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MANAGEMENT OF CHILDREN WITH INTERSEX CONDITIONS: PSYCHOLOGICAL AND METHODOLOGICAL PERSPECTIVES

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Pediatric medicine has undergone considerable upheaval in the past few years over the treatment of children with disorders of sexual differentiation. There have been challenges to all aspects of traditional practice, including sex assignment, genital surgery, the role of the patient and parents in decision-making, disclosure of medical details, the composition of the treatment team, and nomenclature. These challenges have been met with serious attention by pediatricians and other health professionals involved in the care of these children, and there has been considerable discussion of the merits of changes to current practice.¹⁻⁸ This report considers the status of the evidence relevant to treating children with intersex conditions, with particular emphasis on psychological and methodological issues.

BACKGROUND

For 50 years, treatment of children with intersex conditions was guided by the belief that gender identity results from social rearing rather than biological factors, provided that gender-confirming genital surgery is done early in life.^{9,10} Although there have always been questions about this policy, anecdotal evidence generally suggested that it produced good outcome.^{11,12} The policy and the evidence used to support it have recently been subject to detailed scrutiny because of several well-publicized reports. This includes a case of ablatio penis raised female who was unhappy with the assigned sex,^{13,14} conference reports of XY males with absent or malformed penis due to cloacal exstrophy reared as females who declare themselves to be boys,¹⁵ and reports of adverse outcomes from intersex patients.^{16,17}

Several issues have emerged from recent discussions (Table 1). The focus has been on sex assignment and genital surgery, with traditional treatment and challenges often seen in polar terms (Table 2). Discussions have often been acrimonious, and recommendations based

on personal beliefs or anecdotes, although it is clear that the interests of patients are best served by careful application of evidence.

EVIDENCE REGARDING SEX ASSIGNMENT

Determinants of Gender Identity

Decisions regarding sex assignment require recognition of the complexity of gender identity. Gender identity cannot be simply predicted from any single factor; neither is it always consistent with sex of rearing, nor is it simply related to extent of prenatal hormone exposure. The publicized individual with ablatio penis¹⁴ was reared as a boy early in life and it is unclear how this contributed to his gender identity. Another individual with a similar history but with earlier female reassignment had a different outcome, particularly female gender identity.¹⁸ To date, there have been no published systematic studies of individuals with cloacal exstrophy, and case reports indicate variations in gender identity, with no clear indication of the percentage who identify as males or are unhappy as females.^{19,20}

The most systematic evidence regarding gender identity comes from two conditions. Females with congenital adrenal hyperplasia (CAH) overwhelmingly identify as female.²¹⁻²³ The very small minority of females with CAH who are unhappy as females or live as males are not necessarily those with the greatest genital virilization or

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Table 1

Controversies in Treatment of Children with Intersex Conditions

Sex assignment

What criteria should be used?
 What determines gender identity?
 When (if ever) is gender identity fixed?

Genital reconstructive surgery

Is it necessary? (Why?)
 When should it be done?
 What are its benefits and risks?

Decision-making

Who makes the decisions?
 When should decisions be made?
 What information is used to make the decisions?
 What support is available?

Information-sharing

What are the parents told at the time of diagnosis and decision-making?
 What does the child learn and when?
 What support is available?
 What is the best way to share information?

Involvement of mental health professionals

Should psychologists or psychiatrists be part of the diagnosis and treatment team?
 Does counseling to families facilitate decision-making?
 Does routine and continuing counseling to patients and families improve outcome?

the most prenatal androgen excess. Males with micropenis have not been studied as extensively as females with CAH, but they identify as males when reared that way and appear to function well.^{24,25}

There is little systematic evidence to guide decisions about sex assignment in other intersex conditions.²⁰ Recent studies of individuals with micropenis and those with ambiguous genitalia with perineoscrotal hypospadias of varying etiology suggest that gender identity is generally consistent with sex of rearing.^{26,27} But, for several reasons, caution is necessary when generalizing from these studies. First, a substantial proportion of participants (about 25%) were dissatisfied or questioned their sex of rearing. Second, as is typical of retrospective studies, patients who were dissatisfied or atypical were probably underrepresented: 30% of eligible patients did not participate and some participants elected not to answer sensitive questions. Third, outcome was assessed with a few items of unknown sensitivity. Fourth, those reared as boys were subjected to more surgery than those reared as girls.

Recommendations Regarding Sex Assignment

Sex assignment for an intersex child is one of the most difficult decisions made by parents and health professionals, though it is natural to seek simple solutions. But just as it is no longer tenable to assume that gender identity is always consistent with the sex of rearing, evidence indicates that it is equally unwise to consider gender identity to result directly from fetal androgen exposure (inferred from genital appearance or another indicator). Although other aspects of behavior may relate to degree of fetal androgen exposure, gender identity does not. For example, among females with CAH, degree of prenatal androgen exposure (inferred from genetic mutation, salt-wasting status, and degree of genital virilization) is moderately associated with interest in boy-typical activities and sexual orientation.^{23,28-30} but not gender identity.²¹⁻²³ Therefore, it is crucial to separate aspects of outcome (Table 3).

There is sufficient evidence to suggest that 46,XX CAH patients be reared as girls, given the documented good outcomes associated with such rearing. Nevertheless, there are no systematic studies of those reared as boys. It is reasonable to suggest that 46,XY micropenis patients be reared as boys, given the small studies of good outcomes in such cases and the need for surgery with rearing as girls, but it would be helpful to have more evidence comparing quality of life and sexual function in those reared as boys vs. girls. In all other cases, decisions will need to be made with the limited information available from case reports. All children should be assigned as boys or girls. Rearing children as intersex is not advocated by health professionals or activist organizations (including ISNA). Parents and health professionals should realize that an intersex individual may elect to change gender later in life. The accuracy of the sex assignment can only be judged by the patient. It is essential to recognize that gender identity is not synonymous with gender-role behavior or sexual orientation, so that childhood tomboy behavior in girls or homosexuality should not be taken as indications of incorrect sex assignment.

EVIDENCE REGARDING SURGERY

Decisions regarding genitoplasty should be considered in light of the evidence regarding the stated need for surgery. Current practice is predicated on several assumptions: (1) sex-typical genital appearance is necessary for gender identity development consistent with rearing sex and for healthy psychological adjustment; (2) adjustment is hindered by unusual-appearing genitalia, through disruption in parent-child bonding, reactions from caretakers and peers, and difficulty in forming sexual relationships; (3) corrected genitalia are necessary for sexual activity, particularly intercourse. But some intersex patients as adults have

Table 2

Summary of Traditional Care and Current Challenges in the Treatment of Children with Intersex Conditions

Sex Assignment/Gender Identity	Traditional Practice	Challenge
Determinant of gender identity	sex of rearing	prenatal androgen
Stability of gender identity	fixed by age 2	develops throughout life
Role of genitalia	crucial to identity & adjustment	reflect brain masculinization
Decision-maker	physician	family
Genital Surgery		
Rationale	anatomy to match rearing sex	surgery is for comfort of others
Consequences	facilitates gender identity	inhibits gender change
	facilitates adjustment	impairs sexual function
	facilitates sexual intercourse	
Decision-maker	physician	patient

Table 3

Aspects of Outcome in Children with Intersex Conditions

Gender Identity	Sense of self as male or female
Gender-role Behavior	Aspects of behavior that differ between males and females; is multidimensional
Sexual Orientation	Sex of target of sexual arousal
Sexual Functioning	Sexual sensitivity Potential for orgasm Capacity for intercourse, if desired
Psychological adjustment ("quality of life")	Happiness Absence of distress Satisfaction with specific aspects of life e.g., psychosexual adjustment

The surgical outcomes most often studied have been genital appearance and adequacy of genitalia for peno-vaginal intercourse. But the assumptions behind surgery and the concerns of patients make it clear that other outcomes need to be considered, particularly those related to the quality of sexual experience, including sensitivity and satisfaction, and general quality of life (Table 3).

Physical Outcomes of Surgery

There are no systematic outcome data regarding genital appearance and sexual function, especially for current surgical procedures. There are reports of suboptimal cosmetic outcome and self-reported sexual function, but they are based on limited assessments of selected patients with surgery of varying quality.^{26,27,31} Therefore, it is difficult to know how surgery affects sexual function, and the factors that account for variations across individuals. Measures of clitoral responsiveness suggest normal nerve conduction after surgery,³² but it is unclear whether this translates into normal sensitivity. It is also important to remember that intercourse is only one part of sexual activity, and surgery to facilitate intercourse might compromise orgasmic response.

There is optimism that current techniques used by skilled surgeons produce better cosmetic and functional outcomes now than in the past,³³ but confirming evidence is essential. Outcome studies require detailed assessments and comparisons with subjects without intersex conditions, given the complexity of sexual response, the variations in arousal and orgasm among typical individuals without genital surgery,³⁴ and the limitations of self-report in assessing sexual response.³⁵

complained that surgery does not prevent problems and may actually exacerbate them, because of adverse cosmetic and functional outcomes from surgery. These critics further contend that problems arise from the undue focus on the genitalia and not their appearance per se.

Psychological Impact of Genital Appearance

Both physicians and intersex advocates are concerned about psychological problems associated with intersexuality. Physicians suggest that children who look different will have difficulty forming a coherent self-concept, including gender identity, and receive negative reactions from others, with adverse effects on adjustment and life satisfaction. Some intersex advocates argue that problems result from stigma and shame induced by messages from physicians and parents that atypical genitalia are unacceptable.

Neither set of concerns have been empirically validated – or refuted. There are no data showing the relative importance or unimportance of normal-appearing genitalia for psychological outcome. The existence of gender dysphoria in individuals with and without intersex conditions indicates that normal-appearing genitalia are not sufficient for gender identity consistent with rearing sex, but there is no systematic study of the role (if any) that genital appearance plays in the development of gender identity. It is widely believed that boys with a small penis are teased, causing poor peer relationships and adjustment problems. Although this has not been systematically studied, males with micropenis appear to do well.^{24,25} Relevant data from boys with hypospadias who had received genital surgery show psychological adjustment similar to that of control boys, with little relation between adjustment and genital appearance, but depression is associated with more surgery and hospitalizations.³⁶

Evidence from individuals with other physical conditions reinforces the complex contributors to outcome. Problems in individuals with intersex conditions might not arise from specific aspects of the condition or treatment itself, but from the stresses they impose on the patient and the family.³⁷ Children's stress may arise from their own experiences, such as surgery, repeated physical exams and hospitalizations, responses to their unusual genital appearance, or from changes in parent-child interactions brought about by parents' stress. Parent stress may be independent of the child's physical illness or may result from it, for example, from concerns about the child's genital appearance, responsibilities of caring for a sick child, or financial burdens brought about by the child's illness. Additional risk may arise from children's problems with peer relationships,³⁸ but even here the cause is not simple. Peer problems are affected by more than physical appearance, such as frequent school absences and sex-atypical behavior.^{37,39} Furthermore, the association between peer relationships and adjustment is bidirectional: poor peer relations place a child at psychological risk, but poorly adjusted children have difficulty making friends to start.

Psychological Outcome in Intersexuality

Thus, there are many paths by which mental health might be affected in individuals with intersex conditions, but there is no evidence regarding any of them. Further, there is surprisingly little evidence about the ultimate mental health outcomes hypothesized to be affected by these paths, primarily because such studies are difficult. Scientific studies may undersample individuals with problems, but reports from intersex activists may overrepresent those with problems.⁴⁰

The most systematic evidence regarding mental health in intersex individuals comes from females with CAH. Several studies show that their mental health is not different than that of controls, although they may have specific problems with body image and psychosexual function.⁴¹⁻⁴⁶ There are not enough data to know whether outcome is related to genital appearance or surgery.

These results on good adjustment might be surprising in light of assumptions described above. However, they are consistent with evidence that chronic illness, trauma, and other adverse life events have only transient effects on adjustment in the majority of people. Among individuals with a variety of physical disabilities (including quadriplegia), there is often an immediate period of depression, but after a short period (weeks to months), most report positive well-being.^{47,48}

This mismatch between expectation and evidence is an example of the tendency to attribute outcome to the cause that is most salient, in this case, the appearance of the genitalia or the intersex condition itself. But, outcome is influenced by many factors, including temperament and life circumstances. People are not accurate at predicting factors that influence life satisfaction in others because they only focus on a small set of contributors.⁴⁹ This means that attributions about problems among intersex individuals must be validated empirically.

Recommendations Regarding Surgery

The lack of systematic outcome data makes decisions about genital surgery very difficult. There are insufficient data regarding the functional consequences of genital surgery, but there are also insufficient data regarding the effects on a child of living with atypical genitalia. It is likely that the effects of both genital surgery and genital appearance are not the same for all individuals. Perceptions of and responses to the situation may be more important than its objective nature, and psychological support may help families develop coping strategies to foster mental health. It is important to remember that decisions should be made in the best interests of the child and not the parents.

CONCLUSIONS

The discussions surrounding the treatment of children with intersex conditions have crystallized the assumptions and evidence underlying treatment. Changes to treatment must be informed by evidence or, consequently, dilemmas will arise again. Despite gaps in the evidence regarding outcome, there is some information available to guide treatment.

First, sex assignment cannot be based on the assumption that gender identity is determined by either sex of rearing or degree of fetal androgen exposure. Most individuals with 46,XX CAH do well when reared as girls, but there are no systematic studies of those reared as boys. Most individuals with 46,XY micropenis appear to do well when reared as boys, but this approach should be viewed cautiously until there is more evidence about psychological and sexual outcome with male vs. female rearing. There is insufficient evidence regarding other causes of intersexuality and cloacal exstrophy, but all children should be assigned as girls or boys, with the recognition that some may change gender later in life.

Second, decisions about surgery would benefit from systematic evidence regarding functional outcome of current procedures and consequences of atypical genitalia. Sexual function involves more than cosmetic

appearance and the ability to have intercourse. Given the dearth of evidence, assumptions and biases should be clearly articulated to families.

Third, there is a pressing need for additional systematic evidence that addresses the complex determinants of psychological outcome. It is not sufficient to examine outcome only in relation to characteristics of the intersex condition and its treatment. There must be recognition and consideration of the child's temperament, family situation, culture in which the child lives, and benefits of psychoeducational interventions to reduce stress and facilitate coping.

Outcome itself must be defined from the perspective of the patient, and include quality of life. The components of outcome are not interchangeable (Table 3).

Fourth, translation of findings to treatment requires that studies meet important methodological criteria regarding sampling, assessment, and inferences consistent with the limitations of the methodology (Table 4). It is important to avoid being swayed by studies that support preconceptions or provide simple solutions.

Recent debates have improved treatment of children with intersex conditions by forcing an articulation of assumptions and examination of evidence. Resolution of current controversies requires a commitment to

Table 4

Considerations in Evaluating Outcome Studies of Children with Intersex Conditions

Sampling

- What was the population sampled?
- What proportion of potential participants were studied?
- How do the participants compare to the nonparticipants?
- How would results change if nonparticipants have different outcome?
- What was the comparison group?
- Were the samples of intersex and comparison individuals large enough to see effects of clinical significance, including group differences and predictors of outcome?

Outcome Assessment

- Were different aspects of outcome carefully differentiated?
For example, was gender identity measured independently of gender role?
- Was each outcome assessed in detail with reliable and valid measures?
- Were patients compared to controls to be sure that outcome is specific to an intersex condition?
- Were hypothesized predictors of outcome assessed in detail with reliable and valid measures?

Inferences

- Were appropriate statistical comparisons made so that inferences can be made to the population?
- To what populations can results be generalized?
- Can outcome be empirically attributed to intersex condition itself?
- Can outcome be empirically attributed to specific factors related or unrelated to intersex condition?
- Are inferences appropriately qualified in light of (inevitable) methodological limitations?

evidence-based care and a recognition that outcome in intersexuality cannot be simply predicted from medical factors alone.

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Commentary: Intersex Issues - A Series of Continuing Conundrums

Dr. Blizzard has abstracted and commented upon two extraordinarily important manuscripts by Migeon and colleagues. These investigators have provided the first analysis of the long-term outcome of 75 adults with male pseudohermaphroditism or micropenis (46XY or 45X/46XY) managed as children at Johns Hopkins Hospital. These children had been assigned to either the male or female gender. All of 18 patients with feminine external genitalia (androgen insensitivity syndrome or complete gonadal dysgenesis) were raised as females; 5/18 subjects with micropenis (stretched length <1.9 cm) without hypospadias were reared as females. In 39 subjects with ambiguous genitalia, 18 of whom were raised as female and in whom in depth information concerning their "sexuality" was sought, the assigned sex was at least "satisfactory" in the majority. Indeed, those reared as male had greater incidence of atypical external genitalia and greater dissatisfaction with perceived "body image". In general, however, the

outlook for normal adult heterosexual adjustment reared as either male or female was quite good in this group.

Until more complete data are available, these observations can serve as the basis upon which to counsel the parents of a neonate with male pseudohermaphroditism in regard to their choice in the gender assignment of their offspring. Dr. Blizzard correctly states that the "paternalistic" approach to medical practice is no longer tenable.

In my opinion, in the context of this psychosocial emergency, it remains extremely important that the experienced physician assist, perhaps even guide, the parents through the decision making process. In the absence of androgen insensitivity, complete gonadal dysgenesis, deficiency of P450_{side chain cleavage} or 17-hydroxylase/17-20 lyase, and related disorders, it seems most appropriate to rear the incompletely virilized male in the masculine gender if there is at all sufficient penile corpus to do so or to permit its surgical amplification.