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Deciding on Gender in Children with Intersex Conditions

Considerations and Controversies

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Abstract

Biologic factors such as genetic and hormonal influences contribute to gender identity, gender role behavior, and sexual orientation in humans, but this relationship is considerably modified by psychologic, social, and cultural factors. The recognition of biologically determined conditions leading to incongruity of genetically determined sex, somatic phenotype, and gender identity has led to growing interest in gender role development and gender identity in individuals with intersex conditions. Sex assignment of children with ambiguous genitalia remains a difficult decision for the families involved and subject to controversial discussion among professionals and self-help groups. Although systematic empirical data on outcomes of functioning and health-related quality of life are sparse, anecdotal evidence from case series and individual patients about their experiences in healthcare suggests traumatic experiences in some. This article reviews the earlier 'optimal gender policy' as well as the more recent 'full consent policy' and reviews published data on both surgical and psychosocial outcomes. The professional debate on deciding on sex assignment in children with intersex conditions is embedded in a much wider public discourse on gender as a social construction. Given that the empirical basis of our knowledge of the causes, treatment options, long-term outcomes, and patient preferences is insufficient, we suggest preliminary recommendations based on clinical experience, study of the literature, and interviews with affected individuals.

1. Background

Biologic factors contribute to gender identity, gender role behavior, and sexual orientation in humans,[1-4] but this relationship is considerably modified by psychologic, social, and cultural factors.[5-8] Differentiation between biologic sex and an individual's gender, i.e. the psychosocial sex of a person, dates back to John Money,[9] who distinguished between the biologically determined sex and 'gender', a linguistic representation not easily translated into other languages. The gender identity of an individual denotes conscious and unconscious feelings of belonging to one sex or the other. The term gender role refers to what a person does or says to communicate his or her status to others. Gender identity develops in the course of complex interactions of biologic and psychosocial factors, which begins to act even before the time of birth of a child and continues to develop through childhood.[10-13]

Developmental research on the age of attaining gender identity suggests that children can accurately label their sex and place a picture of themselves with other same-sex children by around 24–36 months of age, although considerable variability among children has been found in these abilities. Children differentiate male and female sex on the basis of physical and behavioral characteristics of other individuals (so-called sex typical activities, different levels of activities and aggressions, typical patterns of movement, hairstyle, clothing), and gradually include knowledge of biologic 'body markers' (external genitalia, breasts, body hair) in their understanding of concepts of gender. They will use different sources of information to develop a self-concept of their own

gender: the appraisal and recognition of their own attributes of sex; comparison of their own attributes with those of other people; and the social responses to their own behavior. Whether a period within the first years of life may serve as a critical developmental period in the sense of behavioral imprinting or acquisition of an irrevocable core gender identity, is debatable. For an extensive review of the conceptual issues involved see Ruble and Martin.[6]

2. Atypical Gender Development

The recognition of biologically determined conditions leading to incongruity of genetically determined sex, somatic phenotype, and gender identity has led to growing interest in gender role development and gender identity in individuals with intersex conditions. Individuals with intersexuality develop signs and symptoms of gender identity disorder (GID) relatively more often than the general population;[14] however, a formal diagnosis of GID may be difficult when the primary sex assignment of the child is under controversy. The decision to change gender may not be due to GID but to a shift from a misassigned gender in biologic terms to a correct one. In this context, it is important to realize the wide variation from minor uncertainty in gender identity to the full clinical syndrome of GID, including the wish to change the assigned gender. Psychosocial outcomes of intersexuality may be related to the type of condition, the appearance of external genitalia, influence of hormone exposure both pre- and postnatally, the effects of medical and surgical treatment, social support, and family and cultural background. There are some intersex conditions that cause much greater concern regarding sex assignment than others, such as partial androgen insensitivity syndrome (pAIS), 17β-hydroxysteroid dehydrogenase (17-HSD) type 3 deficiency, or 5α-reductase (5-ARD) type 2 deficiency and congenital adrenal hyperplasia (CAH) in females with excessive virilization. Zucker[15] has provided an excellent review of the salient issues in these conditions.

Studies of genetic males with single gene mutations that impair testosterone formation or action, and consequently prevent development of the normal male phenotype, provide unique insight into the control of gender role behavior.[16] 46,XY individuals with either of two autosomal recessive disorders (17-HSD and 5-ARD) have a predominantly female phenotype at birth and are mostly raised as females but frequently change gender role behavior to male at the expected time of puberty.[17-19] Even with identification of the molecular basis of the conditions, the great variation in phenotype ranging from partial to profound impairment of virilization of the external genitalia is difficult to explain. The rather high rate of sex reversal in these individuals has led to the suggestion that the androgen action in the brain is so pervasive that it can override female sex assignment and female rearing. There is considerable debate in these particular conditions as to whether the child should be gonadectomized before puberty to prevent later virilization and whether this would prevent ambiguity in gender identity.[18]

Genetic males with mutations that impair the function of the androgen receptor (complete androgen insensitivity syndrome [cAIS]) are also raised as females but have consistent female behavior as adults, and gender change rarely occurs in this condition.[20,21] Individuals with pAIS, or related conditions, may be raised as either girls or boys, and apparently generally adapt well to the assigned sex; however, some of the individuals report difficulties in sexual functioning and develop a same-gender orientation.[22-24]

In humans, female sex differentiation does not seem to be dependent on ovarian hormones but may be affected by high levels of circulating androgens as in CAH. Prenatal exposure of XX fetuses to excess androgens may affect later gender role development, and some women with CAH develop gender dysphoria.[25-29] These findings indicate that androgens are important determinants of gender role behavior.[30] Whether gender role behavior in childhood has an impact on gender identity in adult life remains to be evaluated. Recent genetic and neurodevelopmental studies in animals suggest that differences between male and female brains are not entirely a consequence of exposure to sex hormones, but are under the influence of sex-determining genes even before the gonads develop.[31,32]

3. Studies on Psychologic Well-Being

With the exception of studies related to GIDs in individuals with intersex conditions, there are relatively few studies on mental health in this population. In some studies, individuals with intersexuality reported feelings of shame and guilt, anger and sadness, and high scores on measures of depression.[33-35] Generally, no information was available on the personal background and specific experiences leading to such feelings. In contrast, adults with cAIS or pAIS frequently report good emotional health.[20] One follow-up study in children with intersexuality showed psychopathology in 39% of the study group.[36] Puberty may be a particular period of vulnerability in individuals with intersex conditions.[37,38] In one study, 81% of adults with intersexuality received psychotherapy or some other counseling to cope with various aspects of the syndrome.[21] Sample sizes are usually quite small, not allowing generalization of the findings; there is also great variation in conditions, as well as in the types of treatment. This hampers comparisons between groups.

Studies concerned with the impact of diagnosis in parents of newborn children with intersexuality describe strong emotional responses. Feelings of shame and guilt, among others are noted, especially in mothers.[34]

Secrecy about the primary condition and unambiguity towards the child's sex of rearing was often considered a prerequisite of healthy psychosexual development. Anecdotal evidence from patient reports about their experiences in healthcare suggests considerable traumatic impact, especially shame of being different and of not being told the truth by parents and physicians, but also shame about medical examinations and operation of the genitalia and their consequences and impaired potential to enjoy sexual experiences.[23,39-41] The traumatizing effect of repeated medical examinations of intimate parts of the body on a growing child has long been underestimated but is now being recognized. The implications of an early traumatic experience for mental health in affected male or female patients or their relatives may be considerable. It has been suggested that the processes involved in the examinations of intersexual genitalia share characteristics of sexual abuse of children based on observations that:

- repeated examinations on the genitals result in shame, fear, and painful feelings;
- the examinations are frequently carried out against the will of the affected child, but in silent agreement with the accompanying adults, creating a feeling of powerlessness in the child;
- the child has difficulty understanding and adjusting to the situation, due to issues of secrecy;
- the child develops feelings of being different, but is not allowed to speak about it with others;
- the 'collaboration' of the parents and other caretakers with the physicians creates an unresolvable conflict in the child, which will be denied because of his or her dependence on parents or caretakers;
- the traumatic experiences are isolated and may later result in post-traumatic stress syndrome.[42-44] Although such conclusions come from single case reports, their implications have to be taken seriously.

4. Being Born with Ambiguous Genitalia: an Emergency?

The authors assume that all cultures follow a more or less strict binary sex paradigm; however, more anthropologic studies are needed to substantiate this assumption. Western cultures are dominated by a binary sex paradigm. Intersex individuals do not conform to the fundamental assumption: one body – one sex.[45] Following delivery of a newborn with ambiguous genitalia, parents as well as health professionals feel that assignment to the male or female sex must be determined as soon as possible in the best interest of the child; also, because the registry office asks for a distinct statement of female or male sex and, at least in Germany, a corresponding first name of the child within the first few weeks of life. This frequently creates pressure for urgent action, often in striking contrast to the bodily health of the child. Some researchers have suggested that gender assignment must be considered a 'psychological emergency'[46] to be addressed in terms of days or even hours, or that the birth of an infant with ambiguous genitalia is a 'social and potentially medical emergency'.[47] Without doubt, there are cases of medical urgency (i.e. in CAH with salt wasting); however, the psychosocial urgency is postulated without systematic evidence. Long-term studies on the psychosocial effects of prolonged ambiguity are not available. There is some evidence from non-Western society that prolonged ambiguity (often as a consequence of the lack of access to medical intervention) may not lead to impairment of social role functioning and mental health.[48-50]

5. Optimal Gender Policy and Full Consent Policy

Medical and surgical treatments are based on theoretical assumptions and early clinical data that the unambiguous assignment to one gender and the optimal (re)construction of the external genitalia are important prerequisites of normal psychosocial development, social acceptance, and integration. Money and Hampson[51] formulated guidelines for gender assignment in children with ambiguous genitalia. They assumed that gender identity is predominantly determined by psychosocial influences, and accordingly that expedited gender assignment in the newborn period was warranted to avoid prolonged parental insecurity. Surgical genital correction was recommended within the first year of life, preferably not exceeding 18 months of age, to foster early development and unambiguous gender identity and a gender-congruent body image. Gender assignment was to be based on the prognosis of long-term outcome in terms of reproductive capacity, psychosexual functioning, and emotional health taking into consideration the availability of surgical corrections that would lead to optimal functional results in the female or male gender (optimal gender policy).

Increasing evidence of the prenatal influence of sex hormones on the developing brain[1,2,25,31] has led to recommendations that genetic males with micropenis, penile agenesis, or traumatic loss of the penis as well as XY individuals with pAIS, 17-HSD, or 5-ARD and XX individuals with very virilized appearance in CAH, should be reared as male gender.[52] Wilson and Reiner[53] formulated a new paradigm, saying that genital operations in children should be carried out only if the health of the child is at

stake, such as in functional disorders of the urinary tract or repeated infections. Removal of the testicles should be limited to those cases where malignant changes may be expected. In all other cases, these authors recommend the postponement of operations until the children are able to give their consent. The new paradigm was named 'full consent policy'.[54-57] Other authors who still recommend early intervention as well as early correction, however, also advocate full disclosure and detailed informed consent at least from the parents.[58] Some activists hold the position that genital operations that are not medically indicated constitute genital mutilations, and that children should be reared as a third gender.[59] Although more tolerance and acceptance for being different is beneficial for all individuals affected, from a developmental perspective it is not evident that a genderless or third-gender rearing of children, would in fact, always represent a better choice.[60] Some authors point out the potential for psychosocial harm of deferral of all surgery without the specific consent of the affected individual.[61,62] At least in our Western society, the medico-legal system accepts parental discretion in the decisions for and about their children to a large extent, to protect family integrity in terms of cultural and religious beliefs and social values.

6. Long-term Outcomes of Surgical Correction of Ambiguous Genitalia

The goals of corrective genital surgery are to approximate male- and female-typical appearance of external genitalia (to avoid stigma and ambiguity), to make heterosexual coitus possible, and to preserve reproductive ability where feasible. Feminizing genitoplasty can be achieved with approximately 25 different procedures, and there are even more procedures available for masculinizing genitoplasty.[63-67] In retrospective studies of feminizing operations, many procedures left patients with significant impairment of sexual functioning, i.e. insufficient vaginal opening (requiring repeated bougienage), clitoral reduction (resulting in lack of sensation), and inability to achieve orgasms.[68-72] Negative outcomes of masculinizing surgery included reduction of phallic size and erectile problems or dissatisfaction with sexual functioning.[73-75]

Modern techniques, microsurgical procedures in particular, have helped to overcome some of the problems. Today, many surgeons prefer one-stage operations avoiding abdominal access. Pediatric surgeons suggest that outcomes of early surgery are better compared with later corrections, due to the large amount of excess skin that provides excellent pedicled grafts with no tendency to stenosis or shrinking,[76] while others recommend two-stage procedures.[77-79] However, due to complications or less than satisfactory results, a second corrective surgery often becomes necessary. Outcome information, given at oral presentations on modern surgical interventions in intersexuality (claiming the advantages of modern microtechnology), often differ from information in the published literature, based on results from earlier techniques. Even though the era of microsurgery may greatly improve results in the future, the new techniques need to be evaluated in patient samples of sufficient size. It seems to be important to distinguish between the lack of evidence in terms of a lack of data and the lack of evidence of the benefits of surgical interventions in intersexuality in the past. Very few studies up to now have included patient satisfaction as an outcome measure.[23,75,80] In the years to come, patients and professionals will need to provide meticulously collected, representative data from large numbers of patients with standardized treatment protocols if medical decisions are to be based on evidence.

As the conditions are rare and clinical pictures are highly variable, very few surgeons have the opportunity to perform surgery on large numbers of patients. Therefore, personal experience is often limited, which affects overall quality of care. A child-oriented hospital environment that includes the option of rooming-in of a parent, experienced anesthesia and pain management, top quality standards of urologic care, rational choice of procedures and timing in the best interest of the patient, integrated services including pediatricians and others, and, most importantly, respect for the wishes of the child are felt to reduce trauma to a substantial extent. More clinical data are required to establish the psychologically most suitable timing for surgical treatment in childhood. In a recent study, the majority of adult patients with intersexuality were generally satisfied with their sexual functioning; however, 80% of these individuals felt that they preferred operations during adolescence or adulthood.[21,80] For ethical reasons, a randomized trial of late versus early surgery is not feasible, but observational long-term studies on larger numbers of patients may help to clarify the issue. The German Ministry for Education and Science (BMBF) started a large initiative in 2000 to support both basic science and clinical research in rare conditions. Among the ten networks funded is one on disorders of somatosexual differentiation. A central element of the network is a large multi-center, clinical follow-up study on children, adolescents, and adults with intersexuality, including more than 40 institutions, professionals, and self-help groups in Germany for patient recruitment and implementation of a large sustainable clinical database to allow longitudinal studies.[81] Therapeutic strategies should also be developed in close communication with self-help groups, thus ensuring support for patients and families.

The demand for 'evidence-based healthcare' asks for critical evaluation of treatments and long-term outcomes, including not

only the success of somatic (i.e. surgical) interventions, but all aspects of quality of life of the so-affected patients.[35] The ethical implications of the treatment of individuals with intersexuality have been taken up surprisingly late within the medical profession. A particularly difficult ethical question arises from the fact that the surgical interventions are frequently neither life saving nor relevant to health maintenance, but supposedly in the best (long-term) interests of the child.[82-86]

7. Current Debate and Cultural Context

A number of factors have led to a recent public debate of intersexuality beyond the scientific discourse already outlined: open communication of topics related to sexuality appears to be less restricted and more socially acceptable than it was during the 1950s. The international transgender movement and the 'coming-out' of homosexuals as 'being different' as well as the feminist theory of gender as a social construction,[87,88] have all decisively challenged stereotypes of social and biologic gender. Models beyond the heteronormative bisexuality include the perception of hermaphroditism as an ideal combination of maleness and femaleness, a model of gradation, meaning that one's gender may be identified anywhere on a scale ranging from completely male to completely female, and the supposition that more than two genders exist.[45]

On a different trajectory, the proclamation of the rights of children illuminates questions of appropriate participation and representation of children; the recognition of a child's right to an unimpaired physical and emotional development opened the debate on the ill effects of early sexual victimization of children. The increasing number of personal accounts of people with intersexuality in the media documents growing self-confidence in some of the affected individuals. During the last few years, an increasing number of self-help groups[89,90] have been founded, whose members have maintained contact via the Internet. A number of those affected are obviously traumatized and have begun to speak up. Their reports and statements have stimulated research activities and a public debate that would have been impossible without their initiative. As many patients do not wish to express their views publicly, it is difficult to know their wishes.

Culture, and medical options as a part of it, is an important part of the context in which decisions are made on sex assignment of patients with abnormalities of the external genitalia. Cultural differences in dealing with intersexuality and intersex individuals not only influence the patient's own psychosexual development but also medical decisions regarding sex assignment and subsequent management.[91] There is evidence that attitudes concerning gender and sexuality, including the acceptance of intersexuality, differ significantly between various cultures.[15,48-50] Moreover, cultures may significantly change during the lifetime of a patient, which makes prognosis of a therapeutic outcome extremely difficult. Globalization will also have an effect on the way societies cope with sexuality. Thus, cross-cultural studies might allow a new approach to the clinician's interaction with intersexed persons, their families, and their social background, a most important aspect considering the recent discussions and criticisms of patients and individuals affected with intersex disorders.

8. Recommendations

Given that the empirical basis of our knowledge of the causes, treatment options, long-term outcomes, and patient preferences is insufficient, recommendations at this point in time must be made cautiously and should be re-evaluated as knowledge increases.[92] We suggest the following preliminary recommendations based on our clinical experience, study of the literature, and interviews with affected individuals.

- Conditions with nontypical somatosexual development may be caused by a wide variety of mostly genetic errors leading to hormone deficiency or excess, impaired functioning of receptors, and structural abnormalities. Effects on both psychosexual and physical development may vary widely depending on the type, extent, and availability of causal treatment, and may change during the individual's growth and physical development. The identification of an accurate diagnosis (based on clinical findings, enzyme activities, receptor studies, histology of gonads, imaging results, and molecular genetic investigations) is therefore paramount for meaningful counseling of parents, relatives, or affected individuals. Premature decisions leading to irreversible interventions before an accurate diagnosis is established must be avoided.
- Depending on the primary diagnosis, prenatal androgen exposure and possible androgen-dependent physical development in puberty should be taken into account when one attempts to anticipate long-term prognosis for preferred gender. Conditions with very high exposure to androgens are more likely to lead to a preference of male gender in affected individuals compared with those with low androgen exposure. While this may not justify immediate or radical changes in decisions about sex assignment, parents should be aware of this issue.
- In most cases, the birth of an infant with intersexuality is not a medical emergency. All efforts should be directed to reduce anxiety and to support parent-infant bonding to allow time for adaptation and informed consent. Professionals must be aware of their own beliefs and cultural background and should take a

family-centered, culturally sensitive, and open-minded approach.

- Early genital surgery is one of a number of different options. The parents should be fully informed and given the opportunity to judge different possibilities for themselves. A child-orientated hospital environment that includes permitted rooming-in by a parent, experienced anesthesia and pain management, top quality standards of urologic care, rational choice of procedures and timing in the best interest of the patient, and, most importantly, integrated services including pediatricians and others, are felt to reduce trauma to a substantial extent. Surgical interventions should be meticulously documented so that adult patients are able to understand what has happened to them.
- Parents and professionals should be aware that gender identity and gender role development is not highly correlated with the appearance of the external genitalia, at least in pre-puberty, and that surgical corrections may be deferred if parents feel insecure about the decision, in the best interest of the child. Clinicians must provide counseling on the potential effect of stigma, discuss strategies to cope with it, and encourage contact with self-help groups as a source of information as well as social support.
- All children should receive developmentally appropriate information from an early age, and should participate in decision making as soon as possible. Atypical gender role behavior and ambivalence in gender identity should be recognized, accepted, and supported if necessary.
- Early support must be directed at affected children and young people to foster self-acceptance and to cope with feelings of being different and of shame. This requires modifications of the setting of clinical examinations and an environment suitable for children in practices, clinics, and hospitals.[30] Genital examinations may only be performed with permission given by the child in a nonthreatening context. The child should be encouraged to take an active role in deciding whether to show or talk about his or her body, and to ask questions. Examiners should be experienced in documenting and interpreting clinical findings to avoid repeated examinations, feel comfortable to discuss issues of physical development and sexuality, and enjoy communication with children.

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