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Multidisciplinary care for individuals with disorders of sex development

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Abstract

Purpose of review—Recommendations regarding the care of individuals with disorders of sex development include that care be provided by multidisciplinary teams. This article will discuss team composition and function as well as the role of the gynecologist and barriers to such care.

Recent findings—Many barriers to multidisciplinary care exist, but recent reports stress the roles of different team members as well as tools for planning and implementation of such a team that may help to overcome such barriers. All current recommendations include the participation of a gynecologist in the disorders of sex development team. Gynecologists are in the unique position to continue to provide care as these individuals mature into adulthood.

Summary—Multidisciplinary care for patients with disorders of sex development is recommended and gynecologists provide unique expertise.

Keywords

barriers to care; disorders of sex development; multidisciplinary care

INTRODUCTION

Throughout history, the birth of a child with genital discordance has presented special challenges for patients, families and providers. The modern era has seen progress in diagnosis, surgical techniques, understanding of psychological issues and the acceptance of patient advocacy. With these advances as a foundation, the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology organized a 2005 conference to develop guidelines for improving the clinical treatment of 'intersexed' persons. Subsequently, a Consensus Statement on Management of Intersex Disorders was published in *Pediatrics* and was adopted as policy by the American Academy of Pediatrics [1,2].

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Conflicts of interest

There are no conflicts of interest.

The consensus statement first tackles the issue of nomenclature and proposed the use of 'disorders of sex development' (DSD) that has remained controversial among some patient advocacy groups because the word 'disorder' implies that intervention is necessary. This nomenclature takes into consideration the molecular genetic aspects of sex development and thus increases the precision of diagnostic labels, which will in turn allow for better data collection and outcomes research. The statement proposes general categories of 'Sex Chromosome DSD' such as mixed gonadal dysgenesis (e.g., 45,X/46,XY chromosomes), '46,XY DSD' which includes disorders of testicular development as well as disorders of androgen synthesis or action, and '46,XX DSD' which includes disorders of gonadal development, androgen excess (maternal, fetal or placental), and other conditions, such as Mullerian agenesis. DSD classification based on 2005 consensus (modified from [1]) is given as follows:

1. sex chromosome DSD;
 - a. Turners,
 - b. Klinefelter,
 - c. 45,X/46,XY (mixed gonadal dysgenesis, ovotesticular DSD),
 - d. 46,XX/46,XY (chimeric, ovotesticular DSD),
2. 46,XY DSD;
 - a. disorders of gonadal (testicular) development,
 - i. complete gonadal dysgenesis (Swyer syndrome),
 - ii. partial gonadal dysgenesis,
 - iii. gonadal regression,
 - iv. ovotesticular DSD,
 - b. disorders in androgen synthesis or action,
 - i. androgen biosynthesis defect (e.g., 17-hydroxysteroid dehydrogenase deficiency, 5- α reductase deficiency, steroidogenic acute regulatory protein mutations),
 - c. defect in androgen action (e.g., complete androgen insensitivity, partial androgen insensitivity),
 - d. luteinizing hormone receptor defects (e.g., Leydig cell hypoplasia, aplasia),
 - e. disorders of anti-Mullerian hormone and anti-Mullerian hormone receptor (persistent Mullerian duct syndrome),
 - f. cloacal exstrophy,
3. 46,XX DSD;
 - a. disorders of gonadal (ovarian) development,
 - i. ovotesticular DSD,

- ii. testicular DSD (e.g., sex determining region Y gene, duplicate SRY-box 9),
 - iii. gonadal dysgenesis,
- b. androgen excess,
 - i. fetal (e.g., congenital adrenal hyperplasia- 21-hydroxylase deficiency, 11-hydroxylase deficiency),
 - ii. fetoplacental (aromatase deficiency, P450 (cytochrome) oxidoreductase),
 - iii. maternal (luteoma, exogenous, etc.),
- c. vaginal atresia (Mullerian agenesis),
- d. cloacalextrophy.

A 2007 review of 250 individuals cared for by a multidisciplinary Gender Assessment Team in Seattle revealed that 71% of patients presented in infancy. The most common conditions encountered were: congenital adrenal hyperplasia (14%), androgen insensitivity syndrome (10%) and mixed gonadal dysgenesis (8%), which are consistent with other reports. These authors as well as others noted that they failed to establish a diagnosis in 12–25% of their cohort [3■].

Thus it is important to note that the categories of DSD include a wide variety of conditions, some which pose more difficult diagnostic and medical challenges than others. All of these conditions; however, have the potential to significantly impact the well-being of the affected individual throughout their lifespan. Thus, the 2005 consensus statement defined optimal clinical management of persons with DSD and stressed that an experienced multidisciplinary team is essential in providing excellent care as well as addressing the other recommended management of these individuals and their families.

The following is based on literature review, discussion with members of other DSD teams, DSD advocates and our experience with these patients.

MEMBERS OF THE MULTIDISCIPLINARY TEAM

Coincident with the 2005 meeting, the not-for-profit Accord Alliance was founded with a mission to ‘promote comprehensive and integrated approaches to care that enhances the health and well-being of people and families affected by DSD by fostering collaboration among all stakeholders’ [4■]. The Alliance published a manual entitled Clinical Guidelines for the Management of Disorders of Sex Development in Childhood, which addresses all aspects of care including the team members, their roles and how such a team should function [5■].

The Accord Alliance and others recommend that the ideal team include pediatric subspecialists in endocrinology, surgery and/or urology, psychology or psychiatry, gynecology, genetics, neonatology and if available social work, nursing and medical ethics [6■] (Table 1). Often large academic centers and pediatric hospitals have specialists in all

these areas but if they do not there should be at minimum a pediatric endocrinologist, a pediatric urologist or surgeon and a mental health provider, such as psychologist, psychiatrist or social worker. A team coordinator is important both in the creation of the service as well as ongoing functioning [6■]. We found that the person most interested in creating such a team, a physician, served best in the initial planning and implementation of the team but later functioning coordination was maintained by a designated nurse. Others have advocated that a social worker may be the best person for this task as they often are the one member of the team who routinely talks to patients as well as other team members. Regardless of who becomes the ongoing team coordinator, he or she must be committed and be respected by the team members.

To illustrate the myriad of specialists involved in the care of individuals with DSD we can consider the case of a baby born with ambiguous genitalia. It is important that delivery room staff are trained and aware of these conditions so that they can approach the family in a calm and reassuring manner. Part of the role of the members of the multidisciplinary team is to educate providers in the community regarding these conditions. Thus delivery room team members would congratulate the family on the birth of their child, inform them that these conditions are encountered not as rarely as many think, and postpone gender assignment until the multidisciplinary team has completed the initial evaluation. The neonatologist or pediatrician will thus initiate the workup and contact the team.

As salt wasting congenital adrenal hyperplasia (CAH) is life threatening to the newborn, an endocrinologist often needs to be involved in the care of an infant with a DSD from the first few days of life. In addition, the patient with DSD will often need endocrinologic management for their conditions throughout their life. The patient with 46 XX CAH, for example, will require hormonal management to prevent salt wasting, hypertension, further virilization and precocious puberty. Other conditions require evaluation for growth and puberty as the child progresses to adolescence. For example, a patient with 45X or 46 XY gonadal dysgenesis with typical female phenotype will require management to optimize growth, as well as puberty induction and long-term estrogen replacement.

The family will need psychosocial support as soon as the diagnosis is made both for the parents, the child and often other family members, such as siblings [7■]. Counseling should cover a myriad of issues such as what to tell friends and families and how to discuss these issues with the child as he or she grows up; counselors can also facilitate the decision-making process regarding medical, hormonal and surgical options, evaluate for symptoms of distress, and connect families with support groups. DSD support groups are a key partner of the multidisciplinary team for the families with DSD. They allow the family to feel less alone, provide information as well as support. Resources for providers and families are as follows:

1. Accord Alliance—accordalliance.org,
2. DSD—dsdsfamilies.org,
3. Androgen Insensitivity—aisdsd.org,
4. Hypospadias/Epispadias—heainfo.org,

5. Mullerian Agenesis—beautifulyoumrkh.org; mrkh.org,
6. Congenital Adrenal Hyperplasia—caresfoundation.org,
7. Klinefelter Syndrome—genetic.org,
8. Turner Syndrome—turnersyndrome.org.

A significant number of patients do not have a clear diagnosis, especially in cases of 46, XY DSD. As new genomic technologies (such as whole exome sequencing and DSD-chips) become available, the geneticist becomes an integral part of the team [8■,9■]. He or she needs to become involved early in confirming the diagnosis and with a genetic counselor counsel the family about future pregnancies and/or the need to evaluate other family members.

It is important to note that there is significant controversy regarding the surgical management of many of these conditions. Select DSD syndromes are associated with a substantial percentage of individuals who experience gender dysphoria and thus distress with their postsurgical anatomy [10,11■,12■]. In addition, surgery may be associated with complications, such as scarring and stenosis, which can contribute to poor sexual functioning later in life [13,14]. The pediatric urologist, surgeon and gynecologist along with an experienced radiologist can elucidate anatomy, address diagnostic as well as genital surgical options (including not performing surgery in childhood) as well as discuss future fertility [15■].

A bioethicist is often called upon when difficult decisions need to be undertaken with the family. In addition, a bioethicist and the hospital legal team may need to review policies as they pertain to possible effects on fertility and other legal issues. Thus, participation of bioethics in team meetings or easy availability for consultation is essential.

Finally, it is important to note that a significant number of these conditions are associated with other disorders. A recent report from the international DSD registry states that over a quarter of the cases have another condition such as small for gestational age, cardiac renal or skeletal anomalies, as well as central nervous system disorders [16■]. Thus it is important to have access to other specialists, such as nephrologists, cardiologists, neurologists and orthopedic surgeons.

GYNECOLOGISTS' ROLE IN THE MULTIDISCIPLINARY TEAM

The obstetrician is often the first to make the diagnosis of a DSD either antenatally because of findings on genetic testing and ultrasound or immediately after the birth of the infant. Thus, the first point of contact for the family regarding a DSD issue is the obstetrician gynecologist. When the child is evaluated by the multidisciplinary team, the pediatric gynecologist, or a gynecologist with interest and expertise in this area, has a unique role as he or she is better prepared than other specialists to address issues of sexual function and fertility. The pediatric gynecologist or a gynecologist with expertise in DSD can evaluate anatomy, discuss future sexual function and fertility issues as well as the risks and benefits of early surgical treatment (prior to the age of assent). Surgeries can be performed with the pediatric urologist.

As the child grows and reaches adolescence, the gynecologist is again uniquely positioned to assist the family with discussions regarding sexuality and reproductive issues. In addition, many of these conditions are not diagnosed until adolescence when lack of menstruation, pubertal development or virilization elicits a referral to the gynecologist. Thus, the first physician to diagnose many of these conditions when they present in adolescence may be the gynecologist.

Finally, pediatric gynecologists or gynecologists with expertise in DSD are in the unique position to be able to provide care throughout the affected individual's life. Many multidisciplinary teams that currently exist, only provide care to children and adolescents, and it becomes very difficult for these individuals to transition to adult providers who understand their conditions. This has been reported anecdotally by many DSD providers and advocates and there is currently a great deal of interest in the area of transition to adult care for many chronic childhood conditions. Adults with DSD will require hormonal management, fertility and preconception counseling, cancer screening as well as management for osteoporosis and cardiovascular risk factors later in life. The gynecologist can communicate with both pediatric and adult specialists and serve as the central provider for the patient beginning in adolescence. As an example, Sakakibara *et al.* [17] reviewed 57 adult Turner syndrome women and arrived at the conclusion that as most Turner syndrome patients receive hormone replacement therapy from their gynecologist, these physicians should take primary responsibility for these patients with appropriate support from other specialists.

OPERATION OF THE MULTIDISCIPLINARY TEAM

One of the most important decisions the team makes is how they will be accessed by physicians for referrals. As babies are born anytime and certain conditions are urgent (such as in salt wasting congenital adrenal hyperplasia), there needs to be in place an emergency management process. In most cases the pediatric endocrinologist functions as the emergency contact.

It is important to note that creation of a multidisciplinary team is more than just bringing together different specialists [6■]. These specialists will need to create a process for clinical care and decision-making and continuously evaluate and adjust these to best serve their patients and community [6■]. It is important that the team communicate with each other on a regular basis to assure the best care for the patient and family. As there are many areas for which there are no clear management guidelines, the team will need to make decisions with the family given a variety of factors including genetic, endocrine and anatomic findings as well as the individual and the family values and preferences. Among these decisions, gender assignment and surgical management are some of the most difficult. Thus, communication among the team members regarding their unique perspective based on their field of expertise is essential [18]. As it has been noted that parents make different decisions on the basis of who counsels them regarding surgery, it is important for the team members to communicate with the families regarding their different perspectives in an open and caring way [19■■■].

A regular multidisciplinary clinic preceded and followed by a case conference discussion provides an ideal format for such care. The family can see all the providers on the same day, which is an important lifestyle factor especially for families who have to travel long distances to a center with such a team. In addition, the members of the team can discuss all pertinent medical and psychosocial issues before seeing the family, so that there is a clear understanding of the medical condition, as well as after evaluating the family, so as to arrive at a consensus regarding management. We found that providing lunch during the preclinic conference improved participation and that often these discussions modify our individual perspectives when we become aware of other disciplines' issues. Alternatively, separate team meetings to discuss individual cases serve other teams best.

For the team to function properly, it is important to have a team leader and team coordinator [6]. The leader can identify the members of the team as well as begin discussions regarding processes. The team coordinator, often a nurse, can assist with team communication. Our team coordinator, for example, obtains copies of all medical records and distributes them prior to the visit so that members understand the information prior to the meeting.

BARRIERS TO MULTIDISCIPLINARY CARE

In spite of the agreement among experts that multidisciplinary care, including psychosocial support, constitutes best practice, such care is labor intensive and not well compensated [6]. As DSD are individually rare, most hospitals are not aware of these conditions and current recommendations. There is little if any administrative, financial or technical assistance for the creation of such teams. These teams are often started because of the passion (often with little program planning experience) of specialists and subspecialists to provide caring for such individuals [6]. Currently, there is no organization that can define and grant designations of competency and excellence [6]. The possibility for hospitals to receive Centers of Excellence status for DSD care would likely create incentives to fund such care teams and would offer guidance for the process of multidisciplinary care.

In addition, it is often difficult to find subspecialists with knowledge in or the commitment to this area of care, thus the first endeavor of persons attempting to form such multidisciplinary teams is to review their practice structure and location, hospital resources and staff to assess whether the creation of such a team at their particular location is a logical step. It is important that team members continue to review the literature and share expertise. Often one specialty will have deep understanding of a condition (such as the pediatric gynecologist's knowledge of Mullerian agenesis), which the other specialists may not understand well. Specific sites may encounter such few of these patients that a dedicated team may not be realistic and thus the creation of proper referral patterns may best serve the individuals being cared for.

Finally, excellent leadership and communication between team members is required for the team to function properly. It is not unusual for team members to disagree regarding the care of an individual patient [16]. Thus, it is important for the team to discuss and set up processes for conflict resolution in cases of disagreement.

CONCLUSION

Current guidelines recommend multidisciplinary care for persons born with DSD. The complexity of issues faced by these families requires that coordinated care be provided by multiple specialists, including pediatric endocrinology, urology, gynecology, genetics, psychology or psychiatry, often with assistance from bioethics. The pediatric gynecologist has a unique role to play in the care of these patients because of their knowledge and understanding of sexuality and reproductive function as well as their ability to provide care throughout the lifespan of the patient. There are many barriers to multidisciplinary care some of which could be surmounted by official designation of centers of excellence as well as commitment and communication among team members.

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KEY POINTS

- Guidelines recommend that patients with DSD be managed by a multidisciplinary team.
- The gynecologist has an important role to play in the DSD team.
- Barriers to multidisciplinary care can be ameliorated by the availability of Centers of Excellence designation as well as excellent communication among team members.

Table 1**Members of the multidisciplinary team and their roles**

Specialist	Role
Psychologist or psychiatrist	Perform evaluation and management of the mental health needs of the child; assess the child's ability to participate in decision making; assess and facilitate the parent or child relationship; referral for mental health needs of parents
Geneticist or genetic counselor	Perform proper genetic diagnostic tests; provide genetic counseling for the family and child as well as assess for the need to evaluate other family members
Pediatric endocrinologist	Perform evaluation and management of endocrine disorders; provide hormonal management for all endocrine needs including growth and puberty induction
Pediatric urologist	Perform evaluation and management of urologic concerns; perform surgeries after thorough discussion with the team and family
Pediatric gynecologist	Assess female anatomy; perform surgeries of the genital tract with urology when indicated; counsel families and individuals about fertility and sexual function; provide continuity of care during transition to adult providers
Pediatric surgeon	In some institutions general pediatric surgeons provide surgical care
Neonatologist	Provider care for children with DSD and other associated conditions which require care such as salt-wasting
Nursing and social worker	Coordinate care and provide educational help to patients and families. Communicate with the team and family; occasionally provide mental health services; connect families with resources and support services
Bioethicist	Assist in medical decision especially in cases when opinions differ regarding what constitutes the child's best interest; assist in developing hospital policy regarding legal issues
Others	Medical interpreter: it is important to use a trained medical interpreter when English is not the families first language

Modified with permission from [5■].