

THE SURGICAL CHALLENGES OF DISORDERS OF SEX DEVELOPMENT (DSD)

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Summary.- Disorders of Sex Development (DSD) remain a fascinating challenge for the paediatricians, endocrinologists, biologists, psychiatrists, geneticists, radiologists, surgeons and for the whole society. This article aims at highlighting the current controversies and questions met with genital reconstruction in children born with abnormal genitalia. The main current techniques of masculinization and feminization are reviewed with their progress and their problems. The tools of decision used to assign a gender in some newborns with complex DSD are discussed showing that at the dawn of the third millennium, one still does not know why a boy is a boy, and a girl is a girl.

Keywords: Disorders of Sex Development. Hypospadias. Mixed Gonadal Dysgenesis. Congenital Adrenal Hyperplasia. Feminization. Masculinization.

Resumen.- Las Anomalías del Desarrollo Sexual (ADS) siguen siendo un desafío fascinante para los pediatras, endocrinos, biólogos, psiquiatras, genetistas, radiólogos, cirujanos y para toda la sociedad. Este artículo busca destacar las controversias y cuestiones actuales de la reconstrucción genital en niños nacidos con genitales anormales. Se revisan las principales técnicas actuales de masculinización y feminización junto con sus progresos y sus problemas. Se discuten las herramientas de decisión utilizadas para asignar un género en algunos recién nacidos con ADS complejas mostrando que en el amanecer del tercer milenio, uno todavía no conoce por qué un niño es un niño y una niña es una niña.

Palabras clave: Anomalías del desarrollo sexual. Hipospadias. Disgenesia gonadal mixta. Hiperplasia adrenal congénita. Feminización. Masculinización.



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INTRODUCTION

Disorders of Sex Development (DSD) raise challenging issues from all perspectives including reconstructive surgery towards the male or the female gender. The consensus conference of Chicago in 2005 (1) is an attempt to classify these anomalies and to outline the current approaches and controversies met in their management (Table I). Surgical techniques are complex and should only be performed in few selected centres in each country as these patients are limited in number and require a lot of expertise from various specialists who should closely work together.

TABLE I.

PREVIOUS	NEW
o Intersex	o Disorders of Sex Development
o Male pseudohermaphrodite o Undervirilized XY male o Undermasculinized XY male	o 46 XY DSD
o Female PH o Overvirilized XX female o Masculinized XX female	o 46 XX DSD
o True hermaphrodite	o Ovotesticular DSD
o XX male or XX sex reversal o XY sex reversal	o 46 XX testicular DSD o 46 XY complete gonadal dysgenesis

Endocrinologists, geneticists, biologists, psychologists and surgeons constitute the essential environment around a DSD child. A DSD surgeon should be familiar with at least five groups of patients who share some anatomical similarities although having very distinct diagnoses:

1) The severe hypospadias (46,XY DSD) which may be defined as a mal-developed penis with a division of the corpus spongiosum located behind the midshaft of the penis (Figure 1);

2) The mixed gonadal dysgenesis (45,X0/46,XY DSD) and some 46,XX DSDs with an asymmetrical genitalia, a severe hypospadias, an undescended dysgenetic gonad and a mullerian cavity located behind the urethral conduit (Figure 2);

3) The Congenital Adrenal Hyperplasia (CAH) 46,XX patients who require a "de-virilisation" procedure who present with an insufficiently developed vagina which opens into the posterior wall of the urethra, associated with a large genital tubercle (Figure 3);

4) The epispadiac penis which does not belong to the DSD group but involves a dissection of the neurovascular bundles leading to the glans and a dissection of the corpora cavernosa which is very similar to the one performed in CAH patients;

5). The Rokitanski syndrome where substitutive vaginoplasty is sometime needed.



FIGURE 1. Hypospadias: Ventral aspect.

Techniques have been extensively described elsewhere (2-4). Our aim is to point out the major challenges and controversies met in masculinization and feminization surgeries.

Surgery of masculinization

Masculinization surgery is essentially represented by hypospadias surgery which includes three main steps:

1) The complete dissection of the ventral aspect of the penis (ventral radius) and the identification of the degree of severity of the hypospadias. This step allows the correction of the ventral penile curvature in a majority of cases by untethering all the ventral hypoplastic tissues. In rare cases in our experience, a dorsal plication of the albuginea of the corpora cavernosa is needed to straighten the penis. If needed, the TAP (tunica albuginea plication) procedure described by the Philadelphia group (5-7) performed on the apex of the curvature, identified by an erection

test, provides a satisfactory straightening of the penis. It is the merit of Baskin's group (8) to have shown that dissecting the dorsal neurovascular bundles from the corporeal albuginea is not necessary in dorsal corporoplasty as the dorsal midline is almost free of nerves fibers.

2) Once the penis straight, the choice of urethroplasty is essential and really dependent upon the quality of the urethral plate, the length of urethra to be reconstructed and the degree of hypoplasia of the urethra, closely related to the level of division of the corpus spongiosum. The central question is: How safe is a urethroplasty using ventral dysplastic tissues on a long-term basis? If the urethral plate is wide and healthy, many surgeons would perform a Thiersch-Duplay procedure (9) which has the merit of solely using urethral tissues.

However, our experience shows that only few urethral plates are adequate for this procedure. Then comes the TIP (tubularized incised plate) procedure described by Orkiszewski (10) and Snodgrass (11)



FIGURE 2. Mixed gonadal dysgenesis with asymmetrical genitalia, insufficiently developed genital tubercle and a left intra-abdominal streak gonad.



FIGURE 3. CAH

which aims at increasing the width of the urethral plate by performing a midline longitudinal incision of the urethral plate. These authors report that the raw area left in the middle will re-epithelialize and form a urethelium lined conduit. Although this procedure is simple to perform with a reasonably low short-term complication rate (12), its long-term outcome needs to be evaluated as it is unclear whether the reconstructed urethra grows in a satisfactory way. Late inadequacy of the reconstructed urethra in the Thiersch-Duplay and in the TIP procedures are not uncommon in our experience, raising the question of the suitability of using exclusively ventral dysplastic tissues to reconstruct the missing urethra. These concerns have led us to favour the use of dorsal tissues with the Onlay urethroplasty (13) which is a more sophisticated procedure requiring a longer learning curve but providing reasonably good long-term results (14) (Figure 4). One of its advantages is to bring ventrally well-vascularized tissues with a better protein balanced platform which is likely to help the quality of healing (15). One criticism of this technique is the use of non-urethral tissues to repair the missing urethra. The same criticism can be made for the Mathieu procedure which seems to be a little bit out of fashion nowadays although its long-term outcome is quite satisfactory (16) and comparable to the data published for the TIP procedure. It is also a reliable technique for salvage procedure after glanular breakdown. The Koff urethral mobilization (17) is an elegant technique (Figure 5) to relocate the meatus at the apex of the glans by mobilizing the whole penile urethra either in primary cases or in redo cases. This procedure has the advantage of avoiding the use of non-urethral tissue and has in our

experience (18) few complications as long as the indication is well selected. The distal urethra must be healthy otherwise the risk of meatal stenosis is significant. In our practice, we privilege this operation when the length of urethroplasty is short (below 1.5 cm) and when the distal circular urethra is sound i.e. surrounded by spongiosum.

In the most severe hypospadias where the whole ventral radius is hypoplastic, the choice of techniques is several: The Koyanagi procedure (19) and its variant the Hayashi procedure (20) (Figure 6) have our favour. It consists of a full mobilization and a ventral transfer of the lateral tissues and the inner aspect of the preputial hood to reconstitute the urethral plate which is subsequently tubularized. This technique provides excellent cosmetic outcome but urethral complications such as urethrocele or distal stenosis are common leading to a complementary surgical adjustment in most cases (60% redo procedures in our series (14, 21, 22)). Our experience shows that even if most patients require 2 operations, the final outcome is satisfactory. Alternatively two stage procedures (Bracka (23)) using a foreskin graft or buccal mucosa are reliable with a higher risk of proximal stenosis at the junction between the native and the reconstructed urethra. Substitutive tissues such as buccal mucosa find their best indications in redo surgery when local tissues are scarred or insufficient.

Among the procedures commonly used in redo cases, the Inlay urethroplasty is an helpful adjunct in the armamentarium of techniques. It consists of splitting the urethral plate as described in the TIP procedure and grafting the raw area either with buccal mucosa

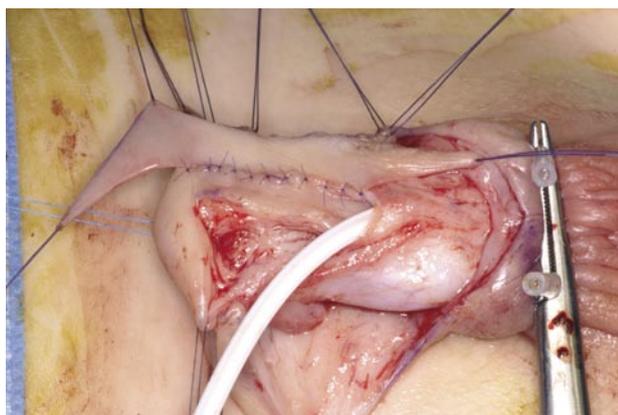


FIGURE 4. Onlay urethroplasty using a pediculated flap of dorsal preputial skin which is transferred ventrally and sutured along the edges of the urethral plate.

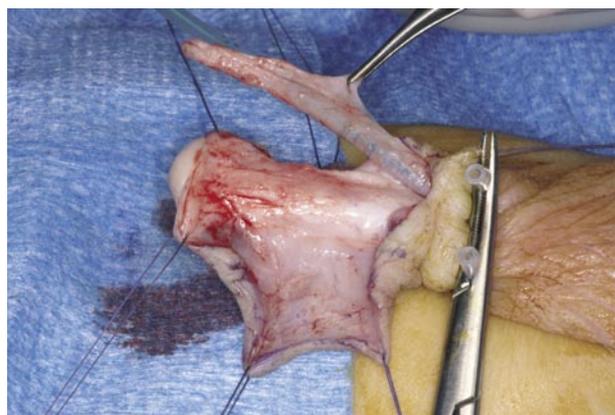


FIGURE 5. The Koff procedure is based on a full mobilization of the penile urethra to relocate the urethral meatus at the apex of the glans.

or with a free graft of prepuce. In our experience, the Asopa-Duckett tube has few left indications when the urethral plate is not preservable and when there is no preputial tissue available. Although the reported rates of complications are very variable (24-26), this procedure uses circular anastomosis which lead to a higher risk of urethral stenosis.

3) The third step of this surgery is the reconstruction of the ventral radius of the penis which involves a meatoplasty, a glanuloplasty and a sleeve skin cover. Some surgeons like to reconstruct the foreskin when it has not been used for the urethroplasty. We favour the circumcision as a reconstructed foreskin often remains asymmetrical and difficult to mobilize.

Whichever procedure used, it may be necessary to prepare the penis with a preoperative hormonal treatment for three main objectives:

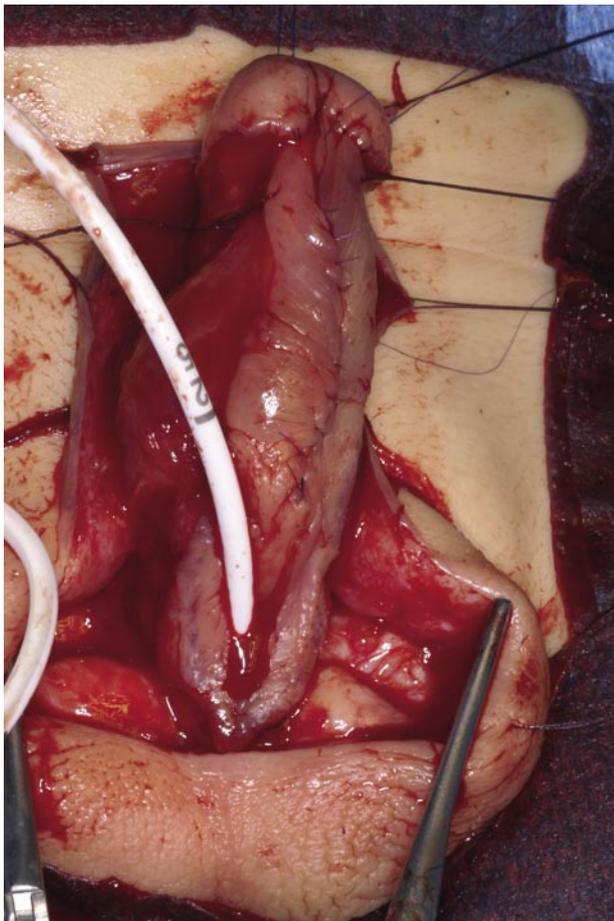


FIGURE 6. The Koyanagi Hayashi procedure involves a full mobilisation of the ventral, lateral and dorsal tissues with their blood supply in order to refashion a full length urethral plate which is subsequently tubularized.

To increase the size of the penis, to downgrade the severity of the hypospadias (27, 28) and to increase the tissular blood supply especially for redo-surgery. Our experience showed that preoperative androgenic treatment given less than 3 months before surgery significantly increased the rate of healing complications (14, 29, 30). This is explained by the role of androgens which slow down the skin healing process as shown by several publications (31-34). We would therefore advise to use androgens when necessary more than 6 months prior to surgery.

Laparoscopic excision of mullerian remnants might be indicated when the patient presents with dysuria and recurrent urinary tract infections (35, 36).

Gonadal surgery is considered when the testis is not intra scrotal (orchidopexy in 1 or 2 stages (37, 38)) or when there is a significant risk of tumours (orchidectomy (39)) which is dependent upon the diagnosis of DSD.

For years, feminization was the "by default" choice in case of complex DSD (40) as the creation of a penetrative conduit was surgically simpler to form than the creation of a phallus. However major progresses have been made with phalloplasty especially with the works done by de Castro and Hoebecke (41-43). It is a challenging procedure which should however be restricted to specific cases submitted to a collegial discussion.

Surgery of feminization

These techniques are mainly used in 46,XX CAH, 45,X0/46,XY DSD, some 46,XY patients oriented in the female gender and in ovotesticular DSD patients who are mostly raised as females. The procedure includes three main steps (Figures 7 A-G): 1) The connection of the mullerian cavity (i.e. vagina) to the pelvic floor (44). The difficulty of this step is related to the level of confluence of the junction between the vagina and the urethral wall. If the confluence is less than 2 cm from the pelvic floor, "top-down" vaginoplasty which exteriorizes the urethra up to the confluence is often used. It is described as partial or total urogenital sinus mobilization (PUM, TUM (45-49)). The exteriorized urethral tissue is used to reconstruct the vaginal introitus. This technique has the advantage of creating a mucosa lined introitus and neatly separating the vaginal from the urethral meatus. One of the criticisms is the potential nerve damage related to the mobilization which may affect the long-term continence of the child (50). Alternatively, for short distance between the perineal floor and the

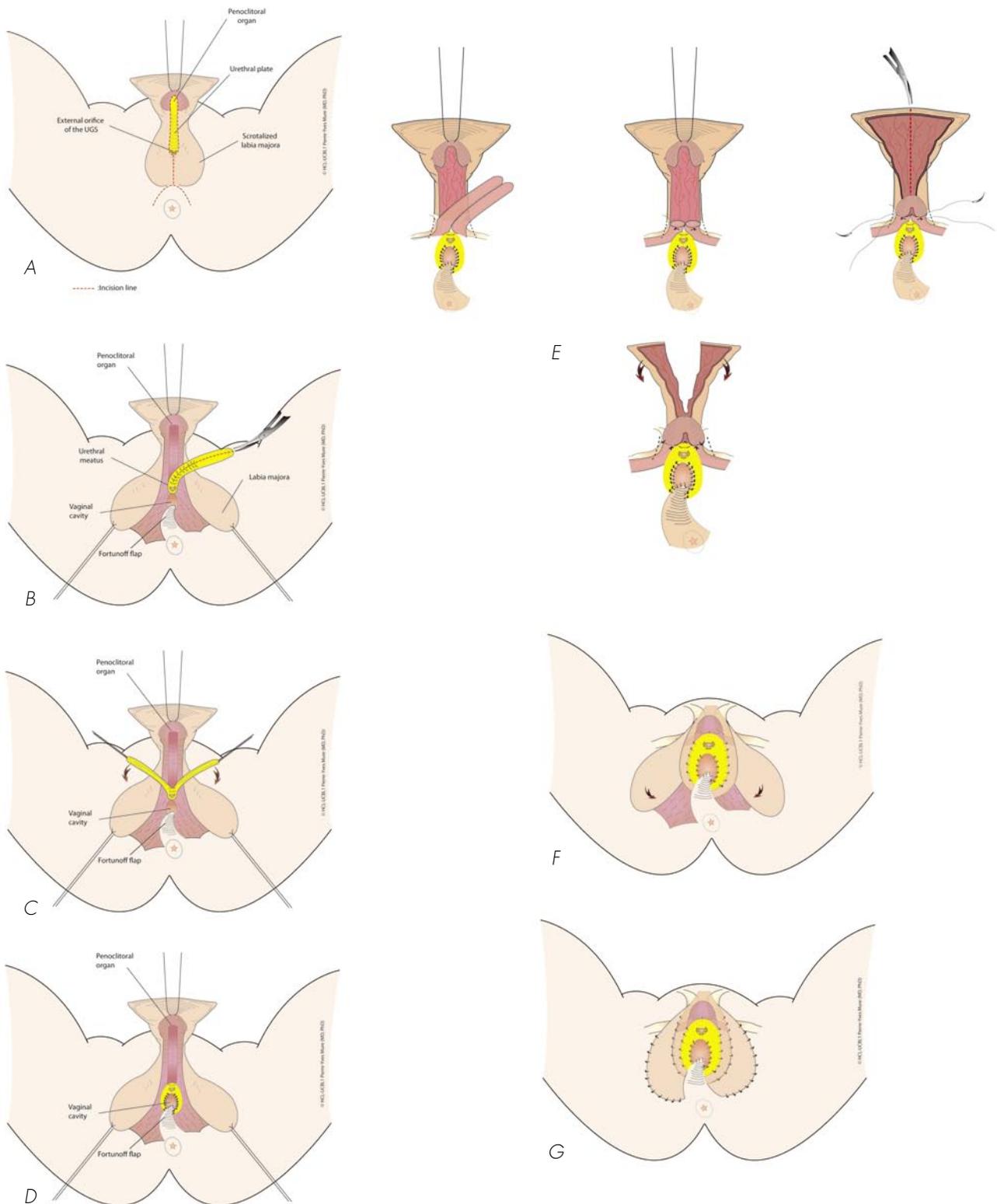


FIGURE 7. The step by step procedure for a CAH patient with a low urethra-vaginal confluence: 7A) Incision lines outlining the genital folds, the midline and the posterior Fortunoff skin flap. 7B) Freeing of the urethral plate off the ventral surface of the corpora. 7C) Midline division of the urethral plate and rotation of the 2 flaps which are subsequently sutures along the edges of the meatal and vaginal mucosa (introitoplasty) (7D). 7E) Close dissection of the 2 corpora cavernosa from their tips down to their bone insertions. 7E) Excision of the corpora. 7E) Anchorage of the clitoris to the corporal stumps. 7E) Midline longitudinal division of the skin shaft and lowering of the 2 flaps which are stitched along the external edge of each urethral flap to refashion the labia minora. 7F) Mobilization and defatting of the labia majora which are reduced and lowered on each side of the operating field. 7G) Final aspect.

confluence, a “down-top” procedure has our favour (51). The vaginal cul de sac is minimally mobilized. The urethral tissues forming the urethral plate sitting on the ventral aspect of the genital tubercle are used to reconstruct the introitus, separate and superficialize the urethral and the vaginal meatus. This technique which creates a mucosal infundibulum should hopefully reduce the number introital revisions often required at puberty with classical techniques.

When the confluence is high close to the sphincter or the bladder neck, the mobilization of the vaginal cup can be done either through a posterior sagittal approach (Peña (52, 53)), or more commonly nowadays laparoscopically (54). The trans-trigonal approach described by Passerini (55) is very rarely performed.

In the Rokitansky syndrome or in the complete androgen insensitivity syndrome (CAIS), a majority of patients may benefit from vaginal dilatations (56). Some of them require a vaginal substitution for which several procedures have been described mainly in adult patients: split-thickness skin grafts of McIndoe (57), tissue expansion (58), rotational cutaneous flap (59), amnion (60) and peritoneum (61) flaps, Vechietti's technique (62, 63), intestinal vaginal reconstruction (64). Reports of these techniques in children (65, 66) are few. Our experience is based on the use of sigmoid bowel (64, 67).

2) One of the main controversies concerning feminization procedures is the clitoral reduction. Several studies showed that surgery of reduction may affect the sensibility of the clitoris and therefore advised not to touch the clitoris if it is less than 3 cm long (68, 69). With the work done by Baskin's team (70) and with the lessons learned from epispadias surgery (71) and hypospadias surgery (72), the dissection of the corpora cavernosa and the preservation of the neurovascular bundles seem to be a lot more secure although one has to wait 15 or 20 years before evaluating the outcome of these new techniques. The full excision of the corpora cavernosa after a circumferential dissection of the neurovascular bundles has the merit of avoiding the classical caverno-cavernostomy used in former techniques and prevents the re-growth of the genital tubercle during the critical period of adolescence when patients are often less compliant with their hormonal substitutive treatment. The preservation of the clitoral blood supply and innervation is far more extensive with the circumferential dissection similar to the technique described by Ransley in epispadias surgery (unpublished data). The anchorage of the clitoris on to the cavernosal stumps gives an excellent cosmetic result and avoids the long mucosal slide

which was often noticed in previous techniques. Alternatively, some authors have suggested to excavate the spongiosal tissue located inside the corpora to reduce its volume and preserve the clitoral neurovascular bundles (73).

3) The last step of this female reconstruction is the formation of the labia minora and the reduction and lowering of the labia majora which gives a satisfactory female perineal appearance (74-76).

The challenge of gender assignment

Newborns with abnormal genitalia raise many challenging questions involving doctors and parents. Paradoxically, the patient is not actively part of the essential discussion concerning his or her Gender Identity i.e. Social Identity. The decision in the neonatal period of a gender has been questioned as some patients felt that doctors should not impose a choice without having more insight concerning the Individual Sex Identity. The challenge at birth is to give a Social Identity or Gender Identity to an individual without knowing what his or her Individual Sex Identity and Behavioral Identity are going to be. This situation has led some specialists to suggest to postpone any decision until the child expresses more clearly his or her own Individual Sex Identity (77). This opinion has raised many controversies and the conference of consensus on DSD of Chicago in 2005 (78) privileged early gender assignment in the most complex genital disorders to avoid unbearable situations for the parents.(79)

The decision taken by the specialist team is based on four groups of indicators: 1) The hormonal, genetic and tissular profiles of the child which may be called the “inside sex”. 2) The anatomy of the genitalia i.e. the size of the genital tubercle and the presence of a mullerian cavity represent the “outside sex” which is the visible part of the iceberg. The future height of the patient might also be a significant criteria to move towards a female gender if the future height is expected to be short. 3) The potential capacity of the patient to have intercourse and children also need to be evaluated and can be defined as the “functional sex”. 4) Perhaps the most important indicators come from the cultural and educational medium of the child and represent the “social sex”. No gender assignment can be made without a full understanding and acceptance of the parents, knowing the fact that their opinion is markedly influenced by the doctors's words. The parents and especially the mother's feelings about the situation are of utmost importance to take the ultimate decision.

Few publications report the long-term outcomes of DSD surgery. Literature is a bit more prolific for hypospadias surgery than for feminization surgery and remains quite opinionated based more on impression than evidence. The collected data from patients or specialists based on observational medicine are often more subjective than objective as they mostly refer to quality of life and integration in the society. Although technical progress have been made for both types of surgery, major genital reconstruction in both males and females often lead to poor functional and cosmetic outcomes with frustrated patients. Since several years, multicentric efforts are made to improve our understanding and management of these complex situations with a better and more consensual approach of the potential determinant factors which may affect the construction of Individual Sex Identity (79).

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