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OPINION

Where medicine meets the boundaries of manhood and womanhood

Louis Gooren

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We are defined by sexual dimorphism. Male and female, the sexes we are (and are perceived to be), affect how we feel, how we behave and how we interact with others. We look around and see all complex creatures, including ourselves, as either male or female. This is so much a part of our daily existence that it reinforces the idea of manhood and womanhood as expressions of a natural order. We regard this division into two sexes as one of the great eternal verities and tend to experience the difference between the sexes as rather absolute. Subjectively, man and woman are seen as opposites, poles apart and mutually exclusive forms of human existence.

In daily medical practice, this duality of the sexes also tends to be regarded as axiomatic. The biological determinants of male and female somatic sexual differentiation have been elucidated and these insights have contributed substantially to the definition and diagnosis of errors of sexual differentiation. As a result, when such errors are encountered, treatments can often be provided to enable subjects to lead more conformable lives as men and women. In some exceptional cases, however, normal medical practice is unable to offer solace to subjects whose manhood or womanhood is troubled.

This contribution looks at some of these unusual conditions. It addresses the sex assignment of newborns afflicted with sexual differentiation errors as well as the phenomenon of transsexualism. Both conditions have their biological aspects, but both also have ramifications into the psychosexual and psychosocial aspects of manhood and womanhood. Both demonstrate that in the practice of medicine, the concepts of manhood and womanhood may extend beyond the confines of traditional biomedical thinking.

VU University Medical Center, Amsterdam 1081HV, The Netherlands
Correspondence: Professor L Gooren (louisjgooren@gmail.com) Current address: 72/1 moo1, T.Palan, A.Doisaket, Chiang Mai 50220, Thailand
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BOYS AND GIRLS, MEN AND WOMEN

Since time immemorial, parents have assigned their newborns to the sex indicated by the morphology of the external genitalia. This empirically based practice seems reasonable enough as it has withstood the test of time; babies that appear to be boys or girls at birth generally do grow up to become normally functioning adult men and women. This means that no major intentional (pedagogic) effort is required to mould baby boys into men and baby girls into women. Manhood and womanhood seem to be intrinsic, biologically determined properties of boys and girls requiring only completion by the hormones of puberty to fully express sexual differentiation and bring about the erotosexual interaction between the two sexes. As the latter is essential for species survival, this would seem to be an inherent, biologically ordained property of all living organisms that depend on sexual reproduction.

The perception of manhood and womanhood as being complementary and this being necessarily so for the survival of the species, has led to the belief that the full spectrum of masculinity and femininity is the product of biological determinism. The strong parallels with the animal kingdom have reinforced this belief. In the biological sciences, the sexual interaction between the sexes is teleologically equated with reproduction. Carnal desire and pleasure are viewed as an embellishment of the incentive to procreate, and not as goals in themselves. The equation of sexuality with procreation has reinforced the idea that man and woman are mutually exclusive but interdependent poles, each presupposing the other and neither existing on its own.

INTERSEXED STATES

It has been part of the human experience that some babies at birth will present ambiguities of the genitalia. The homespun wisdom of medically unsophisticated people would usually guide them to assign the baby to the sex it most closely resembled in external genital appearance on the assumption that nature's 'intentions' were thus best heeded. After all, this is merely an extension of the existing common practice which assumes that the present and future masculinity and femininity can be inferred from a (casual) inspection of the external genitalia.

As is often the case, this commonsense approach is in fact sensible. As the research of Professor John Money from 1950 on has clearly demonstrated, in children with ambiguous genitalia, the sex that a child is assigned and reared in is a significant factor in future self-awareness of being male or female,[1] though other factors, mainly prenatal exposure to androgens, should not be dismissed.

Trying to 'read nature's intentions' in regard to the sex of the newborn took a different turn and gained scientific momentum when the biological principles governing the development of male and female gonads and genitalia were gradually elucidated starting from the middle of the 19th century. The microscopic examination of the gonad and its classification as ovary or testis was the basis of Klebs's classification of hermaphroditism from 1876.[2] Klebs recognized true hermaphrodites as possessing both ovarian and testicular tissue. This was in contrast to pseudohermaphrodites, who possessed either an ovary with genitalia that appeared male, or a testis with female-like genitalia. Klebs and his contemporaries assumed that the gonadal tissue would determine the 'true' core sex, including sexual outlook and sexual desires, even in those cases where the actual genital status and later self-awareness of being man or woman, was at odds with the nature of the

gonad. Klebs's classification gained the power of a medical doctrine: the nature of the gonad, ovary or testis, was the ultimate criterion of masculinity or femininity and consequently the nature of the gonad was also the divining rod for sex assignment of intersexed subjects.

It was assumed that other characteristics of sex, such as self-awareness of being man or woman and sexual attraction to the opposite sex, would submit to the authentication of the criterion of the gonadal sex. This reasoning has subsequently been abandoned. Now most experts would agree that biological characteristics (such as chromosomal pattern, nature of the gonad, and so on) are not sufficient to provide reliable indicators for determining a person's 'true' sex status as a man or woman.[3–7] Though relevant, they presently do not fully govern the decision to assign a particular sex to a newborn with ambiguous genitalia. A widely adopted policy is to arrive at a prognosis on the 'optimal sex' for the newborn, the elements of which are an overall sex-appropriate appearance with stable gender identity, good sexual function (preferably combined with reproductive function if attainable), minimal medical/surgical procedures, and a reasonably fulfilling life hampered as little as possible by the condition.[4–8] The extensive experience with this policy has vindicated the view that self-awareness of being man or woman is not exclusively dependant on biological determinants of sex alone (chromosomes, gonads, genitalia and hormones). While these are not irrelevant, other factors, still largely unidentified, also play a significant role. And of course sex assignment and the consequent rearing of the child as a member of that sex is certainly very significant.

TRANSSEXUALISM/THE SUBJECTIVE EXPERIENCE

In order to understand the phenomenon of transsexualism, it is useful to introduce some technical terms. For example, gender identity is a person's inner sense of being male or female. This develops in early childhood and is strengthened by the hormonal changes of puberty. For most people, such a term has little relevance as the male or female bodies they possess never leave them in any doubt about whether they are men or women.

Transsexuals are another matter. While they are lucidly aware of the physical reality of their bodies, this conflicts with their inner sense of being male or female, and is a source of great distress in their lives. Transsexualism can be best defined as an extreme form of gender dysphoria, which is a discrepancy between gender identity/role on the one hand and the actual physical characteristics of the body on the other. In transsexualism, the gender identity/role of the one sex coexists with the primary and secondary characteristics of the other sex in one and the same person. To the non-transsexual, this problem is so alien and unimaginable that it is difficult to sympathize with the transsexual's predicament.

With most types of suffering, such as the loss by death of a loved one, we can identify with the feelings of those we are close to, and share in their grief. To understand and sympathize with transsexuals is, in the first instance, more of a cerebral act, though one cannot escape the awareness that their plight is genuine and heart-felt. Male readers may be able to get some sense of the transsexual's dilemma by imagining how they would feel if they suddenly developed prominent breasts. This is not entirely theoretical; it is the medical condition known as gynaecomastia. The female equivalent would be experiencing a marked deepening of the voice and the development of male pattern beard and body hair growth. This is also a real condition that is not all that rare. Though these conditions are usually medically insignificant, the subjective experience of them can be a painfully humiliating diminution of one's manhood or womanhood. Transsexuals live permanently in this state of feeling betrayed by their physical selves. They feel trapped in their bodies: 'I felt my body was a prison cell. There were no windows. I could not breathe; I could not get out, I did not have the key'.

Medical evaluation of transsexuals reveals no objective signs of intersexuality that can be detected with existing techniques of assessing biological parameters of sex. Therefore, in traditional medical practice, a transsexual will be advised to undergo psychotherapy in an attempt to adjust the body concept (which is perceived as a mental function) to concur with the actual physical reality of the body. On the face of it, this might seem a reasonable approach, but the transsexual will view such advice as improper and even insulting since it is totally at odds with his or her own perception. To the transsexual, the problem is not in the mind, but in the body.

Transsexualism/transgenderism/homosexuality

Transsexualism must be distinguished from homosexuality. In erotic and sexual imagery and/or practice, homosexuals are attracted to persons with the same genital morphology. Like heterosexuals, a homosexual's sexual pleasure comes from the physical functioning of his or her sexual organs. The only difference is that sexual gratification can only be obtained in encounters with a person with the same apparent sex. By contrast, transsexuals experience the physical functioning of their sex organs as estranged from their selves. They seek physical reassignment, to the fullest extent possible, to the sex they feel themselves to be.

In recent times, an increasing number of people have been presenting themselves who only want to rid themselves of the characteristics of the natal sex without seeking further sex reassignment, or who want only partial adaptation to the opposite sex ('the lady with the penis'). They seek to have an in-between sex status. There may be a social transition to the opposite sex, but sometimes only on a part-time basis. For this category, the term 'transgenderism' has been proposed. There are difficulties with transgenderism from a medical ethical viewpoint. Should a subject's self-assessment of gender status prevail and does medicine have an ethical obligation to provide care for those who seem to genuinely find themselves in an in-between gender status through no choice of their own, and to assist them to live in peace with that gender status?

Prevalence

Calculations of prevalence data are likely to be influenced by the prevailing social climate and provisions for medical treatment. Another factor is definition of the condition; prevalence/incidence studies sometimes make no clear distinction between transsexuals and other subjects with transgenderism. The prevalence of transsexualism as assessed in The Netherlands and based on numbers of people seeking sex reassignment, is 1 : 11 900 men and 1 : 30 400 women.[9] These figures are very stable. They are somewhat lower than those of Singapore but higher than those in Sweden. Incidence data in Sweden and The Netherlands show a very constant pattern over time. Recent data from Japan indicate a prevalence of 1 : 25 000 men and 1 : 11 000 women.[10] Larger countries like the United States are harder to gauge. Figures are usually determined from the numbers attending clinical programs, but some may turn elsewhere and the bigger the country is, the less precise the calculation. Nevertheless, increasing numbers of people with 'gender identity disorder' are seeking help in North America.

The 3 : 1 ratio of males/females encountered in the Western world is not universal.[9] For instance, in Serbia, the ratio is close to

1 : 1,[11] and in Japan 1 : 2.[10] There is no good explanation for this sex difference, neither for the geographical variation.

Parts of Asia have, traditionally, demonstrated a tolerant attitude towards people who express gender nonconformity.[12–14] This may be related to the fact that their cultures do not view transsexualism as an expression of moral depravity but rather as an expression of the diverseness of nature, including human nature. It has been hypothesized that in cultures with a rigorous definition of manhood and womanhood, men who fail to fulfill the exigencies of manhood would resort to a transsexual state, but in the author's experience, this is not the case.

Transsexualism in the medical discourse

Transsexualism has always met with a great deal of scepticism and equivocation in medicine. Its diagnosis and particularly hormonal and surgical treatment are unorthodoxies in medical conduct. The transsexual's complaint that the sexual differentiation of his or her body is a source of unease strikes both layman and physician with disbelief; it is not something one can immediately sympathize with. The wish to 'tamper' with the sexual integrity of a correctly functioning body must seem abhorrent to the outsider. Further, if the transsexual succeeds in conveying the message that life is miserable and not worth living unless 'the body is adapted to the mind', how certain can it be that this conviction will never change? In other words: will irreversible medical interventions be regretted later in life in the course of the ongoing process of evaluating things differently as one grows older and wiser?

For the medical profession, the treatment of transsexualism represents a major departure from its traditional mode of operation. Normally, a subjective complaint of a patient is verified by physical examination complemented nowadays by the objectivity of diagnostic technology. If the outcome of the investigations is in concordance with the subjective complaint of the patient, a medical intervention is undertaken. But if that is not the case, the patient is reassured or may be advised to seek psychological help. With the present state of the art up to 2004, transsexualism presently has no (patho)biological substrate which would permit its verification in clinical practice according to the above diagnostic strategy. Adagia such as 'in dubio abstine' and 'primum non nocere' still enjoy respect in medicine and the medical profession is still reserved as to hormonal and surgical treatment.

Those in the medical field who have set out to undertake sex reassignment of transsexuals have met strong reservations from the peer group. Can it be ethically and medically defended that tissue, healthy by standards of medical pathology, is tampered with solely on the grounds of the purely subjective assertion of the transsexual that life in the natal sex is intolerable? Can hormones and the surgical scalpel actually correct whatever has gone wrong in the apparently 'psychological' process of gender identity and role formation? Is not one of the tenets of psychotherapy (in particular psychoanalysis) that errors in our psychological development can be undone provided that the will and the commitment to invest in psychotherapy are present? Arguments that transsexuals can be 'cured' by psychotherapy have never been corroborated by clinical studies providing evidence. Naturally, they may benefit from psychotherapy to help them cope with their predicament, but there seems to be no hope that it will fundamentally solve their gender identity disorder.

The counter-argument to those who provide sex reassignment is that they have no cure to offer either. Can a transsexual who has undergone hormonal and surgical sex reassignment truly be said to have become a member of the new sex? The answer emerges if one reflects on what medicine in general has to offer to the sufferings of mankind, appropriately phrased by John Money in 1971:[15] 'Some illnesses are acute, time-limited, and subject to therapeutic arrest or reversal, followed by return to health. These, in the Hippocratic tradition, the physician aims to cure. Other illnesses are chronic, progressive and deteriorative. For these the physician is less ambitious. He aims to ameliorate or palliate, with whatever treatment is available, the suffering they engender. Still other illnesses or conditions are chronically, though not progressively disabling. For these the physician's goal is ameliorative plus rehabilitative.

Transsexualism is not a reversible condition, judging by today's therapeutic techniques. Nor is it a progressively deteriorative condition, but it does represent a chronic disability, requiring a patient's life to be rehabilitated. Sex reassignment—social, hormonal, surgical, and legal—is an ameliorative and rehabilitative treatment for transsexualism. There cannot be a cure for this condition in the absence of a clearly formulated etiology so far not discovered'.

As Money et al. observes, a true cure is relatively rare in medicine; rehabilitation is the most common sort of help that can be offered. By way of comparison, a young person paralysed and crippled in a traffic accident may be enormously helped by an orthopedically inspired but 'unnatural' surgical transposition of tendons aimed at improved mobility and a corresponding reduction of dependence on others. Such an intervention, in no way defensible in a healthy person, can be in the best interests of a person in this unhappy circumstance. It is not a cure, but an attempt to rehabilitate a person stuck in this situation. It demonstrates that improvement of the health of the whole person can legitimately take precedence over the health of individual body parts. In fact, the situation of the transsexual is not essentially different.

Sexual differentiation of the brain

In the daily practice of medicine, we deal with verifiable biological criteria of sex (chromosomal patterns, nature of the gonad and genitalia, and sex hormone levels), but there is little attention for another dimension of sexual differentiation: the sex of the brain. It can be argued that this does not usually pose an issue since the sex of the brain almost always conforms to other specifications of sexual differentiation.

From the beginning of the 20th century, studies in rats, mice and other lower mammals have made it apparent that sexual differentiation does not stop with the development of the external genitalia into male or female sex organs (the usual criterion for labelling creatures as male or female). Rather, this development is succeeded by a corresponding differentiation of the brain to match that of the gonad and genitalia. This sexual differentiation of the brain can be demonstrated neuroanatomically. It expresses itself not only in sex-dimorphic sexual behaviour (such as copulatory positions) but also in sex-dimorphic non-sexual behaviour such as aggression, defence of territory and caring for the young. The paradigm of this step in the sexual differentiation process of lower mammals is similar to preceding ones: in the presence of androgens (normally produced by the testis of the fetus), a male brain differentiation occurs; if no androgens are present (the normal situation in females), a female brain differentiation follows. This process has been termed the organisation, or 'wiring' of the brain to prepare it for future sexual and reproductive behaviour in accordance with the gonadal/genital status.[16] This programming laid down during the fetal period or shortly thereafter becomes activated by the hormones of puberty.[16]

As this aspect of sexual differentiation is androgen-dependent, it has been possible to experiment with it in lower mammals. It does seem that a male copulatory pattern can be induced in a rat with a female gonadal/genital differentiation. Similarly, a female copulatory pattern can be induced in a male rat by depriving it of androgenic stimulus at the time of the brain's sexual differentiation.[16]

In clinical studies of transsexuals, it has not been possible to demonstrate any hormonal disruptions at any point that display patterns typical of the opposite sex.[3] However, intersexed subjects exposed to an atypical hormonal environment at the supposed time of brain sexual differentiation do show that prenatal androgen exposure affects their future gender role and may induce a degree of masculinity.[3] In lower mammals, it is now well established that exposure of the brain to androgens during the critical period of sexual differentiation induces male brain development, while lack of exposure to androgens results in a female brain; also, that male and female rat brains differ in their neuroanatomical structures.

Naturally, there has been an effort to determine whether these neuroanatomical differences can also be found in humans. Several researchers have anticipated such differences because of the close parallels between lower mammals and humans in the process of sexual differentiation of the gonads and genitalia. And indeed sex differences in the size and shape of certain nuclei in the hypothalamus have been described in the human, though replication studies are still needed to corroborate the findings (for review, see Refs. 16 and 17).

In the past decade, post-mortem research on the brains of transsexuals at the Dutch Brain Research Institute has been able to demonstrate that one of the brain nuclei that is sex-dimorphic in the human, the bed nucleus of the stria terminalis, shows all the characteristics of female differentiation in a sample of male-to-female transsexuals.[18–20] This observation was refined, and it could further be shown that the one brain of a female-to-male transsexual available for post-mortem examination showed a male differentiation of the bed nucleus of the stria terminalis.[20]

This finding of a biological index of female brain differentiation in male-to-female transsexuals could mark a conceptual turning point in the approach to transsexualism. For the medical profession, transsexuals could be 'rehabilitated' from mentally disturbed to sufferers of a sexual differentiation disorder, namely, of the brain. Also, medical insurance policies could be (legally) obliged to pay for the costs of sex reassignment similar to other forms of intersexed states and the legal system could be held to treating transsexuals analogously to other intersexed individuals. The public might also begin to change its attitude towards this startling phenomenon. The establishment of a biological basis to transsexualism may well have consequences that will reverberate throughout society. At this time, however, brain imaging techniques are not sufficiently refined to detect in living subjects what the post-mortem research has indicated. For this reason, these neuroanatomical differences in transsexuals are not yet part of the diagnostic process.

SUMMARY

Manhood and womanhood, and all shades in between, are part of medicine. While solutions are mostly technical and based on insights into biomedical science, issues in medical care arise that cannot currently be satisfactorily solved on the basis of biomedical science alone. Disorders of sexual differentiation and the phenomenon of transsexualism require a different approach. The self-experience of belonging to one sex or the other weighs on the medical decisions to be made for the well-being of subjects in these situations. This marks the point where medicine becomes an art as well as a science. Some may conceive statements of this nature as woolly. It goes without saying that no treatment procedure is beyond verification by biostatistical methods. Increasingly, studies prove that the above approach helps people to live fuller lives.[7,21–24]

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