2014). Transition of care for adolescents with disorders of sex development. Nature Reviews. Endocrinology, 10(7), 436-442. http://dx.doi.org/10.1038/nrendo.2014.62

Cull, M. L., & Simmonds, M. (2010). Importance of support groups for intersex (disorders of sex development) patients, families and the medical profession. Sexual Development, 4, 310-312.

Dalke, K. B., Baratz A, & Greenberg, J. A. (2020). Protecting children with intersex traits: legal, ethical, and human rights considerations. In: M. Legato (Ed.), The Plasticity of Sex (pp. 207-224). Cambridge: Academic Press

Danon, L. M., & Krämer, A. (2017). Between Concealing and Revealing Intersexed Bodies: Parental Strategies. Qualitative Health Research, 27(10), 1562–1574. https://doi.org/10.1177/1049732317697100

Delimata, N., Simmonds, M., O'Brien, M., Davis, G., Auchus, R., & Lin-Su, K. (2018). Evaluating the term 'Disorders of Sex Development': A multidisciplinary debate. Social Medicine, 12(1), 98-107.

de Roo, C., Lierman, S., Tilleman, K. Peynshaert, K., Braeckmans, K., Caanen, M., … de Sutter, P. (2017) Ovarian tissue cryopreservation in female-to-male transgender people: insights into ovarian histology and physiology after prolonged androgen treatment. Reproductive BioMedicine Online, 34(6):557-566.

de Roo, C., Tilleman, K,, T'Sjoen, G. & De Sutter, P. (2016). Fertility options in transgender people. International Review of Psychiatry, 28(1), 112-119.

Dessens, A.B., Slijper, F.M., & Drop, S.L. (2005). Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. Archives of Sexual Behavior, 34:389-97.

DeVita, T., Bishop, C., & Plankey, M. (2018). Queering medical education: Systematically assessing LGBTQI health competency and implementing reform. Medical Education Online, 23(1), 1-8. http://dx.doi.org/10.1080/10872981.2018.1510703

de Vries, A. L., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2007). Disorders of sex development and gender identity outcome in adolescence and adulthood: understanding gender identity development and its clinical implications. Pediatric Endocrinology Reviews 4, 343-351.

de Vries, A. L. C., Roehle, R., Marshall, L., Frisen, L., van de Grift, T. C., Kreukels, B. P. C., & dsd-Life Group. (2019). Mental health of a large group of adults with disorders of sex development in six European countries. Psychosomatic Medicine, 81(7), 629-640. doi:10.1097/PSY.0000000000000718

DSD-TRN. http://dsdtrn.org/.

Duranteau, L., Rapp, M., van de Grift, T. C., Hirschberg, A. L., Nordenskjöld, A., & dsd-Life Group. (2021). Participant- and clinician-reported long-term outcomes after surgery in individuals with complete androgen insensitivity syndrome. Journal of Pediatric and Adolescent Gynecology, 34(2), 168-175. doi:10.1016/j.jpag.2020.11.01

Ediati A., Juniarto, A. Z., Birnie, E., Okkerse, J., Wisniewski, A., Drop, S., . . . Dessens, A. (2017). Social stigmatisation in late identified patients with disorders of sex development in Indonesia. BMJ Paediatrics Open, 1(1), e000130. doi:10.1136/bmjpo-2017-000130

Ellens, R. E. H., Bakula, D. M., Mullins, A. J., Scott Reyes, K. J., Austin, P., Baskin, L., . . Wolfe-Christensen, C. (2017). Psychological adjustment of parents of children born with atypical genitalia 1 year after genitoplasty. Journal of Urology, 198(4), 914-920. doi:10.1016/j.juro.2017.05.035

Ernst, M. E., Sandberg, D. E., Keegan, C., Quint, E. H., Lossie, A. C., & Yashar, B. M. (2016). The lived experience of MRKH: sharing health information with peers. Journal of Pediatric and Adolescent Gynecology, 29(2), 154-158.

Fisher, A.D., Ristori, J., Fanni, E., Castellini, G., Forti, G., Maggi, M. (2016) Gender identity, gender assignment and reassignment in individuals with disorders of sex development: a major dilemma. Journal of Endocrinology Investigation, 39(11):1207–1224.

Fleming, L., Knafl, K., Van Riper, M., (2017). How the child's gender matters for families having a child with congenital adrenal hyperplasia. Journal of Family Nursing, 23(4), 516-533.

Furtado, P. S., Moraes, F., Lago, R., Barros, L. O., Toralles, M. B., & Barroso, U. Jr. (2012). Gender dysphoria associated with disorders of sex development. Nature Reviews Urology 9(11),620-627.

Godfrey, L. M. (2021). Mental health outcomes among individuals with 46,XY disorders of sex development: A systematic review. Journal of Health Psychology, 26(1), 40-59.

Gong, E. M., & Cheng, E. Y. (2017). Current challenges with proximal hypospadias: We have a long way to go. Journal of Pediatric Urology, 13(5), 457-467. doi:10.1016/j.jpurol.2017.03.024 doi:10.1016/j.jpurol.2017.03.024

Griffiths, D.A. (2018). Shifting syndromes: Sex chromosome variations and intersex classifications. Social Studies of Science, 48(1), 125-148. doi: 10.1177/0306312718757081

Grimstad, F., Kremen, J., Streed, C.G., & Dalke, K.B. (2021). The health care of adults with differences in sex development is changing: Time to prepare clinicians and health systems. LGBT Health. Online ahead of print.

Grynberg, M., Fanchin, R., Dubost, G., Colan, J. C., Brémont-Weil, C., Frydman, R., &Ayoubi, J. M. (2010). Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. Reproductive BioMedicine Online, 20(4), 553-558.

Hines, M. (2015). Increased cross-gender identification independent of gender role behavior in girls with congenital adrenal hyperplasia: Results from a standardized assessment of 4-to 11-year-old children. Archives of Sexual Behavior, 44(5), 1363-1375.

Hines, M., Constantinescu, M., & Spencer, D. (2015). Early androgen exposure and human gender development. Biology of Sex Differences, 26(6), 3-

Hollenbach, A., Eckstrand, K., Dreger, A. & AAMC Advisory Committee on Sexual Orientation, Gender Identity, and Sex Development (2014). Implementing Curricular and Institutional Climate Changes to Improve Health Care for Individuals Who Are LGBT, Gender Nonconforming, or Born with Dsd: A Resource for Medical Educators. Washington DC: Association of American Medical Colleges.

Houk, C.P., & Lee, P.A. (2010) Approach to assigning gender in 46,XX congenital adrenal hyperplasia with male external genitalia:replacing dogmatism with pragmatism. Journal of Clinical Endocrinology and Metabolism, 95:4501–4508

Hughes, I. A., Houk, C., Ahmed, S. F., Lee, P. A., & LWPES/ESPE Consensus Group. (2006). Consensus statement on the management of intersex disorders. Archives of Disease in Childhood, 91, 554-563.

Hughes, I. A., Nihoul-Fékété, C., Thomas, B., & Cohen-Kettenis, P. T. (2007). Consequences of the ESPE/LWPES guidelines for diagnosis and treatment of disorders of sex development. Best Practice & Research Clinical Endocrinology & Metabolism, 21, 351-365.

Hullmann, S. E., Fedele, D. A., Wolfe-Christensen, C., Mullins, L. L., & Wisniewski, A. B. (2011). Differences in adjustment by child developmental stage among caregivers of children with disorders of sex development. International Journal of Pediatric Endocrinology, 2011(1). https://doi.org/10.1186/1687-9856-2011-16

Human Rights Watch (2017). "I want to be like nature made me": Medically unnecessary surgeries on intersex children in the U.S. https://www.hrw.org/sites/default/files/report_pdf/lgbtintersex0717_web_0.pdf;

Interprofessional Education Collaborative Expert Panel. (2011). Core competencies for interprofessional collaborative practice: Report of an expert panel. Washington, D.C.: Interprofessional Education Collaborative

Johnson, E. K., Rosoklija, I., Finlayson, C., Chen, D., Yerkes, E. B., Madonna, M. B., … Cheng, E. Y. (2017). Attitudes towards “disorders of sex development” nomenclature among affected individuals. Journal of Pediatric Urology, 13, 608.e1-608.e8

Jones, C. (2020). Intersex, infertility and the future: early diagnoses and the imagined life course. Sociology of Health and Illness, 42(1):143-156.

Joseph, A. A., Kulshreshtha, B., Shabir, I., Marumudi, E., George, T. S.., Sagar, R., ... Ammini, A. C.. 2017. "Gender issues and related social stigma affecting patients with a disorder of sex development in India." Archives of Sexual Behavior, 46(2): 361-367.

Karkazis, K., Tamar-Mattis, A., & Kon, A. A. (2010). Genital surgery for disorders of sex development: implementing a shared decision-making approach. Journal of Pediatric Endocrinology and Metabolism, 23(8). https://doi.org/10.1515/jpem.2010.129

Khalili, J., Leung, L. B., & Diamant, A. L. (2015). Finding the perfect doctor: identifying lesbian, gay, bisexual, and transgender–competent physicians. American Journal of Public Health, 105(6), 1114–1119. https://doi.org/10.2105/ajph.2014.302448

Kon, A. A. (2015). Ethical issues in decision-making for infants with disorders of sex development. Hormone and Metabolic Research, 47(5): 340-343.

Krege, S., Eckoldt, F., Richter-Unruh, A., Köhler, B., Leuschner, I., Mentzel, H. J., . . . Richter-Appelt, H. (2019). Variations of sex development; The first German interdisciplinary consensus paper. Journal of Pediatric Urology, 15(2), 114-23.

Kreukels, B.P.C., Köhler, B., Nordenström, A., Roehle, R., Thyen, U., Bouvattier, C., ... Cohen-Kettenis, P.T. (2018). Gender dysphoria and gender change in disorders of sex development/ intersex conditions: results from the dsd-LIFE study. Journal of Sexual Medicine, 37(4), 777-785.

Lampalzer, U., Briken, P., & Schweizer, K. (2021). Psychosocial care and support in the field of intersex/diverse sex development (dsd): Counseling experiences, localization and needed improvements. International Journal of Impotence Research, 33(2), 228-242.

Lee, P. A., Houk, C. P., Ahmed, S. F., & Hughes, I. A. (2006). Consensus statement on management of intersex disorders. Pediatrics, e488. https://doi.org/10.1542/peds.2006-0738

Lee, P. A., Nordenström, A., Houk, C. P., Ahmed, S. F., Auchus, R., Baratz, A., . . . the Global DSD Update Consortium. (2016). Global disorders of sex development update since 2006: perspectives, approach and care. Hormone Research in Paediatrics, 85(3), 158-180.

Liang, J. J., Gardner, I. H., Walker, J. A., & Safer, J. D. (2017). Observed deficiencies in medical student knowledge of transgender and intersex health. Endocrine Practice:Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 23(8), 897–906. https://doi.org/10.4158/EP171758.OR

Liao L, Simmonds M. A values-driven and evidence-based health care psychology for diverse sex development. Psychology & Sexuality. 2013:1-19

Lin-Su, K., Lekarev, O., Poppas, D., & Vogiatzi, M. G. (2015). Congenital adrenal hyperplasia patient perception of ‘disorders sex development’ nomenclature. International Journal of Pediatric Endocrinology, 2015(1), 1-7. doi: 10.1186/s13633-015-0004-4

Lundberg, T., Hegarty, P., & Roen, K. (2018). Making sense of ‘Intersex’ and ‘DSD’: How laypeople understand and use terminology. Psychology & Sexuality, 9(2), 161-173. doi: 10.1080/19419899.2018.1453862

Mattawanon, N., Spencer, J. B., Schirmer, D. A., & Tangpricha, V. (2018). Fertility preservation options in transgender people: A review. Reviews in Endocrine and Metabolic Disorders, 19:231–242

Mazur, T., Cohen-Kettenis, P. T., Meyer, W. J., Meyer-Bahlburg, H. F., & Zucker, K. J. (2007). Survey of HBIGDA membership on treatment of disorders of sex development (DSD). International Journal of Transgenderism, 10(2), 99–108. https://doi.org/10.1080/15532730802182276

Mendoza, N., & Motos, M. A. (2013). Androgen insensitivity syndrome. Gynecological Endocrinology, 29(1), 1-5. Doi: 10.3109/09513590.2012.705378

Meyer-Bahlburg, H. F. L. (2019). “Diagnosing” gender? Categorizing gender-identity variants in the Anthropocene. Archives of Sexual Behavior 48(7), 2027-2035. doi: 10.1007/s10508-018-1349-6,

Meyer-Bahlburg, H. F. L. (in press). Psychoendocrinology of congenital adrenal hyperplasia. In: New, M. I., Lekarev, O., Parsa, A., Yuen, T. T., O’Malley, B., & Hammer, G. D. (Eds.). Genetic steroid disorders (2nd Ed.). London, Waltham, San Diego: Academic Press/Elsevier.

Meyer-Bahlburg, H. F. L. (under review). The timing of ‘normalizing’ genital surgery in somatic intersexuality: surveys of patients’ preferences.

Meyer-Bahlburg, H.F.L., Dalke, K.B., Berenbaum, S.A., Cohen-Kettenis, P.T., Hines, M., Schober, J.M. (2016). Gender assignment, reassignment and outcome in disorders of sex development: Update of the 2005 Consensus Conference. Hormone Research in Paediatrics, 85(2), 112-118.

Meyer-Bahlburg, H. F. L., Khuri, J., Reyes-Portillo, J., & New, M. I. (2017). Stigma in medical settings as reported retrospectively by women with congenital adrenal hyperplasia (CAH) for their childhood and adolescence. Journal of Pediatric Psychology, 42(5), 496-503. doi: 10.1093/jpepsy/jsw034

Meyer-Bahlburg, H. F. L., Khuri, J., Reyes-Portillo, J., Ehrhardt, A. A., & New, M. I. (2018). Stigma associated with classical congenital adrenal hyperplasia in women’s sexual lives. Archives of Sexual Behavior, 47(4), 943-951. doi: 10.1007/s10508-017-1003-8

Meyer-Bahlburg, H. F. L., Reyes-Portillo, J. A., Khuri, J., Ehrhardt, A. A., & New, M. I. (2017). Syndrome-related stigma in the general social environment as reported by women with classical congenital adrenal hyperplasia. Archives of Sexual Behavior, 46(2), 341-351. doi: 10.1007/s10508-016-0862-8

Miller, L., Leeth, E. A., Johnson, E. K., Rosoklija, I., Chen, D., Aufox, S. A., & Finlayson, C. (2018). Attitudes towards ‘disorders of sex development’ nomenclature among physicians, genetic counselors, and mental health clinicians. Journal of Pediatric Urology, 14(5), 418.e1-418.e7. doi: 10.1016/j.jpurol.2018.08.009

Money, J., & Lamacz, M. (1987). Genital examination and exposure experienced as nonsocomial sexual abuse in childhood. Journal of Nervous and Mental Disease, 175(12), 713-21.

Mouriquand, P. D. E., Gorduza, D. B., Gay, C.-L., Meyer-Bahlburg, H. F. L., Baker, L., Baskin, L. S., . . . Lee, P. (2016). Surgery in disorders of sex development (DSD) with a gender issue: If (why), when, and how? Journal of Pediatric Urology, 12, 139-149.

National Academies of Sciences, Engineering, and Medicine. (2020). Understanding the Well-Being of LGBTQI+ Populations. Washington, DC: The National Academies Press. https://doi.org/10.17226/25877.

Pasterski, V., Mastroyannopoulou, K., Wright, D., Zucker, K. J., & Hughes, I. A. (2014). Predictors of posttraumatic stress in parents of children diagnosed with a disorder of sex development. Archives of Sexual Behavior, 43, 369-375.

Pasterski, V., Prentice, P., & Hughes, I. A. (2010). Consequences of the chicago consensus on disorders of sex development (DSD): Current practices in europe. Archives of Disease in Childhood, 95(8), 618. http://dx.doi.org/10.1136/adc.2009.163840

Pasterski, V., Zucker, K. J., Hindmarsh, P. C., Hughes, I. A., Acerini, C., Spencer, D., … Dalke, K. B. (2021). The Health Care of Adults with Differences in Sex Developments is Changing: Time to Prepare Clinicians and Health Systems. LGBT Health. Online ahead of print.

Pasterski, V., Zucker, K. J., Hindmarsh, P. C., Hughes, I. A., Acerini, C., Spencer, D., … Hines, M. (2015). Increased cross-gender identification independent of gender-role behavior in girls with congenital adrenal hyperplasia: results from a standardized assessment of 4- to 11-year old children. Archives of Sexual Behavior, 44(5), 1363-1375.

Pediatric Endocrine Society (PES). (2020). Position Statement on Genital Surgery in Individuals with Differences of Sex Development (DSD)/Intersex Traits. Available at https://pedsendo.org/clinical-resource/position-statement-on-genital-surgery-in-individuals-with-differences-of-sex-development-dsd-intersex-traits/. Accessed 15 July 2021.

Rapp, M., Duranteau, L., van de Grift, T. C., Schober, J., Hirschberg, A. L., Krege, S., . . dsd-Life Group. (2020). Self- and proxy-reported outcomes after surgery in people with disorders/differences of sex development (DSD) in Europe (dsd-LIFE). Journal of Pediatric Urology. doi:10.1016/j.jpurol.2020.12.007

Richards, E. G., Farrell, R. M., Ricci, S., Perni, U., Quintini, C., Tzakis, A., & Falcone, T. (2021). Uterus transplantation: state of the art in 2021. .Journal of Assisted Reproduction and Genetics. Online ahead of print.

Roberts, C. M., Sharkey, C. M., Bakula, D. M., Perez, M. N., Delozier, A. J., Austin, P. F., … Mullins, L. L. (2020). Illness Uncertainty Longitudinally Predicts Distress Among Caregivers of Children Born With DSD. Journal of Pediatric Psychology, 45(9), 1053–1062. https://doi.org/10.1093/jpepsy/jsaa069

Roen, K. (2019). Intersex or diverse sex development: Critical review of psychosocial health care research and indications for practice. Journal of Sex Research, 56(4-5), 511-528. doi:10.1080/00224499.2019.1578331

Rolston, A. M., Gardner, M., Vilain, E., Sandberg, D. E. (2015). Parental reports of stigma associated with child's disorder of sex development. International Journal of Endocrinology 2015:980121

Rosenwohl-Mack, A., Tamar-Mattis, S., Baratz, A. B., Dalke, K. B., Ittelson, A., Zieselman, K., & Flatt, J. D. (2020). A national study on the physical and mental health of intersex adults in the U.S. PloS One, 15(10), e0240088. doi:10.1371/journal.pone.0240088

Rothenberg, S. S., van Batavia, J. P., & Kolon, T. F. (2016). Fertility in disorders of sex development: A review. Journal of Pediatric Urology, 12(6):418-425.

Rothenberg, S. S., Witchel, S. F., Menke, M. N. (2019). Oocyte cryopreservation in a Transgender Male Adolescent, New England Journal of Medicine, 28;380(9):886-887.

Ryan, C., Russell, S. T., Huebner, D., Diaz, R., & Sanchez, J. (2010). Family acceptance in adolescence and the health of LGBT young adults. Journal of Child and Adolescent Psychiatric Nursing, 23(4), 205–213. https://doi.org/10.1111/j.1744-6171.2010.00246.x

Safer, J.D., & Tangpricha, V. (2019a). Care of the transgender patient. Annals of Internal Medicine, 171(1), ITC1-ITC16. Doi: 10.7326/AITC201907020

Safer, J. D., & Tangpricha, V. (2019b). Care of transgender persons. New England Journal of Medicine, 381(25), 2451-2460. Doi: 10.1056/NEJMcp1903650

Sandberg, D. E., Gardner, M., Kopec, K., Urbanski, M., Callens, N., Keegan, C. E., … Siminoff, L. A. (2019). Development of a decision support tool in pediatric differences/disorders of sex development. Seminars in Pediatric Surgery, 28(5), 150838. https://doi.org/10.1016/j.sempedsurg.2019.150838

Sandberg, D. E. & Mazur, T. (2014). A noncategorical approach to the psychosocial care of persons with DSD and their families. In B. P. C. Kreukels, T. D. Steensma, & A. L. C. de Vries (Eds.), Gender Dysphoria and Disorders of Sex Development: Progress in Care and Knowledge (pp. 93-114). Springer Science+Business Media New York. https://doi.org/10.1007/978-1-4614-7441-8_5

Schützmann, K., Brinkmann, L., Schacht, M., & Richter-Appelt, H. (2009). Psychological distress, self-harming behavior, and suicidal tendencies in adults with disorders of sex development. Archives of Sexual Behavior, 38(1), 16-33.

Schweizer, K. H., Brunner, F., Gedrose, B., Handfort, C., & Richter-Appelt, H. (2017). Coping with diverse sex development: Treatment experiences and psychosocial support during childhood and adolescence and adult well-being. Journal of Pediatric Psychology, 42(5), 504-519.

Sermondade, N., Benaloun, E., Berthaut, I., Moreau, E., Prades, M, Béranger, A., …Dupont, C. (2021). Reproductive functions and fertility preservation in transgender women: A French case series. Reproductive BioMedicine Online, 43(2), 339-345.

Siminoff, L., & Sandberg, D. (2015). Promoting shared decision making in disorders of sex development (DSD): Decision aids and support tools. Hormone and Metabolic Research, 47(05), 335–339. https://doi.org/10.1055/s-0035-1545302

Speiser, P. W., Arlt, W., Auchus, R. J., Baskin, L. S., Conway, G. S., Merke, D. P., . . . White, P. C. (2018). Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An Endocrine Society Clinical Practice Guideline. Journal of Clinical Endocrinology and Metabolism 103(11), 4043-4088.

Stark, T., Shoag, J. E., & Poppas, D. P. (2019). Eliminating early surgery for disorders of sex development: Risking adverse outcomes in 46,XX CAH. Journal of Urology, 201(5), 871-3.

Tamar-Mattis, S., Gamarel, K. E., Kantor, A., Baratz, A., Tamar-Mattis, A., & Operario, D. (2018). Identifying and counting individuals with differences of sex development conditions in population health research. LGBT Health, 5(5), 320-324. doi: 10.1089/lgbt.2017.0180

Therell, B. L. (2001). Newborn screening for congenital adrenal hyperplasia. Endocrinology and Metabolism Clinics of North America, 30(1), 15-30.

Thyen, U., Ittermann, T., Flessa, S., Muehlan, H, Birnbaum, W., Rapp, M., … dsd-LIFE group (2018). Quality of health care in adolescents and adults with disorders/differences of sex development (DSD) in six European countries (dsd-LIFE). BMC Health Service Research, 18(1), 527.

Thyen, U., Richter-Appelt, H., Wiesemann, C., Holterhus, P. M., & Hiort, O. (2005). Deciding on gender in children with intersex conditions: considerations and controversies. Treatments in Endocrinology, 4(1), 1-8.

Timmermans, S., Yang, A., Gardner, M., Keegan, C. E., Yashar, B. M., Fechner, P. Y., … Sandberg, D. E. (2018). Does patient-centered care change genital surgery decisions? The

strategic use of clinical uncertainty in disorders of sex development clinics. Journal of Health and Social Behavior, 59(4), 520–535. https://doi.org/10.1177/0022146518802460

Timmermans, S., Yang, A., Gardner, M., Keegan, C.E., Yashar, B.M., Fechner, P.Y., … Sandberg, D.E., (2019). Gender destinies: assigning gender in Disorders of Sex Development-Intersex clinics. Sociology of Health & Illness, 41(8), 1520-1534.

Tiryaki, S., Tekin, A., Yagmur, İ., Őzen, S., Őzbaran, B., Gökşen, D., … Avanoğlu, A. (2018). Parental perception of terminology of disorders of sex development in Western Turkey. Journal of Clinical Research in Pediatric Endocrinology, 10(3), 216-222. doi: 10.4274/jcrpe.0007

Tishelman A.C., Shumer D.E., Nahata L. (2017). Disorders of sex development: pediatric psychology and the genital exam. Journal of Pediatric Psychology 42(5), 530-543.

van Batavia, J. P., & Kolon, T. F. (2016). Fertility in disorders of sex development: A review. The Journal of Pediatric Urology, 12(6):418-425.

van de Grift, T.C., Cohen-Kettenis, P.T., de Vries, A.L.C., & Kreukels, B.P.C.; on behalf of dsd-LIFE. (2018). Body image and self-esteem in disorders of sex development: A European multicenter study. Health Psychology, 37(4), 334.

Weidler, E. M., Baratz, A., Muscarella, M., Hernandez, S. J., & van Leeuwen, K. (2019). A shared decision-making tool for individuals living with complete androgen insensitivity syndrome. Seminars in Pediatric Surgery, 28(5), 150844. https://doi.org/10.1016/j.sempedsurg.2019.150844

Weidler, E. M., & Peterson, K. E. (2019). The impact of culture on disclosure in differences of sex development. Seminars in Pediatric Surgery, 28(5), 150840. https://doi.org/10.1016/j.sempedsurg.2019.150840

Weinand, J.D., & Safer, J.D. (2015). Hormone therapy in transgender adults is safe with provider supervision; a review of hormone therapy sequelae for transgender individuals. Journal of Clinical and Translational Endocrinology, 2(2):55–60

Wisniewski, A. B, & Sandberg, D. E. (2015). Parenting children with disorders of sex development (DSD): A developmental perspective beyond gender. Hormone and Metabolic Research, 47(5), 375-379.

Wolfe-Christensen, C., Wisniewski, A. B., Mullins, A. J., Reyes, K. J., Austin, P., Baskin, L. Mullins, L. L. (2017). Changes in levels of parental distress after their child with atypical genitalia undergoes genitoplasty. Journal of Pediatric Urology, 13(1), 32 e31-32 e36. doi:10.1016/j.jpurol.2016.10.024

Yang, J.H., Baskin, L.S., Disandro, M. (2010) Gender identity in disorders of sex development: review article. Urology,75,153–159.

Yogyakarta Principles.org. (2007). Yogyakarta Principles. Yogyakarta Indonesia 2006. yogyakarta.org.

Yogyakarta Principles.org. (2017). The Yogyakarta Principles plus 10. Geneva: Yogyakarata Principles.

Zelin, N. S., Hastings, C., Beaulieu-Jones, B., Scott, C., Rodriguez-Villa, A., Duarte, C., . . . Adami, A. J. (2018). Sexual and gender minority health in medical curricula in New England: A pilot study of medical student comfort, competence and perception of curricula. Medical Education Online, 23(1), 1-14. http://dx.doi.org/10.1080/10872981.2018.1461513

Zucker, K. J., Cohen-Kettenis, P. T., Drescher, J., Meyer-Bahlburg, H. F. L., Pfäfflin, F., Womack, W. M. (2013). Memo outlining evidence for change for gender identity disorder in the DSM-5. Archives of Sexual Behavior, 42, 901-914