European Journal of Endocrinology (2001) **145** 365–376 ISSN 0804-4643

INVITED REVIEW

A psycho-endocrinological overview of transsexualism

A Michel, C Mormont[1] and J J Legros

Department of Clinical Psychology, University of Liège, Liège, Belgium and [1]Endocrinology Service, Unit of Psychoneuroendocrinology, University of Liège, Liège, Belgium

(Correspondence should be addressed to A Michel, University of Liège, Department of Clinical Psychology, Boulevard du Rectorat – B33, B-4000 Liège, Belgium; Email: aude.michel@ulg.ac.be)

Abstract

The technical possibility of surgical sex change has opened up a debate concerning the legitimacy and utility of carrying out such an intervention at the request of the transsexual. Diagnostic, psychological, medical and ethical arguments have been brought forth, both for and against. Nonetheless, anatomical transformation by surgical means has currently become a practice as the frequency of serious gender identity disorders is constantly progressing.

After a brief introduction, the present paper will consider typological, aetiological and epidemiological aspects of transsexualism. Treatment of the sex change applicant is then defined and discussed in terms of psychological, psychiatric, endocrinological and surgical aspects. Finally, the question of post-operation follow-up will be examined.

European Journal of Endocrinology **145** 365–376

Introduction

Throughout history, there have been a number of persons suffering from a major discordance between their physical appearance and their gender identity, but who have not had the opportunity of benefiting from a medical solution. Today, thanks to medical progress, such individuals can now be relieved of their gender identity disorder and frequently find a result in the gender dysphoria experience through surgical sex reassignment.

The first surgical case (consisting of a complete sex change: operation, hormone administration and post-operative follow-up), performed by a Danish team, received major media attention from the tabloid press (1). This case involved Georges Jorgensen, a photographer and ex-GI, who went to Denmark for the operation. At the same time, albeit in New York, Benjamin, an endocrinologist and sexologist, published one of the first scientific articles on the subject (2). In December 1953, during a symposium held by the *Association for Advancement of Psychotherapy*, Benjamin and Gutheil coined the term 'transsexualism'.

The possibility of sex change then resulted in an impressively large number of sex change requests around the world (1). Today, surgical sex change operations are more and more practised, often carried out by specialised interdisciplinary teams. The request may also occur in quite different circumstances, leaving the consulting physician amazed when faced with such an unusual request.

The object of this article is to present, beyond a definition of the disorder, a general outline of the etiological, epidemiological, diagnostic, treatment and rehabilitative aspects of transsexualism.

Definition

The first definition of the term transsexualism dates from 1953, coined by Benjamin who associated biological normality with the conviction of belonging to the opposite sex and the sex reassignment request. In this sense, the transsexual is characterised by an unshakeable conviction of belonging to the opposite sex, presenting a most extreme gender identity disorder. Gender identity (gender identity refers to an identity experience expressed in terms of masculine or feminine 'belongingness', independent of the anatomical reality of the sex) is therefore totally in disharmony with corporal reality, forcing the individual to request sex reassignment surgery.

Transsexualism as a particular nosological category (gender dysphoria syndrome) was included in the *Diagnostic and Statistical Manual of Mental Disorders*, edn III (DSM-III) in 1980 (3), but was then removed from DSM-IV where it was assimilated into sexual identity disorders (4). DSM-IV therefore no longer adopted the view that the difference between transsexuals and other forms of gender dysphoria was an interesting differential criterion. Therefore, as a consequence, highly heterogenous cases are regrouped together in DSM-IV.

Typology

There are two types of sex change applicants. They may include the masculine transsexual (male to female, hereafter referred to as MF), where the male (karyotype XY) demands feminisation, or the feminine transsexual (female to male, hereafter referred to as FM), where the female (karyotype XX) aspires to a masculinisation of her body.

Although these two types of sex change applicant both demand a surgical transformation, they present certain differences. Compared with MF, FM applicants are younger when they ask for interventional surgery (5–10), have more frequently adopted reversed behaviour ('tomboy' versus 'sissy') (7, 10, 11), have a higher educational level, are employed in more stable jobs (6, 11, 12 (except in studies 7, 10)), are more frequently single at the time of the diagnostic phase (6, 7, 10, 11), present a less marked psychopathology (e.g. less likely to attempt to commit suicide (6, 7, 10, 11, 13)) and, finally, are more likely to adopt a homosexual sexuality (7, 11).

Apart from the above-mentioned fundamental distinction, other sexual dysphoric typologies have been proposed (14–27) and are based on particular aspects (choice of sexual object, the presence of transvestite behaviour, etc.). Among these, the typologies presented by Person & Ovesey (23–24) and by Blanchard (16) are considered fundamental. The former proposes a classification based on, among other aspects, the age of the subject at the time of the request, and the intensity of the subject's dysphoria (present or not since childhood), whereas the latter classification is based on the nature of the choice of sexual object. Both the subject's age at the time of the request and the choice of the sexual object are two essential prognostic factors (16, 28–31).

Aetiology

The aetiology of transsexualism remains uncertain in spite of the hypotheses that, for 40 years, have attempted to mark out the factors that interferring with biological, psychological and social processes of the construction of gender identity will explain the appearance of transsexualism (32).

The biological perspective

The majority of studies looking at biological factors in transsexual subjects fall within one of three areas of research (32).

Gender identity disorders in subjects presenting perinatal hormonal abnormalities

Gender identity disorders may be the consequence of an atypical hormonal environment such as congenital adrenal hyperplasia, resistance to androgens or even exogenous hormonal impregnation (the absorption of diethylstilboestrol treatment during pregnancy). In the majority of cases, these subjects do not develop towards transsexualism (33–43). Some researchers have documented changes in behaviour (e.g. behaving as a tomboy) and sexual orientation (44–48) in these subjects, although others have not done so (40, 49).

Alteration of gonadotrophin secretion

Based on perinatal sexual differentiation of the neuroendocrine areas of the central nervous system (CNS), regulation of luteinizing hormone (LH) seems to be a good indicator of sexual brain differentiation. These observations are based on animal experiments conducted by Dörner in the 1970s. The induction of an androgenic deficit (versus hyperandrogenia) during the sexual differentiation of the brain in male (versus female) rats resulted in the appearance of reversed sexual behaviour (50).

On the contrary, based on the observation of transsexuals, it has been shown that the the specific sexual response of LH to oestrogen ('positive' feedback in females, 'negative' feedback in males) is not definitely fixed during the perinatal period. Indeed, Gooren (51) observed, in MF transsexuals, negative oestrogen feedback before hormonal therapy (i.e. in accordance with their anatomical sex) while, after hormonal feminisation, the same subjects presented positive oestrogen retro-control.

Sexual morphological differentiation in the brain

Several studies have revealed sexual morphological differences in the CNS (both in terms of dimension and form), in particular, in the hypothalamic nuclei.

Based on morphometric analyses, an early study examining the preoptic area of the hypothalamus of human subjects suggested the existence of a sexually dimorphic nucleus (SDN). This nucleus was found to be twice as large and contained twice as many cells in male compared with female subjects (52). Other authors have shown that the anterior preoptic hypothalamus is the site of other SDN (53). These researchers also took an interest in the interstitial nucleus of the anterior hypothalamus (INAH), which can be divided into four distinct parts (INAH-1 to INAH-4). According to Allen *et al.* (53), zones INAH-2 and INAH-3 are larger in males than in females. A few years later, Allen & Gorski (54) observed that the anterior commissure of the brain was wider in female subjects.

Few studies have been carried out on transsexual subjects. The first study by Swaab & Fliers (55) was based on three MF subjects, and revealed the presence

of particular characteristics in the hypothalamic structures. Two of the subjects presented a large suprachiasmatic nucleus and a small SDN, whereas the last subject showed the opposite configuration. Ten years later, Zou *et al.* (56) were the first researchers to show the presence of a feminine structure of brain zones (BSTc) in male transsexuals. This study showed that the MF transsexuals presented a bed nucleus of the stria terminalis (BSTc) of the size and form of those of heterosexual women. This structuring of the brain was not due to a concomitant intake of hormones, as the authors failed to find a similar configuration in non-transsexual subjects who, for medical reasons, had to take a similar hormonal therapy.

The psychological perspective

Aside from the constitutional factors considered during the pre- and perinatal periods, various psychological and social aspects also play an important role in the aetiology of transsexualism. Psychological theories can be placed into two distinct categories: one envisaging transsexualism as the result of a non-conflictual process, where gender identity is precociously fixed (57–65), and the other considering transsexualism as a conflictual process, where gender identity is not fixed and continues to remain ambiguous throughout development (23, 24, 66–72).

The non-conflictual hypothesis

Here, transsexualism is considered to be an entirely particular phenomenon, so that its aetiology must be clearly distinguished from both perversions and atypical sex change requests. In addition, 'true' transsexualism is explained by the proximity (emotional as well as corporal) of the mother–son relation as a happy and prolonged symbiosis, where the boy identifies himself with the gender of his mother (64, 65).

According to this hypothesis, the individual who presents gender identity disorders has possessed, since early infancy, a nucleus of the feminine gender. This femininity has been adopted in a non-conflictual manner by the family system (where most often it is the mother who has gratified this reversed gender identity).

The conflictual hypothesis

Although different theories involving the conflictual hypothesis have been proposed, they all share a similar supposition, namely, that the sex change request is a 'pathological compromise formation' (71). In this context, transsexualism is considered a defence against homosexuality (73, 74), a form of perversion (72, 75), a narcissistic disorder (76–79) or a perturbation of the separation–individuation phase (80).

There is general agreement that transsexualism appears as a manifestation of a personality disorder, borderline type (68, 81–85). Referring to the theories of Kernberg (86, 87), it is argued that transsexuals present various characteristics similar to those of borderline subjects (chronic anxiety, diffuse and floating anxiety, depression, isolation, weak tolerance for stress, etc.) and, furthermore, are considered as consequences of a fundamental default of the structuration of the self, where femininity and masculinity appear to be insufficiently integrated.

Epidemiology

The prevalence of transsexualism is particularly difficult to evaluate. Most centres involved in treating gender identity disorders estimate that they treat the majority of the transsexuals of their country and therefore only refer to data based on their clinical practice in order to determine transsexual prevalence rates (8, 14, 59, 88, 89). However, not all transsexuals contact specialised services. Some are treated by their psychiatrists and independent surgeons, others through illegal channels (90).

Prevalence rates vary depending on the country and the era. For example, at the end of the 1960s, the estimated prevalence of transsexualism was much lower in the USA (1:100 000 men and 1:400 000 women (59)) than in Sweden (1:37 000 men and 1:103 000 women) (90)). Later studies, carried out in England (1:34 000 men and 1:108 000 women) (91)), Australia (1:24 000 men and 1:150 000 women) (92)), as well as in Germany (1:42 000 men and 1:104 000 women (9)) confirm the previous prevalence rates established by Walinder (93). DSM-IV regrouped these different results and therefore report an average prevalence of 1:30 000 men and 1:100 000 women (4) (Table 1).

The men–women difference varies depending on the era, country and study. Apart from Poland, there are more men than women amongst sex change applicants; the ratio being 8:1 to 2.5:1 and, on average, 3:1 (three times more men than women). The Polish exception (sex ratio of 1 man for 5 (96) or 5.5 women (97)) has not yet been adequately explained. Some researchers argue that this may be due to different diagnostic criteria in Poland, whereas others have argued that this may be due to differing conceptions of the feminine role in Eastern European, compared with Western countries (98). However, these hypotheses have not been adequately investigated (Table 2).

Treatment strategies

At present, most transsexual treatment clinics refer to the recommendations given in the standards of care set out by the Harry Benjamin International Gender Dysphoria Association (HBIGDA) (100), which sets out minimal criteria for the treatment of transsexual

Table 1 Prevalence rates of transsexualism – a review of the different studies.

Study	Country	MF	FM	Total
Walinder 1968 (93)	Sweden	1:37 000	1:103 000	1:54 000
Pauly 1968 (59)	USA	1:100 000	1:400 000	
Hoenig & Kenna 1974 (91)	England	1:34 000	1:108 000	1:53 000
Ross *et al.* 1981 (92)	Australia	1:24 000	1:150 000	1:42 000
O'Gorman 1982 (94)	Ireland	1:35 000	1:100 000	1:52 000
Eklund *et al.* 1988 (88)	The Netherlands	1:18 000	1:54 000	
Tsoi 1988 (95)	Singapore	1:2900	1:8300	
Bakker *et al.* 1993 (89)	The Netherlands	1:11 900	1:30 400	
Weitze & Osburg 1996 (9)	Germany	1:42 000	1:104 000	1:48 000

applicants. In the HBIGDA, all gender identity disorder interventions are required to arise from an interdisciplinary team which includes psychiatrists, psychologists, endocrinologists and surgeons. The standards of care determined by the HBIGDA advocate treatment in two phases. The first stage consists of establishing a diagnosis based on precise and commonly accepted criteria (DSM-IV) and the second stage, or the real-life test, confronts the subject with the everyday reality that the subject will meet once she/he has successfully completed the sex change process.

At the University of Liège, sex reassignment surgery in gender dysphoria is considered to be a serious intervention which cannot be carried out without the full assurance that the sex change applicant has truly thought out his/her request and has balanced out the consequences. In this context, long-term psychotherapeutic work preceding the intervention is, if not obligatory, at least strongly recommended.

The diagnostic phase

The transsexual requests assume different forms. It is thus appropriate to detect, among individuals who suffer from diverse forms of gender dysphoria, those who fulfil the requirements of a transsexual diagnosis and who, as a last resort, would benefit from surgical sex change.

Table 2 Sex ratio in transsexualism – a review of the different studies.

Study	Country	M:F sex ratio
Walinder 1968 (93)	Sweden	2.8:1
Benjamin 1966 (14)	USA	8:1
Pauly 1968 (59)	USA	4:1
Hoenig & Kenna 1974 (91)	England	3.2:1
Ross *et al.* 1981 (92)	Australia	6.1:1
O'Gorman 1982 (94)	Ireland	3:1
Brzek & Sipova 1983 (96)	Poland	1:5
Tsoi 1988 (95)	Singapore	2.9:1
Godlewski 1988 (97)	Poland	1:5.5
Burns *et al.* 1990 (99)	England	3:1
Bakker *et al.* 1993 (89)	The Netherlands	2.5:1
van Kesteren *et al.* 1996 (8)	The Netherlands	3:1
Weitze & Osburg 1996 (9)	Germany	2.3:1

During the diagnostic phase, there are two objectives: to assess the amplitude of gender dysphoria and the degree of transsexual conviction and to give information concerning the treatment procedure, including both the possibilities and the limitations of surgery.

Even though well-defined criteria are available to the psychologist and psychiatrist, the diagnosis of transsexualism remains difficult; in particular concerning the evaluation of such aspects as authenticity, duration and intensity of the gender dysphoria. For example, in order to convince the examiner, the transsexual candidate frequently tends to exaggerate his/her personal history. Also, the objectivity of the testimony is often difficult to evaluate, especially since in the majority of cases it is impossible to obtain authentic third party information (e.g. parents, spouse, other close relations), as they either endorse the request personally or are opposed to it. Under such conditions, a prolonged and meticulous assessment (through cross-checking and repeating questions) is necessary in order to come to an adequate diagnosis. This phase lasts a minimum of 6 months, but can last up to 12 months.

To begin with, the major objective here is to identify those cases that present psychological (such as psychotic syndromes, perversions or occasional transsexual crises (perturbed or fragile gender identity)) or biological perturbations (intersexual states or endocrine disorders), and this in the most reliable way possible. The amplitude of the dysphoria is then assessed based on a thorough review of the subject's medical history.

Differential diagnostic issues

Anatomical–biological disorders As stated in DSM-IV, it is appropriate to ensure that the sex change applicant does not correspond to a diagnosis of intersexuality: 'the affection is not concomitant to an affection responsible for a hermaphrodite phenotype'. It is important that there is a congruence between the genital organs of the sex change applicant and the

genetic reality of the applicant's karyotype, and that the existence of different biological disorders has been discarded (see The biological perspective, page 366).

Psychopathological disorders *Psychosis*. It is well known that delusion thought related to sexual identification is a classic theme in schizophrenia. The prevalence of gender identity disorders in schizophrenics is frequent (15–25% depending on the study), and delusion revolving around the theme of sex change has been observed in these subjects (101–111).

Although higher than in the general population, the frequency of schizophrenia in the sex change application population remains relatively small (2.8% in the study by Hoenig & Kenna (91); 4.9% in Walinder (112), 6.9% in de Cuypere (111) and 16% in Lothstein & Roback (113)). In light of these frequency rates, caution is recommended when establishing a diagnosis.

'Cross dressing' and transvestism. When wearing the clothing of the opposite sex, the transvestite experiences a playful pleasure or the release of his anxiety, whereas the transsexual simply feels as if she/he is wearing the clothes of a person of the subject's 'true' sex. Also, the majority of transvestites do not show any aversion for their sexual organs, and do not ask for genital modifications. When the transvestite's behaviour is repetitive, it is no longer a question of 'cross dressing' but of transvestism. The passage from 'cross dressing' to transvestism is therefore relative to the frequency and the duration of a 'cross dressing' period.

In some special cases, there may be a sex change request. This occurs most often in transvestites older than 40 years and where the act of wearing feminine clothes has lost its erotic power. Under these conditions, the transvestite will not only want to *appear feminine*, but will also want to *be a woman*. These cases reveal late-onset transsexualism and therefore deserve a transsexualism diagnosis.

Homosexuality. Homosexuality refers to the choice of a sexual object, a choice that brings the homosexual towards a person of his own gender and thus towards someone of the same sex as the subject. Thus, the male homosexual feels male, loves a male, but does not wish to live as a woman, nor to be castrated.

Other disorders. Transsexual requests can also be observed in subjects in transsexual crises (following depression, genital dysmorphophobia, impotence), in perverted patients (from marginal milieus such as prostitution), or even from cases of masochism or suggested transsexualism (114). Such sex change requests come very often from subjects with a fragile gender identity who are going through a difficult period in their lives. Surgical transformation is viewed by these subjects as a miracle solution to their problems. It is clear that a surgical solution is not an appropriate intervention for these patients.

Assessment of the intensity of the gender identity disorder

Finally, it is important to assess the amplitude of the gender dysphoria, its appearance modalities (psychosexual development, manifestation ('cross dressing' phases)), and its impact on the sexual functioning of the subject (e.g. sexual behaviour, sexual orientation). In this context, periods of 'cross dressing' should be meticulously analysed through questions concerning when this type of behaviour first appeared, the adopted form (associated or not to a sexual pleasure), the nature of the clothes, etc.

Questioning of sexual behaviour is also important in order to better understand the applicant's values and attitudes in regard to his sex. Finally, questions concerning masturbation, sexual relations (their nature and satisfaction) and the genital areas (Is there an aversion for genital organs? Does the subject accept that a partner touch his genitals? etc.) would be appropriate in this context (115).

Information concerning the treatment procedure

This final aspect of the diagnostic phase cannot be considered a diagnostic element *per se*. It consists of informing sex change candidates of the possibilities, but also of the limitations of surgery and sexual conversion. Very often, the expectations of candidates clearly exceed the possibilities of reassignment surgery; in that case the task of the team would also be to confront subjects with the unreality of their requests and/or expectations.

The majority of clinicians (17/19) interrogated by Peterson & Dickey (116) follow-up the sex change applicant for at least 3 months (this phase can in certain cases be extended to 2 years) before making a precise diagnosis.

The real-life test: a social integration phase

The objective of the real-life test is to make sure that the patient takes on the appearance of the desired sex in everyday activities, both social and professional, for at least 1 month. During this period, the subject receives a medical certificate justifying the wearing of clothing of the opposite sex to reduce worries associated with the possibility of having to prove his identity (which would reveal his true sex, in spite of appearing to belong to the opposite sex). Also, the sex change applicant must choose a new first name, dress in accordance with his new gender, inform his/her different social partners of

Table 3 Role of the endocrinologist in the interdisciplinary group for the management of transsexualism.

Phase of the reassignment	Role of the endocrinologist	Methodology
Pre-inclusion phase	Confirms absence of endocrine disorders (mainly intersexuality)	Anamnesis and clinical evaluation
	Controls absence of contraindication for further hormonal treatment	Karyotype Basal biological and endocrine check-up Dynamic neuroendocrine test (TRH, OGTT) (optional)
Pre-surgical (pre-castration) (see A1 and A2; Table 6)	Absence of undesirable clinical and biological side-effects (Table 5)	Anamnesis and clinical evaluation Basal biological and endocrine testing (each 3–6 months)
Post-surgical (post-castration) (substitutive therapy)	Absence of undesirable side-effects Control of a good 'physiological' equilibrium	Anamnesis and clinical evaluation Basal biological and endocrine testing (+PSA?) Dynamic tests if mandatory (TRH, OGTT) Osteodensitometry (each 1–2 years)

TRH, thyrotrophin-releasing hormone test; OGTT, oral glucose tolerance test; PSA, prostate specific antigen test.

his future sexual reassignment, and live correctly in his/her new gender role.

During this period, which may last from 12 to 18 months, the sex change candidate must supply proof of his social life and integration (e.g. a certificate of attendance at school, work, etc.). This allows an evaluation of the degree of conviction. Indeed, everyday confrontation with reactions from the social milieu represents one of the major difficulties in sexual conversion. A (simulated) sex change inevitably radically disrupts the subject's social environment. Relations with parents and colleagues and close relations are all perturbed. During the real-life test, therapy may also focus on the subject's confrontation of hostile reactions in his/her environment.

However, a number of sex change applicants attempt to avoid this test, or they try to reduce it to a minimum, as they consider it a waste of time. For example, certain applicants are persuaded that their change will be accepted without problem by their colleagues and that they have nothing to prove. Others argue that presenting themselves in the role before being operated on will result in them being the victim of a hoax (and therefore they must obtain this transformation). Yet others argue that, since they own their own body, they have a right to have recourse to such a surgical intervention, even if this transformation turned out to be an error (107).

Not all treatment centres consider psychotherapeutic follow-up to be necessary (108). Cohen-Kettenis & Walinder (117) noted that several clinicians refuse to comply to the sex change request without such a investigation. Supportive psychotherapy may be used in this context, where issues such as the consequences of reassignment surgery (loss of a partner, contact with children, work, etc.) and eventual disorders indirectly linked to the gender dysphoria (109) may be taken up in treatment sessions.

Hormonal therapy

Although the psychologist and the psychiatrist play the major roles at the various phases of the gender identity diagnosis and reassignment, the endocrinologist must also be involved in the very first step of the process. As summarized in Table 3, the endocrinologist's role will be first to detect unknown intersexual disease through careful anamnesis, clinical examination and basal hormonal check up. The karyotype is also evaluated because it is mandatory to obtain administrative permission for reassignment of sex in Belgium. Although some patients suffering from intersexual status did consult our group, we have, however, never diagnosed such an unknown pathology in the patients referred to our group for a gender identity problem.

When the diagnosis of transsexuality is ascertained, the endocrinologist must then control the absence of absolute contraindications (see Table 4) and carefully explain to the patients the possible undesirable side-effects of various hormonal treatments (see Table 5). Even at this first step, patients should also be aware that the hormonal treatment after castration will be life long to avoid well-known metabolic and psychophysiological problems secondary to sexual steroid deficiency. Recent reviews on hormonal treatments have been published by Futterweit (118) and by Cohen-Kettenis & Gooren (119): a summary of the general guidelines is given in Table 6.

Hormonal treatments differ slightly from one group to another particularly in the 'precastration' phase. In MF, the Amsterdam group systematically prescribes antiandrogen; we limit this prescription to those males in whom oestrogens alone do not significantly modify facial hair pilosity.

Among the biological and endocrinological data, a blood PSA assay might be interesting in both sexes since some rare cases of prostatic carcinoma in a

Table 4 Contra-indications of hormonal treatment in transsexual patients (after Futterwut *et al.* 1998, modified (118)).

	MF (XY)	**FM** (XX)
Absolute contraindication	Severe diastolic hypertension Thrombophlebitis or thromboembolic disease Cerebrovascular disease Severe hepatic dysfunction	
Relative contraindication	Heavy cigarette consumption Family history of breast cancer Hyperprolactinaemia Marked obesity (WHR>0.95)	Overt diabetes Marked hypertriglyceridaemio and/or hypercholesterolaemic Marked obesity (WHR>0.90)

WHR, weight to height ratio.

genetic male (XY) after more than 10 years of oestrogen therapy have been described (118) and since recent data indicate an increased PSA level in a genetical female (XX) receiving androgen therapy (120).

Although there is an increase in the number of thrombo-embolic disorders in oestrogen-treated MF patients (less marked, however, since the use of transdermal oestrogens after the age of 40), the mortality of MF transsexuals is similar to that of the normal population (121). Very exceptionally, the development of a pituitary prolactin-secreting micro-adenoma has been described (122); we have recently observed a 3 mm hypophysial microadenoma (prolactin and growth hormone (GH)?) in a hyperoestrogenized MF patient: the image and endocrine abnormalities disappeared after a decrease in the dose of oestrogen. Other metabolic and endocrine effects of the treatment (123) include: increase in bone density (124), decrease in plasma insulin-like growth factor-I (125) and decrease in hair growth and sebum formation (126).

The use of progesterone for 10–15 days to 'mimic' physiological fluctuations of gonadal steroid hormone is still controversial and, as a rule, not prescribed. In our experience, however, a few patients suffering from abnormal psychological irritability and mammary tenderness may be given oral natural progesterone with some psychological and clinical benefits. In FM patients, androgen treatment induces a constant increase in the haematocrit and a slight decrease in

Table 5 Favourable ('wanted') and unfavourable ('unwanted') side-effects of hormonal treatment in transsexual patients.

	MF (XY)	**FM** (XX)
Favourable side-effects (wanted, phase A1 and A2)	*Psychological* Secondary to body transformation *Biological* Decreased blood testosterone Increased blood oestradiol *Anatomical* Mammary gland hyperplasia Decreased erection Decreased facial hair Modification of speech Gynoid fat deposit	*Psychological* Increased libido Increased subjective wellbeing *Biological* Increased blood testosterone Decreased blood oestradiol and progesterone *Anatomical* Amenorrhea Decreased breast volume Increased facial hair (+androgenic alopoecia) Modification of speech Increased muscular strength Android fat deposit
Unfavourable side-effects (unwanted)	*Psychological* Depression (mainly secondary due to the use of anti-androgens) Abnormally decreased libido *Biological* ↑Bilirubin ↑Prolactinaemia ↓FSH, LH ↑GH responsiveness *Anatomical* Thrombophlebitis Mammary cancer Residual prostate cancer	*Psychological* Pathological aggression Psychotic syndrome Abnormally increased libido *Biological* ↑Erythrocytosis ↓HDL cholesterol ↑Bilirubin ↓FSH, LH Diabetes ↑PSA (?) *Anatomical* Haemorrhagic liver cysts Facial acne

Table 6 Summary of hormonal treatment in MF and FM transsexual patients at the different phases of gender reassignment.

Phase	**MF** (XY)	**FM** (XX)
Pre-surgical A.1.: suppression of the original sex characteristics (optional)	LHRH superagonists (i.m. monthly?) and/or spironolactone (100–200 mg/day) or cyproterone acetate (50–100 μg/day)	LHRH superagonists (monthly?) and/or norethisterone acetate (5–10 μg/day)
Pre-surgical A.2.: induction of designed sex characteristics	Ethinyloestradiol (50–100 μg/day) or conjugated oestrogen (1.25–2.50 mg/day) or oestradiol benzoate, oestradiol phenylpropionate (25 mg/2 weeks) *Optional* Spironolactone (100–200 mg/day) or cyproterone acetate (50–100 μg/day)	Norethisterone acetate (5–10 mg/day) or testosterone undecanoate (3 × 80 mg/day p.o.) or testosterone propionate, phenylpropionate, isoaproate, decanoate (250 mg for 2,3 or 4 weeks i.m.)
A1 and A2 maximum 2 years		
B. Post-surgical (post-castration)	Oestrogens (see A.2.) or transdermal form (50–100 μg/day) or subcutaneous implant *Optional* Progesterone (100 mg/day for 2 weeks/month) or classical post menopausal hormonotherapy (+subcutaneous implant?)	Testosterone p.o. or i.m. (see A.2.) or transdermal androgens?

blood high density lipoprotein (HDL) levels. The development of androgenic obesity rarely leads to type 2 diabetes: a family history of diabetes therefore led us to systematically perform an OGTT before beginning treatment. In those 'at risk' patients advice on diet is mandatory. Increase in facial hair growth (126) and modifications of behavioural and cognitive function (increase in spatial ability, decrease in verbal fluency) (127, 128) are well documented and are considered to be very favourable effects of androgen therapy by the patients. It is, however, important to inform FM patients that androgen therapy often leads to endometrial hypertrophy, a putatively precancerous state: this renders hysterectomy nearly mandatory once the real-life test phase has been terminated.

Surgical transformation

Surgical transformation in MF consists of an ablation of the testicles and penis and vaginal plastic surgery. These interventions are frequently accompanied by mammoplasty. In FM, the surgical procedure consists of bilateral mastectomy, ovariectomy, hysterectomy and phallic plastic surgery.

Surgery is most often performed at least 1 year after starting hormonal treatment. The decision to proceed with such an intervention may be reconsidered if there are difficulties in getting past the real-life phase (psychosocial, psychiatric instability) or evidence of substance abuse (e.g. drugs, alcohol) (116). Other reasons for postponing surgical reassignment may include unsatisfactory family support and/or an environment hostile towards the transformation, or an unannounced divorce.

Post-transformation

It is impossible to compel the transsexual to follow long-term assessment (129). Indeed, a major obstacle in conducting follow-up studies is that it is very difficult to find transsexuals who have been operated on, and even more difficult to find those who accept re-assessment (130–132). Therefore, those few who do agree to participate in follow-up studies do not constitute a representative sample of the population of transsexuals who have been operated on.

Apart from this methodological problem, since the first publication by Hertz *et al.* (133), a large number of studies have examined the consequences of sex change and these have been the subject of several reviews (59, 134–141). In the great majority of cases, transsexuals seem satisfied with their transformation, with only about 10% of subjects being unsatisfied. This percentage is lower in FM (6% (135); 9.7% (137); 3% (139))

compared with MF subjects (8.1% (135); 10.3% (137); 13% (139)).

A temporary dissatisfaction can be observed immediately after the sex change. Certain transsexuals find themselves confronted with various difficulties (post-operation pain, surgical complications, dissatisfaction with surgical results, departure of the partner, loss of job, familial conflicts, etc.) and experience a phase of dissatisfaction that can lead to regret in some cases. However, most often this dissatisfaction disappears during the year following the surgical transformation where no other intervention was deemed necessary (142).

More deep regrets are rare. Studies report only less than 1% of FM subjects regretting the intervention, and 1.5% of MF subjects (142, 143). An analysis of the responses shows that these regrets may come from one of three major sources: (1) erroneous diagnosis (certain subjects showed clear signs of psychosis); (2) absence of a real-life test (subjects had not been submitted to this procedure); (3) insufficiently adapted surgical interventional protocol and deceptive surgical results (certain subjects had to wait for long periods of time before proceeding to the surgical intervention; unsatisfactory results from cosmetic surgery).

Finally, dissatisfaction can be so profound that it may lead the subject to suicide. Nonetheless, the rate of suicide has been reported at a little more than 1% in MF and less than 1% in FM (134, 135, 137, 143, 144). However, it must be mentioned that they may not necessarily be attributed directly to the sex change. For example, errors in medication, overdoses, medical complications (not related to the surgical transformation (145)), loss of employment or emotional difficulties (130, 131, 146) may also be related to this fatal gesture.

In addition, according to Pfäfflin & Junge (144), the success of a sexual transformation depends closely on several concrete intervening factors, either before the surgical transformation (keeping in contact with the treatment centre; living in the desired role; receiving hormonal treatment; benefitting from a psychological and psychiatric follow-up) or during and after the transformation (proceeding to a surgical transformation; profiting from quality surgical interventions; proceeding to a change of civil status).

Prognostic issues

As sex change is a major and irreversible transformation, it is most appropriate to identify, before the operation, the factors that would predict a favourable or unfavourable outcome after the operation. Several researchers have concerned themselves with this aspect (30, 31, 147–151).

No less than 20 different negative criteria have been mentioned in the literature (increasing age, personal and social instability, inappropriate physical build, etc.). Although these different factors cannot be considered true contraindications, their presence should suggest caution. Indeed, the appropriateness of surgical transformation lessens in individuals presenting these factors, as there is a greater risk of an unfavourable outcome in these subjects.

Certain criteria for a good prognosis have been defined. Apart from the absence of psychopathology, the most frequently mentioned are mental and emotional stability, that the request was demanded before the age of 30, that subjects have completed an adaptation period (both physical and behavioural) of at least 1 year in the desired sex, that there is an integration of the limitations and direct consequences of surgery, that the subject undergoes preliminary psychotherapy related to the surgical treatment, and the choice of a homosexual sex object.

In light of the various studies mentioned earlier, it is quite clear that surgical anatomical transformation results in largely positive effects. Based on this, and where treatment is carried out correctly from the diagnostic phase to the operation, there is no empirical reason why a sex change request should be refused.

Conclusions

The transsexual suffering from an extreme form of gender dysphoria syndrome often invests all his/her hopes on surgical reassignment. Due to its irreversible character and its considerable consequences, this procedure cannot be performed before a careful analysis of the request has taken place and a gender dysphoria diagnosis (type transsexualism) has been conducted. This diagnosis is difficult and necessitates a multidisciplinary approach. Before proceeding to the surgical sex reassignment intervention, the transsexual should consult an endocrinologist, psychiatrist and psychologist for a period of at least 3 years.

References

1 Hamburger C, Sturup G & Dahl-Iversen E. Transvestism. *Journal of the American Medical Association* 1953 **152** 391–396.
2 Benjamin H. Transvestism and transsexualism. *International Journal of Sexology* 1953 **7** 12–14.
3 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, edn III. Washington DC, 1980.
4 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, edn IV. Washington DC, 1996.
5 Pauly IB. Female transsexualism: part I. *Archives of Sexual Behavior* 1974 **3** 487–507.
6 Dixen JM, Maddever H, van Maasdam J & Edwards PW. Psychosocial characteristics of applicants evaluated for surgical cross-gender reassignment. *Archives of Sexual Behavior* 1984 **13** 269–276.
7 De Cuypere G, Janes C & Rubens R. Psychosocial functioning of transsexuals in Belgium. *Acta Psychiatrica Scandinavica* 1995 **91** 180–184.
8 van Kesteren P, Gooren LJG & Megens J. An epidemiological and demographic study of transsexuals in Netherlands. *Archives of Sexual Behavior* 1996 **25** 589–600.
9 Weitze C & Osburg S. Transsexualism in Germany: empirical data on epidemiology and application of the German transsexuals'

act during its first ten years. *Archives of Sexual Behavior* 1996 **25** 409–425.
10 Landen M, Walinder J & Lundström B. Clinical characteristics of a total cohort of female and male applicants for sex reassignment: a descriptive study. *Acta Psychiatrica Scandinavica* 1998 **97** 189–194.
11 Verschoor A & Poortinga J. Psychosocial differences between Dutch male and female transsexuals. *Archives of Sexual Behavior* 1988 **17** 173–179.
12 Tsoi WF. Developmental profile of 200 male and female transsexuals in Singapore. *Archives of Sexual Behavior* 1990 **19** 595–605.
13 Kockott G & Fahrner EM. Male-to-female and female-to-male transsexuals: a comparison. *Archives of Sexual Behavior* 1988 **6** 539–546.
14 Benjamin H. *The Transsexual Phenomenon*. New York: The Julian Press, 1966.
15 Bentler PM. A typology of transsexualism: gender identity theory and data. *Archives of Sexual Behavior* 1976 **5** 567–584.
16 Blanchard R. Research methods for the typological study of gender disorders in males. In *Gender Dysphoria: Development, Research, Management*, pp 227–258. Ed BW Steiner. New York: Plenum Press, 1985.
17 Buhrich N & McConaghy N. Two clinically discrete syndromes of transsexualism. *British Journal of Psychiatry* 1978 **133** 73–76.
18 Buhrich N & McConaghy N. Three clinically discrete categories of fetishistic transvestism. *Archives of Sexual Behavior* 1979 **8** 151–157.
19 Fisk N. Gender dysphoria syndrome. In *Proceedings of the Second Interdisciplinary Symposium on Gender Dysphoria*, pp 7–14. Eds R Laub & P Gandy. Palo Alto: Stanford University Medical Center, 1974.
20 Freund K, Steiner BW & Chan S. Two types of cross-gender identity. *Archives of Sexual Behavior* 1982 **8** 527–558.
21 Levine SB & Lothstein L. Transsexualism or the gender dysphoria syndromes. *Journal of Sex and Marital Therapy* 1981 **7** 85–113.
22 Meyer JK. Clinical variants among applicants for sex reassignment. *Archives of Sexual Behavior* 1974 **3** 527–528.
23 Person E & Ovesey L. The transsexual syndromes in males: I. Primary transsexualism. *American Journal of Psychotherapy* 1974 **26** 4–20.
24 Person E & Ovesey L. The transsexual syndrome in males: II. Secondary transsexualism. *American Journal of Psychotherapy* 1974 **28** 174–193.
25 Sorensen T. A follow-up study of operated transsexual females. *Acta Psychiatrica Scandinavica* 1981 **64** 50–64.
26 Sorensen T. A follow-up study of operated transsexual males. *Acta Psychiatrica Scandinavica* 1981 **64** 486–503.
27 Stoller RJ. The term transvestism. *Archives of General Psychiatry* 1971 **24** 230–237.
28 Blanchard R. Nonhomosexual gender dysphoria. *Journal of Sex Research* 1988 **24** 188–193.
29 Blanchard R. The classification and labelling of nonhomosexual gender dysphorias. *Archives of Sexual Behavior* 1989 **18** 315–334.
30 Walinder J, Lundström B & Thuwe I. Prognostic factors in the assessment of male transsexuals for sex reassignment. *British Journal of Psychiatry* 1978 **132** 16–20.
31 Kockott G & Fahrner EM. Transsexuals who have not undergone surgery: a follow-up study. *Archives of Sexual Behavior* 1987 **16** 511–522.
32 Cohen-Kettenis PT & Gooren LJG. Transsexualism: a review of etiology, diagnosis and treatment. *Journal of Psychosomatic Research* 1999 **46** 315–333.
33 Kester P, Green R, Finch SJ & Williams K. Prenatal female hormone administration and psychosexual development in human males. *Psychoneuroendocrinology* 1980 **5** 269–285.
34 Beral V & Colwell L. Randomised trial of high doses of stilboestrol and norethiserone therapy in pregnancy: long-term follow-up of children. *Journal of Epidemiology and Community Health* 1981 **35** 155–160.
35 Collaer ML & Hines M. Human behavioral sex differences: a role for gonadal hormones during early developments? *Psychological Bulletin* 1995 **118** 55–107.
36 Dittmann RW, Kappes MH, Kappes ME, Börger D, Stegner H, Willig RH & Wallis H. Congenital hyperplasia: I. Gender-related behavior and attitudes in female patients and sisters. *Psychoneuroendocrinology* 1990 **15** 401–420.
37 Dittmann RW, Kappes MH, Kappes ME, Börger D, Meyer-Bahlburg HFL, Stegner H *et al.* Congenital hyperplasia: II. Gender-related behavior and attitudes in female salt-wasting and simple-virilizing patients. *Psychoneuroendocrinology* 1990 **15** 421–434.
38 Money J & Matthews D. Prenatal exposure to virilizing progestins: an adult follow-up study of twelve women. *Archives of Sexual Behavior* 1982 **11** 73–83.
39 Hurtig AL & Rosenthal IM. Psychological findings in early treated cases of female pseudohermaphroditism caused by virilizing congenital adrenal hyperplasia. *Archives of Sexual Behavior* 1987 **16** 209–223.
40 Lish JD, Meyer-Bahlburg HFL, Ehrhardt AA, Travis BG & Veridiano NP. Prenatal exposure to diethylstillbestrol (DES): childhood play behavior and adult gender role behavior in women. *Archives of Sexual Behavior* 1992 **21** 423–441.
41 Money J, Schwartz M & Lewis VG. Adult herotosexual status and fetal hormonal masculinization and demasculinization: 46,XX congenital virilizing adrenal hyperplasia and 46,XY androgen-insensitivity syndrome compared. *Psychoneuroendocrinology* 1984 **9** 405–414.
42 Reinisch JM, Ziemba-Davis M & Sanders SA. Hormonal contributions to sexually dimorphic behavioral development in humans. *Psychoneuroendocrinology* 1991 **16** 213–278.
43 Slijper FME. Androgens and gender role behavior in girls with congenital adrenal hyperplasia (CAH). *Progress in Brain Research* 1984 **61** 417–422.
44 Ehrhardt AA, Meyer-Bahlburg HFL, Rosen LR, Feldman JF, Veridiano NP, Zimmerman I *et al.* Sexual orientation after prenatal exposure to exogenous estrogen. *Archives of Sexual Behavior* 1985 **14** 57–77.
45 Ehrhardt AA, Meyer-Bahlburg HFL, Rosen LR, Feldman JF, Veridiano NP, Elkin EJ *et al.* The development of gender-related behavior in females following prenatal exposure to diethylstilbestrol (DES). *Hormones and Behavior* 1989 **23** 526–541.
46 Hines M & Kaufman FR. Androgen and the development of human sex-typical behavior: rough-and-tumble play and sex of preferred playmates in children with congenital adrenal hyperplasia (CAH). *Child Development* 1994 **65** 1042–1053.
47 Meyer-Bahlburg HFL, Ehrhardt AA, Feldman JF, Rosen LR, Veridiano NP & Zimmerman I. Sexual activity level and sexual functioning in women prenatally exposed to diethylstilbestrol. *Psychosomatic Medicine* 1985 **47** 497–511.
48 Meyer-Bahlburg HFL, Ehrhardt AA, Rosen LR, Gruen RS, Veridiano NP, Vann PH *et al.* Prenatal oestrogens and the development of homosexual orientation. *Developmental Psychology* 1995 **31** 12–21.
49 Lish JD, Ehrhardt AA, Meyer-Bahlburg HFL, Rosen LR, Gruen RS & Veridiano NP. Gender-related behavior development in females exposed to diethylstilbestrol (DES) *in utero*: an attempted replication. *Journal of the American Academy of Child and Adolescent Psychiatry* 1991 **30** 29–37.
50 Dörner G. *Hormones and Brain Differentiation*. Amsterdam: Elsevier, 1996.
51 Gooren LJG. The neuroendocrine response of luteinizing hormone to oestrogen administration in heterosexual, homosexual, and transsexual subjects. *Journal of Clinical Endocrinology and Metabolism* 1986 **63** 583–588.
52 Swaab DF & Fliers E. A sexually dimorphic nucleus in the human brain. *Science* 1985 **228** 1112–1114.

53 Allen LS, Hines M, Shryne JE & Gorski RA. Two sexually dimorphic cell groups in the human brain. *Journal of Neuroscience* 1989 **9** 497–506.
54 Allen LS & Gorski RA. Sexual dimorphism of the anterior commissure and massa intermedia of the humain brain. *Journal of Comparative Neurology* 1991 **312** 97–104.
55 Swaab DF & Fliers E. A sexually dimorphic nucleus in the human brain. *Science* 1985 **228** 1112–1114.
56 Zou J-N, Hofman MA, Gooren LJG & Swaab DF. A sex difference in the human brain and its relation to transsexuality. *Nature* 1995 **378** 68–70.
57 Baker H. Transsexualism–problems in treatment. *American Journal of Psychiatry* 1969 **129** 118–124.
58 Knorr N, Wolf S & Meyer E. The transsexual request for surgery. *Journal of Nervous and Mental Disease* 1968 **5** 517–524.
59 Pauly IB. The current status of change of sex operation. *Journal of Nervous and Mental Diseases* 1968 **147** 460–471.
60 Stoller RJ. *Sex and Gender:* Vol. 1. *The Development of Masculinity and Femininity.* New York: Jason Aronson, 1968.
61 Stoller RJ. Psychotherapy of extreme feminine boys. *International Journal of Psychiatry* 1971 **9** 278–281.
62 Newman LE & Stoller RJ. Nontranssexual men who seek sex reassignment. *American Journal of Psychiatry* 1973 **131** 437–441.
63 Green R. *Sexual Identity Conflict in Children and Adults*. New York: Basic Books, 1974.
64 Stoller RJ. *Presentations of Gender*. New Haven: Yale University Press, 1985.
65 Stoller RJ. *Sex and Gender:* Vol 2. *The Transsexual Experiment*. London: Hogarth Press, 1975.
66 Meerlo JA. Change of sex and collaboration with the psychosis. *American Journal of Psychiatry* 1967 **124** 263–264.
67 Hoenig J, Kenna J & Youd A. A follow-up study of transsexualists: social and economic aspects. *Psychiatrica Clinica* 1970 **3** 85–100.
68 Volkan VD. Transsexualism: as examined from the viewpoint of internalized object relations. In *On Sexuality: Psychoanalytic Observation*, pp 189–221. Eds TK Karasu & CW Socarides. New York: International Universities Press, 1979.
69 Lothstein LM. *Female-to-Male Transsexualism. Historical, Clinical and Theorical Issues*. Boston: Routledge & Kevan Paul, 1983.
70 Meyer JK. Psychiatric considerations in the sexual reassignment of non intersex individuals. *Clinics in Plastic Surgery* 1974 **1** 275–283.
71 Meyer JK. The theory of gender identity disorders. *Journal of the American Psychoanalytic Association* 1982 **30** 381–418.
72 Volkan VD & Masri A. The development of female transsexualism. *American Journal of Psychotherapy* 1989 **43** 92–107.
73 Socarides C. The desire for sexual transformation: a psychiatric evaluation of transsexualism. *American Journal of Psychiatry* 1969 **125** 1419–1425.
74 Socarides C. A psychoanalytic study of the desire for sexual transformation (transsexualism). *International Journal of Psycho-Analysis* 1970 **51** 341–349.
75 Volkan VD & Berent S. Psychiatric aspects of surgical treatment for problems of sexual identification (transsexualism). In *Modern Perspectives in the Psychiatric Aspects of Surgery*, pp 78–90. Eds JG Howells. New York: Bruner/Mazel, 1976.
76 Chiland C. Homosexualité et transsexualisme. *Adolescence* 1989 **7** 133–146.
77 Lothstein LM. Self object failure and gender identity. In *Frontiers in Self Psychology*, pp 213–235. Ed A Goldberg. Hillsdale, New Jersey: Analytic Press, 1988.
78 Moberley ER. *Psychogenesis: The Early Development of Gender Identity*. London: Routledge & Kevan Paul, 1983.
79 Oppenheimer A. Le désir d'un changement de sexe, un défi pour la psychanalyse. *Psychanalyse à l'Université* 1992 **4** 117–134.
80 Beitel A. Transsexualism and a new type of psychosurgery. *International Journal of Psychoanalytic Psychotherapy* 1978 **7** 366–372.
81 Greenberg N, Rosenwald A & Nielson P. A study in transsexualism. *Psychiatry Quarterly* 1960 **34** 203–235.
82 Golosow N & Weitzman EL. Psychosexual and ego regression in the male transsexual. *Journal of Nervous and Mental Disease* 1969 **149** 328–336.
83 Weitzman EL, Shamoian CA & Golosow N. Identity diffusion and transsexual resolution. *Journal of Nervous and Mental Disease* 1970 **151** 295–302.
84 Kavanaugh J & Volkan V. Transsexualism and a new type of psychosurgery. *International Journal of Psychoanalytic Psychotherapy* 1978 **7** 366–372.
85 Limentani A. The significance of transsexualism in relation to some basic psychoanalytic concepts. *International Review of Psychoanalysis* 1979 **6** 139–153.
86 Kernberg OF. *Borderline Conditions and Pathological Narcissism*. New York: Jason Aronson, 1975.
87 Kernberg OF. *Severe Personality Disorders: Psychotherapeutic Strategies*. New Haven: Yale University Press, 1984.
88 Eklund PLE, Gooren LJG & Bezemer PD. Prevalence of transsexualism in The Netherlands. *British Journal of Psychiatry* 1988 **152** 638–640.
89 Bakker A, van Kesteren P, Gooren L & Bezemer P. The prevalence of transsexualism in The Netherlands. *Acta Psychiatrica Scandinavica* 1993 **87** 237–238.
90 Bourgeois M. Troubles de l'identité de sexuelle. Dysphories de genre et transsexualisme. *Encyclopédie Médico-Chirurgicale* 1988 37299 D20 1-8.
91 Hoenig J & Kenna JC. The nosological position of transsexualism. *Archives of Sexual Behavior* 1974 **3** 273–287.
92 Ross MW, Walinder J, Lundström B & Thuwe I. Cross-cultural approaches to transsexualism: a comparison between Sweden and Australia. *Acta Psychiatrica Scandinavica* 1981 **63** 75–82.
93 Walinder J. Incidence and sex ratio of transsexualism in Sweden. *British Journal of Psychiatry* 1968 **119** 195–196.
94 O'Gorman E. A retrospective study of epidemiological and clinical aspects of 28 transsexual patients. *Archives of Sexual Behavior* 1982 **11** 231–236.
95 Tsoi WF. The prevalence of transsexualism in Singapore. *Acta Psychiatrica Scandinavica* 1988 **78** 501–504.
96 Brzek A & Sipova L. Transsexuelle in Prag. *Sexualmedizin* 1983 **3** 110–112.
97 Godlewski J. Transsexualism and anatomic sex ratio reversal in Poland. *Archives of Sexual Behavior* 1988 **17** 547–548.
98 Reid RW. Aspects psychiatriques et psychologiques du transsexualisme. *Actes du XXIIIe Colloque de Droit Européen*, Vrije Universiteit Amsterdam, 1993.
99 Burns A, Farell M & Brown J. Clinical feature of patients attending a gender-identity clinic. *British Journal of Psychiatry* 1990 **157** 265–268.
100 Walker PA, Berger JC, Green R, Laub DR, Reynolds CL & Wolman L. Standards of care: the hormonal and surgical sex reassignment of gender dysphoric persons. *Archives of Sexual Behavior* 1985 **14** 79–90.
101 Planarsky K & Johnston R. The incidence and relationship of homosexual and paranoid features in schizophrenia. *Journal of Mental Sciences* 1962 **108** 604–615.
102 Gittleson NL & Levine S. Subjective ideas of sexual change in male schizophrenics. *British Journal of Psychiatry* 1966 **112** 779–782.
103 Gittleson NL & Dawson-Butterworth K. Subjective ideas of sexual change in female schizophrenics. *British Journal of Psychiatry* 1967 **113** 491–494.
104 Scherrer P & Pelletier JC. Du transsexualisme à la schizophrénie. *Annales Médicales et Psychologiques* 1972 **130** 609–635.
105 König P. A case of transsexualism in a female schizophrenic patient. *Wien Nervenheilk* 1973 **31** 167–175.
106 Haberman M, Hollingswordt F, Falek H & Michael RP. Gender identity confusion, schizophrenia and 47 XYY karyotype: a case report. *Psychoneuroendocrinology* 1975 **1** 207–209.

107 Edie A. Karo in an Anglo-Saxon Canadian. *Canadian Psychiatry Association Journal* 1976 **21** 389–392.
108 La Torre RA & Piper WE. Gender identity and gender role in schizophrenia. *Journal of Abnormal Psychology* 1979 **88** 68–72.
109 Commander M & Dean C. Symptomatic transsexualism. *British Journal of Psychiatry* 1990 **156** 894–896.
110 Caldwell C & Keshavan MS. Schizophrenia with secondary transsexualism. *Canadian Journal of Psychiatry* 1991 **36** 300–301.
111 De Cuypere G. Schizophrenia and symptomatic trans-sexualism: two case reports. *European Psychiatry* 1993 **8** 163–167.
112 Walinder J. *Transsexualism, a Study of Forty-three Cases*. Göteburg, Scandinavian University Books, 1967.
113 Lothstein LM & Roback H. Black female transsexuals and schizophrenia: a serendipitous finding? *Archives of Sexual Behavior* 1984 **13** 371–386.
114 Breton A. *Le Transsexualisme, Etude Nosographique et Médico-Légale*. Paris: Masson, 1985.
115 Steiner BW. Intake assessment of gender-dysphoric patients. In *Clinical Management of Gender Identity Disorders in Children and Adults*, pp 93–106. Eds R Blanchard & BW Steiner. Washington: American Psychiatric Press, 1990.
116 Peterson ME & Dickey R. Surgical sex reassignment: a comparative survey of international centers. *Archives of Sexual Behavior* 1995 **24** 135–156.
117 Cohen-Kettenis PT & Walinder J. Sex reassignment surgery in Europe: a survey. *Acta Psychiatrica Scandinavica* 1987 **75** 176–182.
118 Futterweit W. Endocrine therapy of transsexualism and potential complications of long term treatment. *Archives of Sexual Behavior* 1998 **27** 209–226.
119 Cohen-Kettenis PT & Gooren LJG. Transsexualism: a review of etiology, diagnosis and treatment. *Journal of Psychosomatic Research* 1999 **46** 315–333.
120 Obeizu CV, Giltay EJ, Yu H, Magklara A, Soosaipillai AR, Gooren JLG *et al.* Serum prostate specific antigen is significantly elevated after testosterone administration in female to male transsexuals. In *ENDO'99 The 81st Annual Meeting of the Endocrine Society*. San Diego, California, 1999, Abstract 0R29-4, 102.
121 van Kesteren P, Asscheman H, Megens J & Gooren LJG. Mortality and morbidity in transsexual treated with cross-sex hormones. *Clinical Endocrinology* 1997 **47** 347–354.
122 Gooren LJG, Assies J, Asscheman H, De Slegte R & van Kessel M. Ostrogen-induced prolactinoma in a man. *Journal of Clinical Endocrinology and Metabolism* 1988 **66** 444–446.
123 Mauras N, O'Brien K, Klein KO & Hayes V. Estrogen suppression in males: metabolic effects. *Journal of Clinical Endocrinology and Metabolism* 2000 **85** 2370–2377.
124 Lips P, Asscheman H, Uitewaal P, Netelenbos JC & Gooren LJG. The effect of cross-gender hormonal treatment on bone metabolism in male-to-female transsexuals. *Journal of Bone and Mineral Research* 1989 **4** 657–662.
125 van Kesteren P, Lips P, Deville W, Popp-Snijders C, Assechman H, Megens J *et al.* The effect of one-year cross-sex hormonal treatment on bone metabolism and serum insulin-like growth factor-1 in transsexuals. *Journal of Clinical Endocrinology and Metabolism* 1996 **81** 2227–2232.
126 Giltay E & Gooren LJG. Effect of sex steroid deprivation, administration on hair growth and skin sebum production in transsexual males and females. *Journal of Clinical Endocrinology and Metabolism* 2000 **85** 2913–2921.
127 van Goozen S, Cohen-Kettenis P, Gooren L, Frijda N & van de Pool N. Gender differences in behavior: activating effects of cross-sex hormones. *Psychoneuroendocrinology* 1995 **20** 343–363.
128 van Goozen S, Cohen-Kettenis P, Gooren L, Frijda N & van de Pool N. Activating effects of androgens on cognitive performance: causal evidence in a group of female to male transsexuals. *Neuropsychobiology* 1996 **32** 1153–1157.
129 Kuiper AJ & Cohen-Kettenis PT. Sex reassignment surgery: a study of 141 Dutch transsexuals. *Archives of Sexual Behavior* 1988 **17** 439–457.
130 Stürup G. Male transsexuals. A long-term follow-up after sex reassignment operations. *Acta Psychiatrica Scandinavica* 1976 **53** 51–63.
131 Hunt DD & Hampson JL. Follow-up of 17 biologic male transsexuals after sex-reassignment surgery. *American Journal of Psychiatry* 1980 **137** 432–438.
132 Stein M, Tiefer L & Melman A. Follow-up observations of operated male-to-female transsexuals. *Journal of Urology* 1990 **143** 1188–1192.
133 Hertz J, Tillinger KG & Westman A. Transvestism. *Acta Psychiatrica Scandinavica* 1961 **37** 283–294.
134 Pauly IB. Male psychosexual inversion: transsexualism. A review of 100 cases. *Archives of General Psychiatry* 1965 **13** 172–181.
135 Pauly IB. Outcome of sex-reassignment surgery for transsexuals. *Australian and New Zealand Journal of Psychiatry* 1981 **15** 45–51.
136 Lothstein LM. Sex reassigment surgery: historical, bioethical and theorical issues. *American Journal of Psychiatry* 1982 **139** 417–426.
137 Lundström B, Pauly I & Walinder J. Outcome of sex reassignment surgery. *Acta Psychiatrica Scandinavica* 1984 **70** 289–294.
138 Abramowitz SI. Psychosocial outcome of sex reassignment surgery. *Journal of Consulting and Clinical Psychology* 1986 **54** 183–189.
139 Green R & Fleming D. Transsexual surgery follow-up status in the 1990s. *Annual Review of Sex Research* 1990 **1** 163–174.
140 Michel A. *Le Changement de Sexe: une Métamorphose sans Conséquence?* Unpublished Doctoral Thesis, University of Liège, Liège, 2000.
141 Michel A. Le transsexuel: quel devenir? *Annales Médico-Psychologiques* 2001 **5** 1–11.
142 Pfäfflin F. Regrets after sex reassignment surgery. In *Gender Dysphoria, Interdisciplinary Approaches in Clinical Management*, pp 69–86. Eds WO Bockting & E Coleman. Binghamton, New York: The Haworth Press, 1992.
143 Kuiper AJ. *Transseksualiteit. Evaluatie van de Geslachtsaanpassende Behanding*. Unpublished Doctoral Thesis. Amsterdam: Vrije Universiteit te Amsterdam, 1991.
144 Pfäfflin F & Junge A. *Nachuntersuchungen nach Geschlechusumwandlung: eine Kemmentierte Literatureubersicht 1961–1991*. Stuttgart: Scahttauer, 1992.
145 Walinder J & Thuwe I. A social-psychiatric follow-up study of 24 sex-reassigned transsexuals. *Reports from the Psychiatric Research Center*. St Jorgen's Hospital, University of Gothenberg, Sweden, Akademiforlager, 1975.
146 Hastings M. Postsurgical adjustment of male transsexual patients. *Clinics in Plastic Surgery* 1974 **1** 335–344.
147 Lindemalm G, Korlin D & Uddenberg N. Pronostic factors vs. outcome in male-to-female transsexualism. A follow-up study of 13 cases. *Acta Psychiatrica Scandinavica* 1987 **75** 268–274.
148 Blanchard R, Steiner BW, Clemmensen LH & Dickey R. Prediction of regrets in postoperative transsexuals. *Canadian Journal of Psychiatry* 1989 **34** 43–45.
149 Ross MW & Need JA. Effects of adequacy of gender reassignment surgery on psychology and adjustments: a follow-up of fourteen male-to-female patients. *Archives of Sexual Behavior* 1989 **18** 145–153.
150 Johnson S & Hunt DD. The relationship of male transsexual typology to psychosocial adjustment. *Archives of Sexual Behavior* 1990 **19** 349–360.
151 Doorn CD. *Towards a Gender Identity Theory of Transsexualism*. Unpublished Doctoral Thesis, Vrije Universiteit te Amsterdam, Amsterdam, 1997.

Received 6 April 2001
Accepted 30 May 2001