Disorders of Sex Differentiation: A Pediatric Urologist's Perspective of New Terminology and Recommendations

Julia Spencer Barthold*

From the Division of Urology, Alfred I. duPont Hospital for Children, Wilmington, Delaware

Purpose: In 2005 medical and lay experts convened (the Chicago Consensus), and reviewed and updated nomenclature and treatment recommendations in individuals with congenitally atypical gonadal, chromosomal or anatomical gender. This review summarizes, analyzes and considers the implications of these recommendations in pediatric urology practice.

Materials and Methods: Publications identified in a PubMed® search of 2000 to 2010 as well as relevant prior reports of new concepts and trends in the diagnosis of and treatment for intersex/ambiguous genitalia/disorders of sex differentiation, and responses to the Chicago Consensus were reviewed.

Results: In response to concerns regarding outdated, confusing and/or controversial terms, such as "intersex," "hermaphroditism" and "sex reversal," the consensus statement recommended a new taxonomy based on the umbrella term, "disorders of sex differentiation." Additional categorization based on sex chromosome complement was recommended but not clearly defined and variously interpreted. Routine use of multidisciplinary diagnostic and expert surgical teams, continuing psychosocial and psychosexual care, and full disclosure of alternatives relating to surgery type and timing were recommended. Early gender assignment was advocated but evidence-based guidance to support some aspects of care of affected individuals was insufficient. Pediatric urologists should remain abreast of new data refining the diagnoses and outcomes of disorders of sex differentiation, and ensure that their patients have access to multidisciplinary resources.

Conclusions: Major changes in classification and expectations in the care of individuals with disorders of sex differentiation have occurred in recent years. Increasing focus on determining precise etiology and defining objective outcomes will help more clearly determine appropriate management and prognosis for this heterogeneous group of disorders.

Key Words: abnormalities, genitalia, sex differentiation disorders, evidence-based practice, terminology as topic

Abbreviations and Acronyms

CAH = congenital adrenal hyperplasia

CAIS = complete androgen insensitivity syndrome

DSD = disorders of sex differentiation

GB = gonadoblastoma

PAIS = partial androgen insensitivity syndrome

PGD = partial gonadal dysgenesis

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* Correspondence: Division of Urology, Alfred I. duPont Hospital for Children, 1600 Rockland Rd., Wilmington, Delaware 19803 (telephone: 302-651-5986; FAX: 302-651-6410; e-mail: jbarthol@nemours.org).

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THE care of a child with atypical genitalia represents a challenge due to the complexities involved in diagnosis, gender assignment, surgical repair, and analysis of the long-term impact of each condition and/or its treatment on quality of life. The term "intersex" has been applied to disorders with and without genital ambiguity but the former comprise most cases managed by pediatric urologists. Critical focus on physical and psychosocial outcomes in these individuals has intensified in the last 2 decades. As described in the historical review by Meyer-Bahlburg,[1] by the 1990s nonclinicians expressed increasing dissatisfaction with tradi-

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tional treatment methods, which led to publications questioning the ethics and appropriateness of standard care and nomenclature. These events culminated in a multidisciplinary meeting of medical and nonmedical experts in Chicago in October, 2005 (the Chicago Consensus), which was sponsored by the Lawson Wilkins Pediatric Endocrine Society and the European Society of Pediatric Endocrinology. In 2006 the proceedings were published.[2] They provide a revision of standard nomenclature and updated treatment recommendations in individuals with the newly defined DSD. This review summarizes the background, and the updated nomenclature and treatment recommendations that emerged from the Chicago Consensus, and considers their potential implications for pediatric urology practice.

RATIONALE FOR CHANGE

Pediatric urologists recognized that reappraisal of the traditional approach to treatment for genital ambiguity was needed in response to dialogue with dissatisfied former patients.[3] Interaction with patient advocate groups, such as the Intersex Society of North America (http://www.isna.org/) and the Accord Alliance (/http://www.accordalliance.org/), provided novel perspective and insight into potential suboptimal outcomes of care. In 2001 Daaboul and Frader presented the opposing viewpoints of traditional medical/surgical providers and patient advocates/"activists" in the care of individuals with genital ambiguity.[4] They noted that neither physician imposed gender assignment and limited parental disclosure to prevent transmission of parental doubt about gender identity to offspring (the "traditionalist" or "optimal gender policy"[5] approach) nor deferral of surgery pending full disclosure and consent of the affected individual later in life (the "intersex activist" approach) has clear scientific validity. Consequently they advocated a middle way that allows full parental disclosure and decision making. In 2005 Dreger et al argued that general terms based on gonadal anatomy and phenotypic appearance, such as "male pseudohermaphrodite," "true hermaphrodite" and "sex reversal," are outdated, confusing and potentially harmful to patients and families, eg when the former is used as a scientific term to label a person identifying socially as female.[6] They advocated updating the taxonomy to reflect the primary disease when possible and using specific nomenclature that does not establish or dictate gender assignment or treatment. In 2004 Creighton and Liao summarized the increasing debate on intersex treatment and reiterated their concerns about early surgery in infants born with ambiguous genitalia[5] based in part on experience with the long-term outcome of feminizing genitoplasty.[7]

In response to these and other controversies Chicago Consensus participants recommended replacing the term "intersex" with DSD and discontinuing the use of "hermaphroditism" and "sex reversal." In addition, they made general recommendations regarding the diagnosis of and treatment for DSD. These recommendations influence several areas of critical importance to pediatric urologists, including advances in diagnosis, assignment of gender in infancy, attention to patient psychosocial and sexual needs, and recommended and alternative surgical therapies.

SUMMARY AND IMPACT OF NEW NOMENCLATURE

DSD is defined as a congenital condition associated with atypical chromosomal, gonadal or anatomical sex.[2,8,9] DSD seems intended as an umbrella term with proposed subcategories. Included in the original consensus publications were 46,XY DSD, 46,XX DSD, ovotesticular DSD, 46,XX testicular DSD, sex chromosome DSD and 46,XY complete gonadal dysgenesis. Further diagnostic classification based on a primary genetic defect, if known, is preferred when available, and will ultimately allow limited use of these more general terms.

Since the original summary publications of the Chicago Consensus did not provide exhaustive categorization of disorders into subgroups, discrepancies exist between the DSD classifications used by some investigators and those that may be preferred by pediatric urologists. For example, in a followup publication by Hughes the subcategories included sex chromosome, 46,XX and 46,XY DSD with the latter including gonadal dysgenesis and defects of androgen synthesis or action, disorders that may appear similar phenotypically but show important clinical differences.[9] Although DSD may be useful as a more neutral general term, these general subcategories seem too nonspecific and less useful. Houk and Lee provided a more detailed subclassification in a followup publication.[8] The Appendix summarizes conditions and how they may be categorized based on the DSD nomenclature.[2,8–10] Specific diagnoses are preferable when possible, since they may more clearly predict disease specific outcomes.

Hughes included additional "other" subclassifications under 46,XX and 46,XY DSD that incorporate various isolated genital disorders, such as nonsyndromic hypospadias or cryptorchidism, vanishing testis syndrome and labial adhesions, that are not necessarily congenital or endocrine related.[9] These disorders have not been classified as intersex by pediatric urologists and are not typically associated with the pronounced medical, psychosocial and psychosexual complexity that accompanies many DSD/