Presidenza del Consiglio dei Ministri

ITALIAN NATIONAL BIOETHICS COMMITTEE

MINOR'S SEXUAL DIFFERENTATION DISORDERS:

BIOETHICAL ASPECTS

25th February 2010

PRESENTATION

In this Opinion the National Bioethics Committee deals with the pathologies – that can occur in children in different degrees of gravity and frequency – of "sexual ambiguity" (also called an "intersex" condition), that is, a not harmonious development of the different components of sex (genetic, gonadal, hormonal, phenotypic), where it is difficult for the doctors and parents to assign sex as male or female.

It is a delicate matter of considerable bioethical and bio-juridical interest as it places at the centre of reflection the sexual identity of the child (the different physical, mental and social components), the complex decisions of intervening on the body and psyche by the physician, the manner of providing advice for parents and the children themselves when they reach a sufficient level of awareness, the personal, social and legal implications for those affected by these pathologies.

The Opinion, after placing the problem within a historical and clinical framework, highlights the principle elements of international bioethical guidelines, in order to grasp the problematic issues in bioethical and juridical terms, and reach some important shared recommendations. Including: each medical intervention in DSD cases must have the objective to harmonise elements of disharmony in physical, psychological and social terms; the physician must pay particular attention on a diagnostic level to each objective sign (from the stage of prenatal development) to prearrange any possible therapeutic instrument; any intervention on the body must be guided by the principle of the best interests of the child, avoiding unnecessary mutilation (such intervention should be implemented only in emergencies, as it is preferable to wait until the individual reaches a maturity which allows the expression of consent); the family and the child himself/herself (if able to understand) should be given adequate psychological support and the communication must be careful and gradual, with the provision of appropriate counselling.

The NBC focuses in particular on the so-called "exceptional cases" where there are no objective indications for assigning sex: in these cases it is desirable that parents together with the physician make a shared choice to educate the child as male or female, however particular attention is paid to the emergence of spontaneous inclinations. Juridically, the NBC believes that the current Italian legislation governing the declaration of sex at birth (3rd November 2000) should be integrated with a confidential "annotation", based on rigorous and comprehensive medical certification of the disorder that affects the newborn child, so as to subsequently consent – if necessary – correction of the registry indication through a more simplified procedure compared with that required by current law (that requires surgical medical treatment in accordance with the law on sexual rectification, the Law of 14th April 1982).

The document has been drawn up by the working group coordinated by Prof. Laura Palazzani: with contributions to the group made by Profs. Salvatore Amato, Carlo Flamigni, Francesco D'Agostino, Lorenzo d'Avack, Marianna Gensabella, Aldo Isidori, Assunta Morresi, Andrea Nicolussi, Maria Luisa Di Pietro, Giancarlo Umani Ronchi, Lucetta Scaraffia, Monica Toraldo di Francia, Grazia Zuffa. Special thanks to Prof. Maurizio P. Faggioni, for the two hearings held within the context of the working group and for his valuable suggestions in the drafting of the text. The Opinion was approved in the plenary session on the 25th February 2010 in unanimity of those present: Profs. Salvatore Amato, Luisella Battaglia, Adriano Bompiani,

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Among the absent members that have expressed their approval are Profs. Luisella Battaglia, Stefano Canestrari, Roberto Colombo, Bruno Dallapiccola, Romano Forleo, Silvio Garattini, Alberto Piazza, Rodolfo Proietti.

The President
Prof. Francesco Paolo Casavola

1. Definition

The term "disorders of sexual differentiation"(DSD from now on), refers to the inharmonious development of the different components of biological "sex" that can also influence the structuring of sexual identity and the assumption of gender role.

It is also known as sexual ambiguity or intersex[1]. In the past different expressions have been used such as "androgyne" or "hermaphrodite", to indicate those individuals with a mixture of both masculine and feminine elements present[2].

It is a particularly delicate matter of bioethical and juridical interest, as it puts at stake the health of the minor. The term "minor" indicates a person under the age of 18 and refers to a wide range of ages, including the infant, child, and adolescent: such temporal scope requires articulate bioethical reflection that takes into account the different ages, life situations and levels of awareness. The Opinion intends to highlight the issues of DSD connected with the gradual building of sexual identity, the complex decisions to intervene on the body and the psyche, the manner of informing and communicating between those involved (when possible, physician-parents-minor), the personal, social and juridical implications. Other issues arise in relation to anticipation of the diagnosis of certain pathologies of DSD in the prenatal stage which on one hand allows the possibility of new therapies in the uterus and on the other raise - in some cases- ethical issues in the context of the decision related to acceptance or termination of pregnancy. In this field adequate genetic counselling is particularly important[3].

The NBC, following along the child centred lines drawn from the previous document *Bioethics with Childhood* (1994), intends to propose ethical reflection which focuses on the dignity and interests of the child within the context of the complex issue under examination.

2. Sexual development

Multiple factors contribute to sexual development. The three key factors are: 1. the chromosomes of the zygote (46,XX in females; 46,XY in males); 2. the differentiation of the gonads in ovary and testis; 3. the differentiation of organs responsible for reproduction and development of external genitalia.

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[1] Intersex and middlesex are terms used in English. Intersex is distinct from transsexualism, where the dissonance between biological sex- defined as male or female- and sexual identity recognises its genesis as primarily psychological.

[2] *Androgyne* indicates a being with both sexes present in some myths; *hermaphrodite* comes from the mythical Hermaphroditus, son of Hermes and Aphrodite, who obtained from the Gods the merging of his body with that of his beloved so becoming a hybrid, sharing male and female characteristics. As these expressions show, the subject, treated here as a bioethical issue in terms of certain medical disorders, also has an ancient and widespread history. A number of different myths represent androgyny as a "status of reality preceeding creation and the ordering of the cosmos" (A. Di Nola, *Bisessualita' e androginia*, in *Enciclopedia delle religioni*, Vallecchi, Florence 1970, vo. 1, col. 1144). The book of Genesis itself (1, 27), speaking of the creation of the first human being uses the expression "male and female he created them", which could allude, as emphasised by the ancient exegesis, to a primordial androgyny. The ancientness of the subject and its symbolic radicalness add complexity to the scientific bioethical debate.

[3] Attention should be drawn to the Permanent Conference for relations between the State, Regions, and the autonomous Provinces of Trento and Bolzano: The agreement between the Minister of Health, the Regions, the autonomous Provinces of Trento and Bolzano on the document containing "Guidelines for the activities of Medical Genetics" 15th July 2004. This document advocates that genetic testing should always be accompanied by adequate genetic counselling.

The Y sex chromosome provides the signal for the development of the male gonad, irrespective of the number of female sex chromosomes (X chromosome) present. The absence of Y directs the development of the individual into a female. Therefore, the *genetic sex,* which is formed at the moment of conception in chromosomal 46,XX or 46,XY, can be considered the first event to determine the sex of a person. A series of changes follow on from this, in the cascade which leads to the formation of the female gonad (ovary) or male (testis) and therefore to the definition of the person's *gonadal sex*. Gonads, in turn, secrete hormones that control the development of external genitalia (*phenotypic sex*). There are also other levels of expression of somatic sexuality that contribute to the difference between men/women: for example, blood-chemical parameters and basal metabolism rate.

The *sex of rearing* (*nurture*) and *psychic sex* (*gender*, *role*) are dependent on these events.

Although the formula of sex chromosomes is already defined in the zygote, sexual differentiation in the human embryo starts only after the 6th week. Until then the gonads are identical in both sexes and both the precursors of the tubes and uterus are present, the so-called Mullerian ducts, as well as the precursors of the male efferent ducts, the so-called Wolffian ducts. Undifferentiated gonads appear as bulges in the central portion of the genital ridge. In the presence of testicular determining factor (TDF), 42 days after conception, the first signs of organisation of the testis appear. In the absence of TDF, the gonad develops into female.

Understanding of the initial stages of this complex process were defined in the 40's from animal castration experiments carried out by Jost. Following the removal of genital ridges in rabbit embryos, in the stage preceding differentiation of the gonad, it was seen that internal and external genitalia developed into female, regardless of genetic sex. When a crystal of testosterone (the male hormone produced by the testes) was inserted in place of the removed genital ridge, masculinisation of genitalia occurred even though the Mullerian ducts and therefore the uterus and tubes continued to exist. It has emerged from this result that the basic sex is female; virilisation is related to the secretion of testosterone by the testes; testosterone is not sufficient, however, to complete virilisation, the hormone that inhibits Mullerian structures (AMH) is also necessary.

Jost's intuition has been largely confirmed in the last 25 years, through a series of new acquisitions including, among other things: the identification of the SRY gene (*Sex determining Region Y*), the equivalent of TDF; the discovery of hormone AMH, produced by testis Sertoli cells, which inhibit Mullerian structures; evidence for the production of testosterone by Leydig cells of the testis and its reduction into Dihydrotestosterone (DHT), the hormone that produces virilisation in peripheral tissues, by the a-reductase enzyme. The effectiveness of these hormones depends on the functional integrity of the androgen receptor (AR gene) in target cells. This cascade of events is completed by the action of other genes present on non-sex chromosomes (autosomes) and on the X chromosome, whose proper functioning is critical to obtain the correlation between chromosomal, gonadal and phenotypic sex as well as reproductive function.

The SRY gene is located on the short arm of the Y chromosome. Introduction of the homologue of this gene (SRY) in a female mouse embryo, determines the development into a male. SRY gene encodes a protein of 204 amino acids, which contains a sequence of 79 amino acids, evolutionarily conserved (HGM-box), present in proteins with high affinity for DNA. SRY is expressed in the genital ridges during

differentiation and in many fetal tissues, but not in adult tissues. SRY binds to the promoter of the gene that encodes the anti-mullerian hormone (AMH) inducing expression and preventing the formation of derivatives of the duct of Muller. In addition it controls some enzymes involved in steroidogenesis and therefore in virilization and inhibits DAX1, a gene located on the X chromosome, which in turn acts as a repressor of sexual differentiation. The critical role of SRY in male sex determination is confirmed by the observation that its mutations cause sex reversal. People with this mutation have a chromosome 46,XY, but they are sterile females (Swyers syndrome). This condition arises not only from mutations in the coding or regulatory region of the SRY gene, but also, and more commonly, from loss of a part of the short arm of Y that contains the gene, deriving from an error during pairing of X and Y sex chromosomes in spermatogenesis.

The phenotypic sex of the embryo depends therefore on gonadal sex determination, which is primitively related to the compliment of sex chromosomes and the presence/ absence of the Y chromosome. In humans the Y chromosome is the determinant in male sex. Indeed, in the presence of only one X chromosome (45,X or X monosomy), the phenotype is female and corresponds to Turner syndrome (gonadal dysgenesis with short stature; sterile female). Conversely, the sex complement XXY (47,XXY or Klinefelter's syndrome) and its more complex variant forms (48,XXXY; 49,XXXXY) give rise to a predominantly male sterile phenotype. In the presence of a cellular mosaicism (coexistence of genetically different cell lines) 45,X /46,XY, the phenotype varies from sterile male (when the line XY prevails) to the Turner syndrome (ovarian dysgenesis with short stature when the X line prevails) with intermediate dysgenesis of the gonads and ambiguous genitalia.

The XY sex reversal (male to female) has a heterogeneous origin. An illustrative example is testicular feminization (known as Morris syndrome), in which the subject 46,XY, because of a mutation in the AR gene (androgen receptor) is insensitive to the action of testosterone, and despite having abdominal testis, develops a female phenotype, with dead-end vagina, in the absence of uterus and tubes. This condition can be associated to varying degrees of virilization, when there is only partial insensitivity to testosterone. Other aspects of ambiguity of the external genitalia in 46,XY subjects can be caused by a defect in the alpha-reductase enzyme, which transforms testosterone into the active form of dihydrotestosterone, which results in pseudovaginal perineoscrotal hypospadias, or other enzyme deficiencies in the cascade that leads to the synthesis of testosterone, such as the defect in 17-KS-reductase. In addition, three quarters of the 46,XY male carriers of alterations in the SOX9 autosomal gene have dysgenetic gonads and ambiguous genitalia, up to sexual reversion. Similarly, mutations with loss of function of the autosomal gene SF1 (*Steroidogenic Factor 1*), which regulates the transcription of certain target genes involved in reproduction, steroidogenesis and sexual differentiation in males, produce in subjects with complement XY a female phenotype, with gonadal dysgenesis, uterus and normal Mullerian structures, adrenal hypoplasia.

XX reversion (from female to male) is very rare. The most common form is linked to translocation of the short arm of X of the region containing the *SRY* gene. Sex reversion independent from *SRY* (*SRY*-negative subjects) is exceptional and it is due to the mutation of certain autosomal genes.

Lastly, psychological sex, suffers from the influence of factors of a biological nature (brain imprinting) and also of an educational and relational nature.

3. DSD: classification and description of some clinical aspects

Genetic, gonadal and phenotypic sex– as already stated – are closely related and are defined by the genomic characteristics of the individual. It is implicit that such a complex mechanism such as sex determination and differentiation is subject, with relative frequency, to genetic mutations which result in variable aspects of ambiguity or dysfunction. From the physical point of view, the development of body size of sex organs comes from an undifferentiated structure, which then develops through factors of differentiation, the action of sex hormones and specific determinants encoded in the chromosomes: this process begins with fertilization and ends with puberty, with the development of secondary sexual characteristics. The project is originally set by genetic patrimony and is rich in interaction between the diverse components. If this process does not take place in a regular way, it can produce situations of disharmony in the development of sexual organs.[4]

This state of disharmony between the genetic, gonadal, ductal and phenotypic components can raise important ethical issues for doctors, surgeons and parents at the moment of decision of the so-called "attribution of sex" or "sex assignment", which sometimes requires intervention of physical modification and psychological support for the structuring of sexual identity.

The new classification of DSD distinguishes[5]. 1. DSD from sex chromosome abnormalities; 2. DSD with 46,XY karyotype; 3. DSD with karyotype 46XX. The first group includes Klinefelter syndrome 47, XXY and variant forms; Turner syndrome with 45, XX and variant forms; mixed gonadal dysgeneses with 45, X/46, XY; chimeras 46XX/46XY formed from the fusion of two zygotes. The second group includes: disorders of gonadal development (testis); disturbance of synthesis, sensitivity and the action of androgens; other pathological aspects (e.g. the syndrome of persistent Mullerian ducts, etc.). The third group includes: gonadal developmental disorders (ovary); syndromes with excessive androgens; other pathological conditions (for example agenesis/Mullerian hypoplasia, etc.)

The descriptions of some clinical situations of DSD mentioned in the previous paragraph in relation to their origin, follow as examples.

Among the most well known clinical situations of DSD abnormalities are: Klinefelter syndrome, Turner syndrome and mixed gonadal dysgeneses (previously mentioned in the paragraph above). According to other classification, Klinefelter syndrome and Turner syndrome fall under congenital primary hypogonadism with chromosome aberration[6].

The syndrome of Klinefelter is associated with karyotype 47,XXY, or more rarely with mosaic 46,XY/47,XXY. In patients with Klinefelter syndrome, testicular biopsy shows the presence of fibrous tissue with absence of spermatogenesis in more than 90% of cases. The phenotype is male with gynecomastia (abnormal development of the mammary gland), normal internal and external genitalia and underdeveloped testicles. The Klinefelter syndrome is generally associated with sterility, even if it is possible to produce a low percentage of sperm in 7% of cases.

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[4] D. Frimberger, J.P. Gearhart, *Ambiguous genitalia and intersex*, "Urol. Int.", 2005, 75, pages 291-297.

[5] I.A. Hughes, *Disorders of sex development: a new definition and classification*, "Best Pract Res Clin Endocrinol Metab.", 2008, 22 (1) pages 119-134.

[6] L.S. De Groot, S.L. Jameson, *Endocrinology*, IV edition, Saunders Co. 2001; *Klinefelter Syndrome*, Acts of the SIAMS commission for rare diseases, Padova February 2010.

Turner syndrome is characterised by 45,X chromosome (monosomy X, also known as 45,XO) or a mosaic (45,X/46,XX) or structural defects of the X (deletions, isochromosome of the long arm, ring chromosome). Those affected by the syndrome are phenotypically female, with dysgenetic ovaries, hypoplasia of the uterus and tubes, no pubertal maturation, menarche, do not produce female gametes and show hypoplasia of secondary sexual characteristics. External genitalia maintain a childlike appearance, stature is low, the chest is deformed; intellectual deficit is rare.

Mixed gonadal dysgeneses are associated with genetic mosaicism, abnormal gonadal tissue, ambiguity of the external genitalia, delayed puberty, primary amenorrhea in patients with female phenotype, increase in testicular cancer in patients with male phenotype. In gonadal dysgeneses, phenotypic characters and -particularly- development of the external genitalia are not usually discordant with the other components of sex, except for some forms of mixed gonadal dysgenesis.

In DSD with Karyotype 46,XY and 46,XX phenotypic sex can contrast variably with gonadal sex and the structuring of sexual identity may not correspond to the gonadal sex. While in the past "male pseudohermaphroditism" and "female pseudohermaphroditism" were distinguished, depending on the presence of male or female gonads, today a new classification, better adapted to the different clinical situations, has been proposed[7].

The DSD with karyotype 46,XY include - as previously stated - diverse clinical situations, characterised by incomplete or absent virilisation of external and internal genitalia in patients with karyotype 46,XY and male gonads. Among the various forms of DSD with 46,XY karyotype, we only need remember total peripheral androgen insensitivity and the 5 alpha-reductase deficiency.

Total peripheral androgen insensitivity is the so-called *syndrome of Morris*, a consequence of complete and impaired functioning of androgen receptors in the genital organs and peripheral tissues. Consequently, these individuals does not meet those transformations that are mediated by androgens in males, therefore they have a female phenotype with female external genitalia, dead-end vagina, agenesis of the uterus, internal genital ducts that are not differentiated, male gonads, usually held in the abdomen, inguinal canal or labia. Menarche does not occur, the mammary gland develops normally[8], pubic and axillary hair is absent. These people can not be virilised with hormone therapies. Treatment consists of removal of undescended testes to prevent the risk of cancerous degeneration of the gonads and the administration of estrogen. Expansion of the vagina permits a satisfactory sex life. The phenotypic sex and identity of these people is female [9]. Not only the phenotype but also the level of muscle strength is similar to that of women, that is, to genetically female individuals: this implicates the importance of analogous treatment (consider the problem of possible discrimination in sports).

As previously stated, different forms of partial androgen resistance exist (Lubs syndrome, Rosewater syndrome, Reifenstein syndrome etc.): in these situations there

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[7] See: A. Dreger, C.Chase, A. Sousa et al., *Changing the nomenclature/taxonomy for intersex: A scientific and clinical rationale*, "Journal of Pediatric Endocrinology and Metabolism", 2005, 18, pages 729-733; C.Chase (ed.) Chrysalis: "Journal of Transgressive Gender Identities", Fall/Winter, 1997; Cf. *Consensus statement on management of intersex disorders*, 2006.

[8] Cf. J.M. Morris, *Syndrome of testicular feminization in male pseudo-hermaphrodites* (82 cases). "American Journal of Obstetrics and Gynaecology", 1953, 95, pages 1192-1211. This development is made possible with the action of estradiol, a typically female hormone produced in small quantities from the testes even in normal males and which – in this case –has a markedly feminizing effect because it is not thwarted by male hormones.

[9] A.B. Wisniewski, C.J. Migeon, H. F. Meyer-Bahlburg et al., *Complete androgen insensitivity syndrome: long-term medical, surgical and psychosexual outcome*, "The Journal of Clinical Endocrinology and Metabolism", 2000, 50, pages 2664-2669.

is ambiguity of external genitalia at birth and partial masculinisation during puberty, with variable phenotypic changes.

The deficit of enzyme 5 alpha reductase (Imperato-McGinley syndrome) prevents the formation of an important derivative of testosterone, deidrotestosterone, responsible for the evolution into male external genitalia (testosterone induces the development on male internal genitalia). These people are genetic males who present - at birth - ambiguous external genitalia with failure to close the lip and scrotal folds and agenesis of the scrotum. The internal genitalia, under the control of testosterone, evolve into male. Testes are usually undescended in the inguinal canal along with hypospadias and a small stretch of dead-end vagina. This phenotype often leads to allocation of female registry with correspondent female education. During puberty, in conjunction with increased levels of plasma testosterone, external genitalia progressively virilize, the volume of the penis increases, the testes descend and muscle mass grows: this transformation highlights the condition of DSD. The effects of physical transformation on identity are variable, but there is mostly a new male identification[10] as far as possible fertility in adult life.

Those DSD with karyotype 46,XX include different clinical situations, characterised by the presence of ambiguous external genitalia in patients with chromosome 46,XX. Among the forms of androgen excess there is hyperandrogenism from fetal defects in certain enzymes produced by adrenal 21-hydroxylase, 11-hydroxylase, 3-HSD, from maternal hyperandrogenism, iatrogenic (from progestins or androgens) or from virilising tumors of the ovary or the adrenal glands.

The most widespread form of DSD with Karyotype 46,XX with hyperandrogenism is congenital adrenal hyperplasia 21-hydroxylase enzyme deficiency involved in cortisol metabolism: this condition determines from prenatal life, an overproduction of androgens with consequent virilization of external genitalia. Alterations in development of genitalia are variable, from female phenotype with clitoral hypertrophy, to frankly male phenotype with complete fusion of the labia majora, which can simulate an empty scrotum, with marked clitoral hypertrophy, which looks like a hypospadic or even normal penis, having sometimes a single meatus, urethral and vaginal, at the tip of the male genitalia. Usually, both the uterus and the tubes develop normally. The ovaries maintain for some time their functional potential and this explains the resumption of normal ovarian activity after appropriate therapy or, more rarely, spontaneously. The somatic aspect of patients varies according to virilization of external genitalia: from little or no virilisation in aspect, to a phenotype with masculine physique, that at puberty has short, muscular limbs, abundant hair apparatus, moustache and beard, no breast development, male fat distribution, low and husky voice. In cases of congenital adrenal hyperplasia deficit of 21-hydoxylase (genetic disease that can be suspected in a family where there have been previous cases and therefore also diagnosed prenatally[11]), administration of cortisone can be done even before birth, generally, with good results[12], it is necessary, only in very serious cases, to resort to surgery to remove the clitoral hypertrophy or other aspects of virilization of the external genitalia, allowing a satisfactory sex life and avoiding the difficulties of the structuring of sexual identity linked to virilization. Some

[10] J. Imperato-McGinley at al., *Androgens and the evolution of male gender identity among male pseudo-hermaphrodites with 5 a-reductase deficiency*, "New England Journal of Medicine", 1979, 300, pages 1233-1237.

[11] Otherwise, it can be diagnosed at birth with a blood test of the newborn child.

[12] M.G. Forest, H. Betuel, M.David, *Prenatal treatment in congenital adrenal hyperplasia due to 21-hydroxylase deficiency: up-date 88 of the French multicentric study* , "Endocr. Res." , 1989,15, pages 277-301;
J. Travitz, D. L. Matzger, *Antenatal treatment for classic 21-hydroxylase forms of congenital adrenal hyperplasia and the issues*, "Genet. Med.", 1999, 1, pages 224-230

untreated or inadequately treated individuals, usually assume male sexual identity and find a discrete psychological equilibrium; often resorting to surgery to accentuate the manly appearance of external genitalia.

A specific form of DSD is ovo-testicular DSD, in which the (non functional) structures of the ovary and testis coexist. External genitalia may be ambiguous or differentiated as male or, more often, as female; development of the internal genital tract is constantly ambisexual and the uterus or uterine rudiment is usually present: this explains the observation of menstruation, which, in subjects with male phenotype appeared as cyclical hematuria. Secondary sexual characters of the opposite sex in a predominantly male or female soma may be present. Sex drive is usually low or absent; and sexual identity can be ambiguous[13].

4. The problem of "assignment of sex": a brief excursus

The identification of DSD has undergone modification according to changes in the way of considering sexual differences, the development of knowledge and biomedical technologies.

Sex was traditionally considered primarily a physical anthropological reality aimed at procreation: somatic data constituted the basic criterion for sex determination. The only possible way of facing the problem was that of social and univocal normalization to one sex, the one prevailing biologically. Only in cases of absolute ambiguity (so-called "perfect hermaphrodites") was reference made to subjective perception[14]. In the sixteenth century, with the birth of biological science[15] more rigorous criteria for sexual identification were established in reference to the specific anatomy and physiology of male and female. For males the determining criterion was the presence of testes, and for females the detection of menstrual flow or the presence of the uterus[16].

From the second half of the nineteenth century, physiological discoveries in the definition of sexual characters, lead to recognition of the gonads as the determining factor in the true sex of a person. Therefore, sex could be attributed without delay to the majority of individuals with ambiguous genitalia, possessing male or female gonads; only in extremely rare cases of true hermaphrodites (with gonadal tissues of both sexes) was "uncertain sex" properly referred to and the prevalent sex then sought. In this way, nineteenth century medicine managed to remove the inconvenience of sexual ambiguity and assign with certainty one of the two sexes to each individual[17].

It was from the middle of the twentieth century that the criterion of genetic sex for sexual identification was introduced.

Today, in the light of recent developments in scientific knowledge and technologies, the framework of identification of DSD is highly composite. There is

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[13] There are few long term studies. Among these: C. Elliott, *Why can't we go on as three*? "Hastings Center Report", 1998, May-June, pages 36-39; F.M. Siliper, S.L. Drop, J.C. Molenaar et al., *Long-term psychological evaluation of intersex children*, "Arch. Sex. Behav.", 1998, 2 pages 125-144.

[14] Ulpiano (D. 1, 5, 10) introduces the criterion of prevalent sex, evaluated on the basis of bodily appearance.

[15] In addition to the canonical emphasis on medical report. For a systematic treatment of the issue in historical and theoretical terms in the context of canon law cf. P.A. d'Avack, *Cause di nullita' e di divorzio nel diritto matrimoniale canonico*, Florence 1952, page 91 ff.

[16] The role of the ovaries as agents of feminization was not understood let alone their ovum genetic function, and, in any case, they were not in the investigative possibilities of the medicine of that time: this explains the resorting to other indices of femininity.

[17] On this point: A. Dromurat Dreger, *Hermaphrodites and the medical invention of sex*, Harvard University Press, Cambridge 1998.

the realization that a person's sexuality is not reducible to a single aspect, however relevant: sexuality has physical components (somatic, anatomical and physiological, gonadal and genetic) and psychological. Therefore, the "assignment of sex" for registration of birth and sexual identification in cases of DSD must take into consideration: a) *somatic indices* (phenotypic and gonadal sex): the appearance of the genitals is a determinant for birth registration, the possibility of a satisfying sex life and the mental elaboration of sexual self-identification; *gonadal sex* is relevant to brain *imprinting* (or brain sexualisation), hormonal processing and fertility; b) *psychological indices*, meaning personal identity and social role[18].

5. The treatment of DSD: bioethical and juridical reflection

Generally, in clinical practice there are two different situations that require cogitation and differentiated choices: early diagnosis (at birth or in the earliest years of life) or late diagnosis (in an adolescent child, but also in an adult subject), often in examinations to verify the delay or irregularity of sexual maturation (in adolescence) or the causes of infertility (in adulthood). The medical treatment of DSD on minors has undergone changes throughout history[19]: if in the past children with this condition were not operated on, however since the 1950's medical practice has also begun to provide surgical intervention and has subsequently taken different directions.

5.1 In the 50's there was the spread of *the theories of J. Money* which had an impact in the development of the bioethical guidelines mentioned later in this opinion. Money affirms the irrelevance of genetic and gonadal sexual identity, in the belief that sexual identity (defined as "gender" to distinguish it from the bodily identity) derives from the psychic structure induced as a consequence by family education and socialization. In his opinion, the development of gender identity is a kind of "psychic imprinting" completed within two and a half years from birth and that can be changed later but with serious risks for psychological equilibrium[20]. Money's perspective marks a critical somatic step (or somatic prevalence) towards pragmatic criterion, that is, the criterion of sexual assignment by the physician on the basis of surgical feasibility: in cases of ambiguity, given the complexity of reconstruction of functional male genitalia, it was preferred to assign female sex to the subject, with a corresponding upbringing, regardless of consideration of the physical indices (but also of possible infertility or sexual satisfaction). Money's indication was therefore that of early assignment, in order to facilitate "oriented" *nurture*, even with intervention for demolition and reconstruction and possible hormonal therapy at pubertal age.

It should be mentioned that after World War II, the most discerning work in depth psychology - let us think to W.R. Bion or to D. Winnicot[21] - genuinely tried to

[18] A. Isidori, *L'etica degli stati intersessuali*, in A.A. VV., *Androgen insensitivity syndrome (CAIS/PAIS)*, study day, meeting of the College of Schools specialising in Endocrinology and Metabolic Diseases of Rome, Fatebenefratelli Foundation, Rome, 23rd May 2009.

[19] A.D. Dreger, *A history of intersexuality: from the age of gonads to the age of consent*, "J. Clin. Ethics", 1998, 9, pages 345-349.

[20] Cf. A.D. Dreger, *Ambiguous sex or ambivalent medicine? Ethical issues in the treatment of intersexuality*, "Hastings Center Report", 1998, May-June, pages 24-35.

[21] D. Winnicot, *Playing and Reality* preface by R.Gaddini, Armando, Rome 1974 and *Sulla natura umana* edited by R. Gaddini, Cortina, Milan 1990; W.R.Bion, *The Italian Seminars*, Borla 1985 and *Attention and interpretation* Tavistok Publications, London 1970.

understand the influence of the unconscious and cultural formation, without any denial of the genetic component in the construction of sexual identity. The model supported by Money was criticised [22] regarding the malleability of gender identity. Clinical and scientific evidence have challenged the model of absolute gender malleability. At the clinical level[23], the serious distress experienced by some of the cases treated (feminized males asked to be re-masculinized) has highlighted the problematic nature of sex assignment based on the adopted criteria[24]. At the scientific level, the discovery of the importance of prenatal exposure to sex hormones not only for hypothalamic imprinting, but also for the psychic identification of the child show how not only external psychic factors (family, social and cultural) are determinants, but also biological factors play a role in the defining of body image. These findings show the problematicity of a sex assignment (resulting in surgical alteration of the body) be it consequence of an external decision, based on the medical criteria of surgical practicality[25] or on the subjective preference on the part of the parents[26]. It therefore becomes apparent that there is the need to identify sexuality in a complex interaction between the somatic and psychic dimensions uniquely irreducible solely to the cultural-social factor (socio-cultural and environmental determinism).

However, Money's model has been taken up and valued as regards consideration of the need, following the diagnosis of DSD, of an early assignment, therefore rapid surgical intervention for medical and psycho-social reasons. This line is supported on the basis of the following considerations: a) living with sexual ambiguity involves psychic trauma, which renders individuals incapable of acquiring a harmonious sexual identity; b) living with sexual ambiguity implicates difficulty in acceptance on the part of parents and society. On the basis of prolonged psycho-pedagogical experience, Money's observation on the need for timely intervention in the assignment of sex, for

[22] Included in the criticism is the possible damage from surgical practice (loss of reproductive ability, infections, pain, distress, incontinence); the possible strengthening of the social perception of "sexual abnormality"; asymmetry in the treatment of male and female (the choice of assignment as male was measured on the basis of the possibility to have sexual satisfaction; the choice of assignment as female on the basis of the capability to copulate). K. Kipnis, M. Diamond, *Pediatric ethics and the surgical assignment of sex*, "The Journal of Clinical Ethics", 1998, 9, 4, pages 398-410; H.G. Beh, M. Diamond, *An emerging ethical and medical dilemma: should physicians perform sex assignment surgery on infants with ambiguous genitalia?*, "Mich. J. Gender Law", 2000,, pages 7-38.

[23] Reiner reported a study of 27 children: 25 males who were raised as females, 14 declared themselves to be male. W. Reiner, *To be male or female: that is the question*, "Arch. Pediatr. Adolescent Med", 1997, 151, p. 224; Id, *Case study: sex reassignment in a teenage girl*, "J. Am .Acad. Child. Adolesc. Psychiatry", 1992, 35 (6), pages 799-803; Id. *Sex assignment in the neonate with intersex or inadequate genitalia*, "Am. J. Dis. Child", 1990, pages 1044; Id, *Androgen exposure in utero and the development of male gender identity in genetic males reassigned at birth*, Presented at international Behavioural Development Symposium 2000, May 25-27, 2000; Id., *Gender identity: study questions `sex reassignment`*, "Health Med", May 16, 2000, A17.

[24] The case is well-known of two male twins, one of whom, John at 18 months of life, remained without genitals after a surgical accident. Money decided to feminize him (Joan) and suggested to the parents to bring the child up as a girl. But Joan always showed signs of distress; and at the age of 13 on discovery of the truth decided to resume male sex , and underwent multiple operations to eliminate the signs of feminisation. The alteration of psychic equilibrium brought him to commit suicide at the age of 38. Money publicised the case as empirical proof of his theory. In truth, it must be stated that the child was brought up as male up to 18 months of age, and was feminised only at a year and a half: therefore the distress would seem to confirm not so much the theory of malleability of gender, but rather the theory of the relevance of educational pressure early on in sexual identification. Cf. J. Colapinto, *As nature made him. The boy who was raised as a girl*, New York 2001. A critical review of the theory of Money is S.J. Kessler, *Lessons from the intersexed*, New Brunswick (NJ) 1998. There are other cases reported in literature cf. S.J. Bradly, G.D. Oliver, A.B. Chemick, K.J. Zucker, *Experiment of nurture: ablation penis at two months, sex reassignment at 7 months, and a psychosexual follow-up in young adulthood*, "Pediatrics", 1998, 102 (1), p.9

[25] M.L. Di Pietro, *Aspetti clinici, bioetici e medico-legali della gestione delle ambiguita' sessuali*, "Medicina e Morale", 2000, 50, pages 51-83; B. Dallapiccola, *Genetica della determinazione sessuale*, "I quaderni di Scienza e Vita", 2007 , 2, p. 11 and ff.

[26] Cf. K. Kipnis, M. Diamond, *Pediatrics, ethics and the surgical assignment of sex* cited.

a clear education right from the start (or as soon as possible). This line of thought pays special attention to the methods of communication, considering essential that the truth be learnt from the parents and children themselves, in a non-traumatic manner, and therefore with due caution[27].

5.2 The *guidelines* developed by *M. Diamond and H. K. Sigmundson* (1997)[28] distance themselves from Money and are presented as innovative. These guidelines seek to harmonise sexual identity with adult sex life and fertility, in an attempt to direct therapeutic treatment and education taking into account several factors in the choosing of sex: the dominant phenotype, karyotype, possible fertility, sexual functionality, the hormonal influence in the sexualisation of the brain (above all in males), considering it a criteria that has a substantial effect on the predictability of sexual identity. Careful diagnostic evaluation is recommended before and immediately after birth by pediatric endocrinologists, radiologists, and urologists to avoid delayed diagnosis; it is recommended that the choice of sex should be based on diagnosis, and not on the basis of sexual functionality or external appearance. The need for continuous family support (as for the individual) is indicated to ensure adequate and fair information calibrated to the capacity of comprehension[29], allowing for approval of the choice to focus on the medical treatment objectively believed to be the most appropriate regardless of the desire for social "normalization" and the encouraging of acceptance; confidentiality as regards the family and respect of the patient's body are recommended. Invasive treatments are not recommended for aesthetic reasons (to acquire normal appearance) but only for therapeutic. In rare and extreme cases where diagnosis is not possible and prediction uncertain, postponement of surgery is recommended, the choice of a name that can be used for males and females and an education which leaves room for spontaneous inclinations and free male or female expression, without forcing, until it is the actual individual (having reached sufficient cognitive and emotional awareness and maturity) who is involved in the decision concerning such delicate and crucial elements as personal identification as well as health. There is also the possibility that individuals may refuse surgery and accept their condition of coexistence of organic discrepancies between various sex components.

5.3 *The guidelines of the Intersex Society of North America* (2006)[30] reaffirm the necessity of diagnostic criteria in sexual ambiguity and the importance along with somatic and functional indices also of identification of the genetic and endocrine factors in the prenatal stage[31]; they consider medical and surgical intervention a duty only when faced with a real, present and imminent threat to the individual's physical

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[27] American Academy of Pediatrics Policy Statement, *Timing of elective surgery on the genitalia of male children with particular reference to risks, benefits, and psychological effects of surgery and anaesthesia*, 1996, 97, pages 590-594.

[28] M. Diamond, H.K. Sigmundson, *Management of intersexuality. Guidelines for dealing with persons with ambiguous genitalia*, "Archives of Pediatrics and Adolescent Medicine", 1997, 151, pages 1046-1050. Cf. of the same authors *Sex reassignment at birth: long-term review and clinical implications*, "Archives of Pediatrics and Adolescent Medicine", 1997, 151, page 298.

[29] The guidelines insist on the need to avoid stigmatizing terms (such as: "abnormality") in favour of a kindlier expression (e.g. "rarity").

[30] Intersex Society of North America (ISNA), *Clinical guidelines for the management of disorders for sex development in childhood*, Consortium on the Management of Disorders of sex development, 2006.

[31] W.G. Reiner, *Assignment of sex in neonates with ambiguous genitalia*, "Current Opinion in Pediatrics", 1999, 11, pages 363-365. Cf. also S. Kessler, *Lessons from the intersex*, cited; S. Creighton, C. Minton, *Post vaginal surgery in childhood should be deferred*, "Br. Med. J", 2001, 323 pages 1264-1265.

integrity and in the case of sure empirical indices or predictors, not forcing the patient to a social "normalization" (only in order to gratify the wishes of parents) that could cause damage (the emphasis on "normalization" induces a sense of guilt and shame in parents and a sense of rejection as regards the child). These guidelines recommend, in cases presenting no medical urgency, or objective elements to determine a decision, to delay surgery and postpone hormonal therapy to enable the individual to actively participate in the decision (wherever this may be possible, given the age of the individual), both in relation to the individual's perception of sexual identity, and to the balancing of the risks and benefits of intervening. In this sense the guidelines focusing on the "well-being of the patient" recommend the promotion of a welcoming approach towards the subject and the family who must be told the truth, avoiding every form of stigmatization (making use of appropriate, not objectifying terminology and avoiding photographs or an attitude of "curiosity"), ensuring adequate psychosocial support, through the formation of multidisciplinary teams able to deal with such cases, (consisting of paediatric endocrinologists, gynaecologists, urologists, geneticists, psychologists and psychiatrists, social workers and nurses). According to this perspective, it is not the surgical modification of the child (to conform to normal parameters) that can alleviate the anxiety of parents or favour social acceptance, but rather appropriate support and psychological and educational counselling, whatever the choice (male, female or - in extreme and rare cases – the preserving of the condition of ambiguity).

5.4 *The Consensus Statement on Management of Intersex Disorders* (2006)[32], while not completely abandoning the line inspired by Money, takes account of the non-malleability of sexual identity and the role of sexualization of the brain, and proposes the following indications: care when using nomenclature, to ensure scientific precision, comprehensibility by the subject (so as to find sufficient cognitive and emotional awareness) and the family, so avoiding confusion and stigma; the importance of a careful evaluation of the newborn in the diagnosis and pathogenesis (with reference to genetic data, to genital appearance for self-identification of the body, to the possibility of surgery, the maintenance of fertility and family views, as well as cultural circumstances); the formation of a multidisciplinary team able to address the situation. Early sex assignment is appropriate on the basis of a careful diagnostic evaluation that takes account of objective indicators, considering that each person should be assigned a sex in order to avoid the possible damage of an ambiguous education.

5.5 Along with these bioethical lines, it is important in bio-juridical terms to recall[33] the *decision of the Constitutional Court of Colombia* (1999)[34]. The constitutional ruling recognizes that parents can give consent to treatment as long as it is guaranteed

[32] P.A. Lee, C.P. Houk, Faisal Ahmed, A. Hughes, *Consensus statement on management of intersex disorders*, "Pediatrics", 2006, pages 488-500: document drawn up in the sphere of the International consensus Conference on Intersex , organised by Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology.

[33] As well as the guidelines, it should be noted that the Consensus Conference on Intersex states (Chicago, 2005) and the International Meeting on Anomalies of Sex Differentiation (Rome, 2006) have drawn attention to the medical and legal problems, with particular reference to cases of professional negligence or consent, situations for now of little relevance in Italy and not under discussion in this Opinion. On the subject see R. Cecchi, G, Marrocco, *Stati Intersessuali e questioni medico-legali*, "Rivista Italiana di Medicina Legale", 2009, 1, page 101 ff; J. Greenberg, *Legal aspects of gender assignment,* "The Endocrinologist", 2003, 13,3, page.279.

[34] Sentencia SU-337/99, May 12th 1999, and T.551/00, Aug. 2nd 1999. Cf. also sentencia T-477/95 (www. isna.org/Colombia).

to be based only on the interests of the child and not on their own self-interest. To ensure this, it is necessary that informed consent is "qualified, clear, explicit and based on full recognition of the consequences of the treatment and alternative treatments" (with reference also to the possible postponement of intervention) and that it is "persistent" (in other words, repeated over time) to guarantee the interests of the child (with appropriate psychological support)[35]. Only medical intervention that is necessary can be carried out, namely, those interventions justified on the grounds of protection of the physical integrity and health of the child, also as regards the physical pain resulting from the burden of the operation and the associated risks: no operation can be carried out only for psychosocial reasons (emotional non-acceptance by parents of undefined sex; the parents' need for biological normalisation for social acceptance). For intervention for which there is no data on the benefits or the potential danger for the child (both physical and psychological) or that is irreversible, the consent of the actual subject is required (when informed consent must be gradual and based on the maturity of the child)[36]. It is on this basis, therefore, that the constitutional ruling limits the capacity of physicians and parents to intervene surgically altering children with such pathologies, considering parental consent invalid if not motivated by the best interests of the child[37].

6. The bioethical recommendations of the NBC

6.1 The NBC underlines the delicate bioethical nature of the decisions in cases of sexual ambiguity in minors; there is at stake the issue of the basis of sexual differentiation and the structuring of sexual identity, as an essential element of the personal, individual and relational identity of each subject. The Committee believes it is important to give adequate consideration to each choice in this unusual situation, evaluating case by case, depending on "recognition" of sexual identity within the sphere of a global consideration of the subject, balancing in a dynamic synthesis the biological data (in the case of neonates) and the biological and psychological aspects (in the case of minors with a sufficient level of awareness), aimed at *harmonizing elements of disharmony*. The conception of sexuality as a structuring reality of a person within his/her uni-totality, the way of existing, of relating, of being in the world, prevents the use of *solely* physical and biological criterion, as well as it prevents from showing no regard for body size on sex in order to favour exclusively psychological components.

Harmonization derives from interaction between the biological and socio-cultural dimensions (as opposed to biological determinism on the one hand and socio-cultural determinism on the other), recognizing the importance of the biological component, but also external factors (psychological and environmental) - present during the stages of development of the minor that allow the achievement and expression of a sufficient level of awareness - , even without knowing to `what extent` and `how` they interact, from the well-established evidence that they do interact. Sexuality is not "neutral" at

[35] See also A.D. Dreger (ed.) *Intersex in the age of ethics*. Frederick (MD) 1999; S.E. Sytsma (ed.), *Ethics and Intersex*, Springer, New York 2006 (*International Library of Ethics, Law and the New Medicine*, vol.29); Intersex Society of North America (ISMA); S.E. Preves, *Intersex and Identity: the contested self*, Rutgers University Press, South Brunswick NJ 2003.

[36] The court bases itself on the studies of: A.D. Dreger, cited; J. Schober, M. Diamond; G.L. Warne, *Advances and challenges with intersex disorders*, "Reproduction, Fertility and Development", 1998, 10 (1), pages 79-86.

[37] The first sentence considered not valid the informed consent of the parents for intervention on a two year old child because deeming it as not "qualified and persistent"; and in the second case of an eight year old child because already mature enough to decide

birth even if the boy or girl is at the start of the journey towards sexual identification: there are biological elements (genetic, gonadal, hormonal, and phenotypical) which are interwoven with environmental factors (social and family such as the parents' representation of the sexual identity of their son/daughter).

6.2 The NBC believes that the necessary steps must be taken to provide *accurate and early medical diagnosis* (if possible in the prenatal stage, otherwise during the immediate post-natal stage), of DSD through genetic testing, hormonal blood tests, attention to phenotypical characteristics. Early diagnosis should be accompanied by study of the causes of DSD in order to avoid them, where possible. It is recommended that physicians, harbouring diagnostic doubts at the moment of a birth, should clearly note these down in descriptive form in the medical records. In addition, physicians should be appropriately trained; in the meantime reference health facilities should be adapted, so as to prevent technical incompetence from being responsible for DSD.

In cases of prenatal diagnosis it is essential to implement all available and possible therapeutic interventions. In cases of early postnatal diagnosis, the NBC believes that the decision, of the physician together with the parents, to intervene or not to intervene (surgically and/or with hormonal therapy) should be guided – in the exclusive best interests of the child – by objective criteria (emerging from comprehensive diagnostic tests) without neglecting, when possible, extrinsic criteria (technical facility). Furthermore, the established importance of hormonal factors in the sexualisation of the brain as predictive elements of sexual identification is to be taken into account. The choice to intervene or not to intervene must be guided by the following criteria: therapeutic criteria and medical emergency, gradualness, the predictability of benefits and harm minimization (in the physical and mental sense) with a view to achieve, within a situation of organic pathology, the greatest possible harmony. Particularly those interventions that are irreversible or difficult to be reversed must have objective medical justification. The planning of medical and surgical interventions on the body, must have as an objective not only alteration of the somatic structure for "biological normalisation", but also help the person to set the conditions to achieve, in the best possible way, self realization in physical and psychological harmony. These interventions are not only licit, but also a duty if they represent the only reasonable and possible path in order to ensure - as far as possible – that the person has the future conditions to reach harmonic identification, inclusive of the practice of future sexual activity. The presence of discordant sexual elements, if they do not conform to the plan of being male or female, makes their removal licit as they present a hindrance to realization, at least partially, of this harmony. There should be careful consideration of a balance between somatic indices (phenotypic sex or bodily appearance and gonadal sex in relation to fertility and to brain imprinting) and psychological indices (expected or present).

6.3 The NBC believes that such interventions necessarily require *informed consent*, arising from appropriate consultancy that provides comprehensive information to parents (respecting their emotionality) and to the minor (if able to receive it). In particular, when the interventions involve demolition and are irreversible (or reversible with great reconstruction of the body)[38].

[38] In the case of disagreement between the parents, Italian law provides the possibility of recourse to a tutelary judge who will attribute the right to chose to the parent believed to be most capable of deciding for the good of the child.

It is important within the sphere of consultancy that attention is given to definitions and nomenclature, and that unknown aspects (unknown to the parents or the actual subject, if in possession of sufficient awareness) are not revealed in a brutal manner so as to respect the complexity of the problem both in scientific and existential terms. The choice of the physician must be shared by the parents (responsible for later raising the child) and – as much as possible- by the minor itself, whose interests must be placed at the centre of ethical consideration.

The Convention on Human Rights and Biomedicine[39] (1997) takes into account along with age and maturity, the minor's will. Even if formally the expression of will is for the parents, who have legal responsibility, the substantial consent of the minor – who is the central subject of therapeutic relationship – is to be sought and supported in the context of the complex relational dynamics, involving not only the parents but also the physician.

If the parents' choice, for some reason, did not meet clinical and diagnostic needs, or should they ask for intervention deemed "impossible", the parents' will could not be carried out because not in line with the "best interests" of the minor: it is the physician's undoubtedly delicate duty to make the parents understand the motives behind choices highlighting the biomedical and psycho-social aspects.

6.4 The NBC believes that in some *exceptionally difficult cases* (i.e. in cases in which there is no objective data for the assignment of sex[40]), it may not be appropriate to proceed immediately to demolition and/or reconstructive surgery because this may not be compatible with the actual evolution of sexual identity. It is not always easy to explain the situation to parents and, above all, justify possible delays in the surgical definition of physical sex. However, surgical definition can not be dictated by "haste" in rectification of sex for individual preferences or social expectations. It is the physician's duty in advising parents to make them understand that in some extreme cases *watchful waiting* may be necessary (as dictated by the difficulty to establish a priori the degree of sexualisation of the brain and to predict the probability of acceptance of sex by the minor).

In cases of postponed intervention, the minor should also be gradually involved in the decision – according to the gaining of sufficient awareness – because, especially in the most difficult cases, the choice of the physician and parents may conflict with the sexual identity that is structuring. In these exceptional cases of genital ambiguity (when at birth objective data are not sufficient) the problem arises, for the parents, regarding the choice of upbringing. The NBC deems appropriate that it should be oriented towards male or female, with great attention to observation and spontaneous inclinations and to the gradual emergence of sexual awareness in the minor.

The NBC, faced with such complexity and problematicity, believes it is important that the decision regarding sex assignment should be shared by both parents and physicians and properly supported in psychological terms. Furthermore, it is also believed necessary that – when possible - the child should be heard and accompanied by adequate psychological support until post-pubertal time.

In cases where the subject has already developed a congruent sexual identity with the phenotypic sex that is the opposite of the genetic and gonadal sex and does not

[39] *The Convention for the Protection of Human Rights and the Dignity of the Human Being with regard to the application of Biology and Medicine: Convention on Human Rights and Biomedicine* (Oviedo 4th April 1997): art. 6 c.2 "The opinion of the minor shall be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity".

[40] For example, the rare cases of ovotesticular DSDs described above

manifest the desire for sex correction, the information regarding the situation directed at the patient must be given with great caution as it could be destabilizing for mental balance[41]. However, the truth must be told: a lie could only ruin the relationship of trust between the family and physician and could lead to the conviction of being affected by such a "repulsive" pathology even to avoid talk of it.

6.5 It is right to reflect, particularly on cases of genital ambiguity in which at birth objective data are not sufficient to attribute sex and on consequent legal formalization – in the short time as provided by Italian Law – of the declaration of birth[42]. This involves cases in which there is a high possibility that the decisions taken may not reflect the dynamics of the psychological and physical development of the child and that may justify a subsequent request for change of sex at the registry office.

In the context of the bio-juridical debate the proposal was made to record at the registry office those children with uncertain attribution of sex *as such*, therefore avoiding their being registered as male or female[43]. This hypothesis is unacceptable on the basis of certain arguments: firstly it would legally institutionalize, surreptitiously and not clearly, registration of a *tertium genus*, not legally recognised in our regulatory system and this would cause serious changes in its systemic balance; secondly this would give rise to, even if against all good intentions, real legal stigmatization of the person, with unpredictable psychological and social consequences, but undoubtedly highly risky; furthermore it is – regarding these disorders, anomalies and pathologies – a hypothesis just the opposite of specific sexual identity, that expresses a condition of uncertainty in assignment of sex and it makes no sense to build a third identity on uncertainty.

The NBC deems appropriate that the legislature should provide (compatibly with the principle of non-availability of civil status), at the time of official birth registration of the newborn as male or female, the possibility that the registrar records "an annotation", based on rigorous and comprehensive medial certification, not of uncertain attribution of the sex of the newborn, but of the *pathology* itself. Such an annotation, confidential and strictly respectful of the privacy of the minor, could enable the competent magistrate, should a better and different clinical evaluation of the case be reached, to authorise upon request by the person concerned, a correction of the registry indication (due to incorrect attribution at birth), following more simplified procedures compared to those required by the law now in force[44].

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[41] E. G. Howe, *Intersexuality: What should care providers do now*, "J. Clin. Ethics", 1998, 9, 4, pages 334-337.

[42] In Italy the D.P.R. 3rd November 2000 number 396 (art. 30) requires that the *declaration of birth* is made within 3 days after birth in the Directorate of Health of the hospital or nursing home where the birth took place or within 10 days at the Registry Office of the city where the child was born or the parents' town of residence. In the declaration explicit indication is also required regarding the sex of the child (art. 29) and the name of the child must match the sex (art. 35). If the declaration is made after more than 10 days from birth (late declaration, art. 31), this is admissible by the registrar only if the declarant specifically indicates the "reasons for the delay". The declarant must give reasons for the delay and this delay is reported to the Public Prosecutor. In cases of non declaration or late declaration without specifying the "reasons for delay", the registrar reports to the Public Prosecutor to promote "rectification proceedings" (art.32).

[43] J. Butler, *Undoing gender*, Routledge, New York 2004.

[44] For the cases of DSD described above correction at the registry office is more appropriate than rectification of sex, regulated by the Italian Law of 14th April 1982, number 164, *Rules concerning rectification of sexual attribution*. This law does not explicitly distinguish cases of transsexualism and cases of DSD. In cases of DSD where it is difficult to assign sex with certainty at birth, and to which a male or female sexual identity is assigned nevertheless, it is essential to check over time the development of physical and psychological sexual identity (that can be congruous to that declared or may be opposed to what was declared at registration). The law demands the determining of phenotypic sex and congruency between phenotypic sex and the registered and social sex: in cases of DSD phenotypic sex can be defined during growth and may not need surgical treatment, if not for aesthetic or functional improvements. It is for this reason that it is appropriate, specifically in the case of DSD, to refer to registry correction (in cases of mis-assignment at birth), rather than the rectification of sex.

7. Conclusions

Following on from this clinical, ethical and juridical reflection, the NBC recommends:

1. that where diagnosis is possible on the basis of objective and updated medical and clinical parameters, it must be recognized that it is the preeminent best interest of the child to be raised (in keeping with the diagnosis received) as a male or female;

2. that in cases of absolute genital ambiguity (where objective data are missing at birth), it is appropriate that the assignment of sex be agreed by parents and physicians and a consequent male or female education, along with the necessary psychological support and particular attention to the possible emergence of a sexual identity different from the one initially assigned;

3. that any possible surgical intervention will not cause unnecessary mutilation of the child, and as much as possible, not involve the loss of fertility potential and the conditions for possible satisfactory sexual activity; that thorough evaluation of the whole clinical situation is ensured by physicians, taking into account, but not bound by, the environmental, social and cultural factors;

4. that in the case of deferral of possible surgical intervention, waiting until the person is capable of expressing consent, adequate psychological support in the structuring of sexual identity will be given to the minor;

5. that when, in the context of ambiguity of sexual development, a discrepancy should arise between the assigned sex and the development of sexual identity, – after the required medical examinations and provision of necessary psychological support - the change of sex at the registry office shall be facilitated legislatively;

6. that research in this field will be encouraged (for the furthering of knowledge into the causes of these pathologies and the therapeutic possibilities); that diagnosis of these pathologies will be carried out with scientific expertise and the provision of any possible therapeutic intervention, when necessary;

7. that seeing the importance of early diagnosis and treatment for the health of the minor, that observance of the principle of equity will be ensured in the accessing of the most advanced diagnostic methods and equipment, working to also overcome the qualitative differences between health facilities in the country;

8. that there will be special attention given to counselling and informed consent as regards the parents and the minor (if possible); - for this purpose – promotion of the training of health personnel able to, in addition to their scientific and technical competence, also focus specifically on the psychological dimension of the patient and the family;

9. that long-term studies will be encouraged with particular reference to complex clinical cases in order to identify additional elements that may give a contribution to the difficult decisions in this field.