

ORIGINAL RESEARCH—INTERSEX AND GENDER IDENTITY DISORDERS

The Treatment of Adolescent Transsexuals: Changing Insights

Peggy T. Cohen-Kettenis, PhD,^{*§} Henriette A. Delemarre-van de Waal, MD, PhD,^{†§} and Louis J. G. Gooren, MD, PhD^{‡§}

^{*}Department of Medical Psychology, VU University Medical Center, Amsterdam, The Netherlands; [†]Department of Pediatric Endocrinology, VU University Medical Center, Amsterdam, The Netherlands; [‡]Department of Endocrinology, VU University Medical Center, Amsterdam, The Netherlands; [§]Institute for Clinical and Experimental Neurosciences, VU University Medical Center, Amsterdam, The Netherlands

DOI: 10.1111/j.1743-6109.2008.00870.x

ABSTRACT

Introduction. Treatment of individuals with gender identity disorder (GID) has in medicine nearly always met with a great deal of skepticism. Professionals largely follow the Standards of Care of the World Professional Association for Transgender Health. For adolescents, specific guidelines have also been issued by the British Royal College of Psychiatrists.

Aim. To describe the stepwise changes in treatment policy which, in recent years, have been made by the team of the Gender Identity Clinic at the VU University Medical Center in Amsterdam, The Netherlands.

Methods. The first step taken to treat adolescents was that, after careful evaluation, (cross-sex hormone) treatment could start between the ages of 16 and 18 years. A further step was the suppression of puberty by means of gonadotropin-releasing hormone analogs in 12–16 year olds; the latter serves also as a diagnostic tool. Very recently, other clinics in Europe and North America have followed this policy.

Results. The first results from the Amsterdam clinic show that this policy is promising.

Conclusions. Professionals who take responsibility for these youth and are willing to help should yet be fully aware of the impact of their interventions. In this article, the pros and cons of the various approaches to youngsters with GID are presented, hopefully inciting a sound scientific discussion of the issue. **Cohen-Kettenis PT, Delemarre-van de Waal HA, and Gooren LJG. The treatment of adolescent transsexuals: Changing insights. J Sex Med 2008;5:1892–1897.**

Key Words. Transsexualism; Gender Identity Disorder; Sex Reassignment; Gender Dysphoria; GnRH Analogs; Adolescents

Introduction

Sex reassignment for individuals with gender identity disorder (GID), often called transsexuals, has in medicine nearly always met with a degree of skepticism and equivocation [1–5]. McHugh [5], for example, stated that he found it hard to understand how the belief of a man “that he is a woman trapped in a man’s body differs from the feelings of a patient with anorexia nervosa that she is obese despite her emaciated, cachectic state. We don’t do liposuction on anorexics. So why

amputate the genitals of these patients?” (p. 111). Rather than seen as a way to relief psychic pain, sex reassignment is regarded as “tampering” with the integrity of a healthy body. Such views are even more outspoken when it comes to the treatment of young people. It is felt that, if ever, only in adulthood gender identity is sufficiently consolidated to allow for decisions regarding invasive, and irreversible interventions such as hormonal and surgical therapy [2].

With the state of the art medicine in 2008, the (patho-) biological basis of GID is still poorly

understood, and its diagnosis relies totally on psychological methods. Research on post mortem brains of male-to-female transsexuals (MtFs) and one female-to-male transsexual (FtM) has demonstrated that one of the sex-dimorphic brain nuclei, the central part of the bed nucleus of the stria terminalis, shows all characteristics of opposite—sex differentiation [6,7]. Unfortunately, these brain structures are too small in size to visualize with presently available imaging techniques of the brain, and the (temporal) relationship between the development and size of these brain structures and the development of a GID is far from clear. This implies that the diagnosis of GID still relies on a subjective report of a person verified by a mental health professional using diagnostic criteria as spelled out in the widely used psychiatric classification system Diagnostic and Statistical Manual of Mental Disorders IV-TR [8]. Because of the far-reaching nature of the interventions, professionals largely follow the Standards of Care [9] of the World Professional Association for Transgender Health, formerly called the Harry Benjamin International Gender Dysphoria Association. For adolescents, specific guidelines also exist of the British Royal College of Psychiatrists [10]. In both guidelines, the diagnostic process is lengthy and takes place in several stages. This is important because 80–95% of the prepubertal children with GID will no longer experience a GID in adolescence [11–13]. First, there is a diagnostic phase in which the actual diagnosis of GID is made, and an estimation is made of potential risk factors for post-treatment regret. Then, during a phase called the “real life test” or “real life experience,” both clinician and patient check whether the applicant is able to live satisfactorily in the desired gender role. Only if the real life experience had been successful, the applicant will be eligible for sex reassignment surgery (SRS).

Some find a diagnostic process as described, especially for young applicants, a less than solid foundation for a medical intervention impinging on the physical integrity of the body [2]. They refer to classical medical ethical adages such as “in dubio abstinere” (when in doubt, abstain from intervention) and “primum non nocere” (first, do no harm). For a long time, health professionals have waited till their patients have reached young adulthood, or, in general, the age of legal consent to medical treatment, even though these adolescents make very clear that they find their pubertal physical changes unbearable.

Besides the professional consideration that the condition can only be diagnosed with certainty in adulthood (see also below), some health care providers might also fear disapproval of the peer group, reactions of the correctional medical boards, or litigation.

Changes in Policy

The Amsterdam VU university medical center treats 98% of the Dutch transsexuals. About 20 years ago, when a few adolescents with an overwhelming and clear-cut GID came to the attention of clinicians [14], the decision was taken to start the sex reassignment (SR) procedure before adulthood. Despite many years of psychotherapy, gender dysphoria had not abated in these youngsters. Many of the problems they were struggling with seemed to be the consequence rather than the cause of their GID. They were very lucid about their situation, had no psychopathology that would obtrude their self-assessment, and were able to cope with the process of transitioning to the other sex. There was also strong parental support for the treatment decision. This convinced us to make a change in policy and we decided to treat subjects younger than 18 years hormonally. Males were treated with anti-androgens first and with estrogens a few months later provided they appeared to do well; females were treated first with progesterone to stop menstrual bleeding and androgens later [15]. The minimum age set then for this treatment was 16 years. Although, in the Netherlands, adolescents are from the age of 16 years on legally competent to make decisions on their medical treatment, parents were required to endorse the request for treatment, which always was the case. Parents had been involved in the earlier diagnostic process and were of the conviction that hormonal and subsequent surgical treatment was the only acceptable solution to alleviate the suffering of their child.

In several studies this protocol has been evaluated [16–18]. From these studies it appeared that the youth who were selected for early hormone treatment (starting between 16 and 18 years) no longer suffered from gender dysphoria, and that 1–5 years after surgery, they were socially and psychologically functioning not very different from their peers. Their scores on various psychological instruments, such as a shortened Dutch form of the Minnesota Multiphasic Personality Inventory and the Symptom Check List-90 [19], were considerably more favorable than scores of a group of

subjects who had been treated in adulthood in the Amsterdam clinic, and scores were in the normal range as compared to normative samples. By contrast, there was also a cohort of adolescents presenting with gender dysphoria, who after long-term assessment (which, depending on the degree of gender dysphoria and nonrelated pathology, could take a year or even longer) were not deemed eligible for early treatment, and they did not pursue SR at later ages. So, the burden of the GID, the unabating pursuit of SR, and clinical assessment provided by our clinic appeared to provide acceptable selection criteria for good candidates for SR before adulthood. Over the last 5–6 years the age of adolescents applying for SR has dropped considerably. It is no longer unusual to have 12-year-olds presenting at gender identity clinics with the wish to undergo SR. Most are accompanied and supported by their parents. These youngsters are no longer willing to wait for many years, knowing that the alienating experience of development of the secondary sex characteristics of their biological sex by then will have been completed and can only be incompletely reversed at a high price of medical interventions. Clinics with a good deal of experience with gender dysphoric juveniles such as in Gent, Boston, Oslo, and Toronto recently started to offer (or refer for) medical interventions before the age of 16 years provided hormonal puberty has started, and has progressed to at least Tanner stage 2. Other criteria for a start with gonadotropin-releasing hormone (GnRH) analogs are: (i) a presence of gender dysphoria from early childhood on; (ii) an increase of the gender dysphoria after the first pubertal changes; (iii) an absence of psychiatric comorbidity that interferes with the diagnostic work-up or treatment; (iv) adequate psychological and social support during treatment; and (v) a demonstration of knowledge and understanding of the effects of GnRH, cross-sex hormone treatment, surgery, and the social consequences of sex reassignment. Treatment consists of administration of GnRH analogs blocking the hormonal puberty of their biological sex. No cross-sex hormones are administered at this stage. In our view, these early hormonal interventions should not be considered as sex reassignment per se. Their effects are reversible. By blocking, delaying or “freezing” puberty by means of GnRH analogs time is “bought” [20]. The peace of mind of the adolescent provides more opportunity to explore with the mental health professional the applicant’s wish for SR thoroughly. The prospect of the

alienating experience of developing sex characteristics, which they do not regard as their own, will not occur. It is also proof of solidarity of the health professional with the plight of the applicant. Yet many professionals are reluctant to treat youth with GID with GnRH analogs. They reason that before a GID can be regarded as unremitting, the brain must have been fully exposed to the hormones of puberty of the sex one is born in. There is, however, no evidence from brain research to support this contention.

Arguments Pro-Pubertal Delay

There are a number of reasons for allowing adolescents to start with the GnRH analogs.

First, delaying the start of treatment (even under 16 years) has its psychological drawbacks. Some individuals who have shown a pattern of extreme cross-sex identification from toddlerhood onwards develop psychological problems, such as depression, suicidality, anorexia, or social phobias, which are consequences of the agony about the pubertal physical development rather than comorbidity unrelated to the GID. This burden can adversely affect social and intellectual development. Patients and their parents often report that halting the physical features of puberty is an immediate relief of the patients’ suffering.

Second, pubertal suppression may give adolescents, together with the attending health professional, more time to explore their gender identity, without the distress of the developing secondary sex characteristics. The precision of the diagnosis may thus be improved.

Third, the child who will live permanently in the desired gender role as an adult may be spared the torment of (full) pubescent development of the “wrong” secondary sex characteristics (e.g., a low voice and male facial features for the ones who will live as women, and breasts and a short stature [males are on average 12 cm taller than women] for the ones who will live as men). This is obviously an enormous and life-long disadvantage. Ross and Need [21] found that postoperative psychopathology was primarily associated with factors that made it difficult for transsexuals to pass postoperatively successfully as members of their new sex. If the adolescents would make a social gender change without receiving hormone treatment, they may fail to be perceived by others as a member of the desired sex and be easy targets for harassment or violence.

Fourth, early treatment will likely make certain forms of surgery redundant or less invasive (e.g., breast reduction in FtMs and maxillo-facial surgery in MtFs).

Fifth, follow-up studies among adult transsexuals show that unfavorable postoperative outcome seems to be related to a late rather than an early start of the sex reassignment procedure (for reviews, see [22–24]). Age at time of assessment also emerged as a factor differentiating two groups of MtFs with and without postoperative regrets [25].

Sixth, youth who have no access to regular treatment may try to find illicit sources of medication (Internet and older peers) and turn away from any professional health care all together.

There is increasing evidence that GID is not a matter of choice or caused (solely) by environmental factors, such as poor parenting. We are still far from understanding which factors are necessary or sufficient for an atypical gender identity development [26]. Biological factors do seem to play a role [6,7,27–29] and may contribute to persistent GID (see below).

Arguments Against Pubertal Delay

Some assume that it is not possible to make a definitive diagnosis of GID in adolescence, because in this developmental phase gender identity is still fluctuating; others fear that preventing secondary sex characteristics to develop will inhibit a “spontaneous formation of a consistent gender identity, which sometimes develops through the ‘crisis of gender’” (see also [30]). These points raise the question of what is actually known about the persistence of GID in juveniles. If childhood GID does not persist over time it would be less than desirable to provide early somatic treatment. As mentioned earlier, symptoms of GID at prepubertal ages decrease or even disappear in a considerable percentage of children (estimates range from 80–95%) [11,13]. Therefore, any intervention in childhood would seem premature and inappropriate. However, GID persisting into early puberty appears to be highly persistent [31]: at the Amsterdam gender identity clinic for adolescents, none of the patients who were diagnosed with a GID and considered eligible for SR dropped out of the diagnostic or treatment procedures or regretted SR [16–18]. Even some of those who were not eligible to start treatment before the age of 18 years because of serious psychiatric comorbidity, extremely adverse living circumstances, or a combination of both,

persisted in their wish for SR. Because their other problems had to be addressed before they were regarded eligible to start SR successfully, their treatment was usually delayed until after 18 years of age.

Another potential risk of blocking pubertal development relates to the development of bone mass and growth, both typical events of hormonal puberty, and of brain development. In theory, peak bone mass may not be achieved and/or there might be body segment disproportion. However, the first data of a Dutch cohort of adolescents who have been treated with GnRH analogs suggest that, after an initial slowing in bone maturation, it significantly caught up after the commencement of cross-sex steroid hormone treatment [32]. A parallel may be drawn with children with a (constitutionally) delayed puberty who are similarly exposed to sex steroids beyond the normal age of puberty. There are indications that these children develop a lower bone mineral density than children who go through puberty at a normal age but the differences are not large [33]. It has also been reported that these differences might be attributed to the methods of measuring properties of bone [33,34]. Body proportions, as measured by sitting height and sitting-height/height ratio, remained in the normal range [32]. Early treatment may result in a final height for MtFs that is in the normal female range. For FtMs, a timely administration of oxandrolone may result in acceptable male height [32]. Effects of suppression of the hormones of puberty on brain development are currently studied, and not known yet. Clinically, there seem to be no effects on social, emotional, and school functioning, but potential effects may be too subtle to observe during the follow-up sessions by clinical assessment alone.

Finally, for the MtFs a non-normal pubertal phallic growth, the genital tissue available for vaginoplasty may be less than optimal. However, appropriate adjusted techniques exist to deal with the shortage of tissue [35].

Ethical and Legal Aspects

Are adolescents able to make their own decisions when it comes to medical treatment? According to Dutch law, adolescents from 16 years on are legally competent to make a treatment choice, even without parental consent, because it is assumed that they are able to fully understand the pros and cons of a treatment. These, and possible alternative treatments, should have been explained

completely and repeatedly to the patient in the course of the diagnostic procedure. Under Dutch law, if children are between 12 and 16, they can also make treatment decisions, but at this age they still need the consent of their parents.

Some argue that it is not possible to give valid informed consent to hormonal suppression of puberty, because the risks of it are partially unpredictable. Giordano [30] points out that if it were impossible to consent to interventions whose outcome is uncertain, much medical research involving human beings would be unethical. Indeed, much research is done *because* the outcome is not known. Naturally, in order to give valid consent, the applicant must receive as complete as possible information about treatment, and has to be informed about the unknown risks of each stage of therapy. The person will then consider and weigh the unknown risks of treatment and the potential benefits on one side, and all the known psychological and physical effects of nontreatment on the other. It will be clear that in the case of a complex treatment such as SR, informed consent is not given at a single point in time. Rather, it is a process during which the adolescent is progressively more able to understand what the decision is all about.

Finally, in judging the desirability of hormonal pubertal suppression as a first but reversible phase in the sex reassignment procedure, one should not only take consequences of the intervention into account. Rather, one should also consider the consequences of nontreatment. Nonintervention is not a neutral option, but has clear negative life-long consequences for the quality of life of those individuals who had to wait for treatment until after puberty. It may lead to irresponsible and risky, unhealthy actions of the patient in order to get access to the desired medication, distrust against professionals, with negative consequences for other aspects of their health care. It may lead to developmental arrest, and a psychological functioning forever hampered by shame about one's appearance. This implies that "in dubio abstine" may actually be harmful. Not different from other endeavors in medicine, the care for gender dysphoric juveniles must be open to peer review and scientific scrutiny, which has always featured high on the agenda of the Dutch health care for transgendered subjects.

Realizing the potential harmfulness of nonintervention, one may wonder whether not providing treatment may not only be doubtful on ethical grounds, but also have legal implications [36].

In the field of treatment of young adolescents, it may be that the adage "in dubio abstine" needs to be reconsidered. Particularly when there are research opportunities to lessen this "dubium" to the benefit of those who suffer from gender dysphoria.

Corresponding Author: Peggy T. Cohen-Kettenis, PhD, Department of Medical Psychology, PO Box 7057, 1007 MB Amsterdam, The Netherlands. Tel: (31) 20-4442550; Fax: (31) 20-4443077; E-mail: PT.Cohen-Kettenis@vumc.nl

Conflict of Interest: None declared.

References

- 1 Beatrice J. A psychological comparison of heterosexuals, transvestites, preoperative transsexuals, and postoperative transsexuals. *J Nerv Ment Dis* 1985;173:358–65.
- 2 à Campo J, van Os J. Reaction to: "Van Campen YE, Duyx, JHM, Cohen-Kettenis PT. Transseksuele adolescenten voor de behandeling: Achtergronden en functioneren ("Transsexual Adolescents Before Treatment: Background Data and Functioning," Published In *Tijdschr Psychiat*. 2003;45, 193–201). *Tijdschr Psychiat* 2003;45:649–50.
- 3 Chiland C. The psychoanalyst and the transsexual patient. *Int J Psychoanal* 2000;81:21–35.
- 4 Federoff JP. The case against publicly funded transsexual surgery. *Psychiatr Rounds* 2000;4:1–3.
- 5 McHugh PR. Witches, multiple personalities and other psychiatric artifacts. *Nat Med* 1995;1:110–4.
- 6 Zhou J, Hofman MA, Gooren LJ, Swaab DF. A sex difference in the human brain and its relation to transsexuality. *Nature* 1995;378:68–70.
- 7 Kruijver FP, Zhou J, Pool C, Hofman MA, Gooren LJ, Swaab DF. Male-to-female transsexuals have female neuron numbers in a limbic nucleus. *J Clin Endocrinol Metab* 2000;85:2034–41.
- 8 American Psychiatric Association. Diagnostic and statistical manual of mental disorders DSM-IV-TR, 4th edition. Washington, DC: American Psychiatric Association; 2000.
- 9 Meyer W, Bockting W, Cohen-Kettenis PT, Coleman E, DiCeglie D, Devor H, Gooren LJG, Hage JJ, Kirk S, Kuiper AJ, Laub D, Lawrence A, Menard Y, Patton J, Schaefer L, Webb A, Wheeler CC. The Standards of Care of the Harry Benjamin International Gender Dysphoria Association, 6th version. *Int J Transgenderism* 2006;5. Available at: <http://www.symposium.com/ijt>.
- 10 DiCeglie D, Sturge C, Sutton A. Gender identity disorders in children and adolescents: Guidelines for management. London, Royal College of Psychiatrists; Council Report CR63; 1998.
- 11 Cohen-Kettenis PT. Gender identity disorder in the DSM? *J Am Acad Child Psy* 2001;40:391.

- 12 Drummond KD, Bradley SJ, Peterson-Badali M, Zucker KJ. A follow-up study of girls with gender identity disorder. *Dev Psychol* 2008;44:34–45.
- 13 Zucker KJ, Bradley SJ. Gender identity disorder and psychosexual problems in children and adolescents. New York/London: Guilford Press; 1995:283–301.
- 14 Cohen-Kettenis PT, Pfäfflin F. Transgenderism and intersexuality in childhood and adolescence; Making choices. Thousand Oaks: Sage; 2003:131–51.
- 15 Gooren LJ, Delemarre-van de Waal HA. The feasibility of endocrine interventions in juvenile transsexuals. *J Psychol Hum Sex* 1996;8:69–74.
- 16 Cohen-Kettenis PT, van Goozen SH. Sex reassignment of adolescent transsexuals: A follow-up study. *J Am Acad Child Adolesc Psychiatry* 1997;36:263–71.
- 17 Smith YL, van Goozen SH, Cohen-Kettenis PT. Adolescents with gender identity disorder who were accepted or rejected for sex reassignment surgery: A prospective follow-up study. *J Am Acad Child Adolesc Psychiatry* 2001;40:472–81.
- 18 Smith YL, van Goozen SH, Kuiper AJ, Cohen-Kettenis PT. Sex reassignment: Outcomes and predictors of treatment for adolescent and adult transsexuals. *Psychol Med* 2005;35:89–99.
- 19 Kuiper AJ, Cohen-Kettenis PT. Sex reassignment surgery: A study of 141 Dutch transsexuals. *Arch Sex Behav* 1988;17:439–57.
- 20 Cohen-Kettenis PT, van Goozen SH. Pubertal delay as an aid in diagnosis and treatment of a transsexual adolescent. *Eur Child Adolesc Psychiatry* 1998;7:246–8.
- 21 Ross MW, Need JA. Effects of adequacy of gender reassignment surgery on psychological adjustment: A follow-up of fourteen male-to-female patients. *Arch Sex Behav* 1989;18:145–53.
- 22 Cohen-Kettenis PT, Gooren LJ. Transsexualism: A review of etiology, diagnosis and treatment. *J Psychosom Res* 1999;46:315–33.
- 23 Pfäfflin F, Junge A. *Geschlechtsumwandlung: Abhandlungen zur Transsexualität*. Schattauer: Stuttgart; 1992.
- 24 Pfäfflin F, Junge A. Sex reassignment: Thirty years of international follow-up studies. A comprehensive review, 1961–91. 1998. Available at: <http://www.symposium.com/ijt/books/index.htm>.
- 25 Blanchard R, Steiner BW, Clemmensen LH, Dickey R. Prediction of regrets in postoperative transsexuals. *Can J Psychiat* 1989;34:43–5.
- 26 Gooren LJ. The biology of human psychosexual differentiation. *Horm Behav* 2006;50:589–60.
- 27 Coolidge FL, Thede LL, Young SE. The heritability of gender identity disorder in a child and adolescent twin sample. *Behav Genet* 2002;32:251–7.
- 28 Henningson S, Westberg L, Nilsson S, Lundstrom B, Ekselius L, Bodlund O, Lindstrom E, Hellstrand M, Rosmond R, Eriksson E, Landén M. Sex steroid-related genes and male-to-female transsexualism. *Psychoneuroendocrinology* 2005;30:657–64.
- 29 Knafo A, Iervolono AC, Plomin R. Masculine girls and feminine boys: Genetic and environmental contributions to atypical gender development in early childhood. *J Pers Soc Psychol* 2005;88:400–12.
- 30 Giordano S. Gender atypical organisation in children and adolescents: Ethico-legal issues and a proposal for new guidelines. *The International Journal of Children's Rights* 2007;15:365–90.
- 31 Wren B. Early physical intervention for young people with atypical gender identity development. *Clin Child Psychol Psychiatry* 2000;5:220–3.
- 32 Delemarre-van de Waal HA, Cohen-Kettenis PT. Clinical management of gender identity disorder in adolescents: A protocol on psychological and paediatric endocrinology aspects. *Eur J Endocrinol* 2006;155:S131–7.
- 33 Vanderschueren D, Vandenput L, Boonen S, Lindberg MK, Bouillon R, Ohlsson C. Androgens and bone. *Endocr Rev* 2004;25:389–425.
- 34 Bertelloni S, Baroncelli GI, Ferdeghini M, Saggese G. Normal volumetric bone mineral density and bone turnover in young men with histories of constitutional delay of puberty. *J Clin Endocrinol Metab* 1998;83:4280–3.
- 35 Kapoor R, Sharma DK, Singh KJ, Suri A, Singh P, Chaudhary H, Dubey D, Mandhani A. Sigmoid vaginoplasty: Long term results. *Urology* 2006; 67:1212–5.
- 36 Whittle S. *Respect and equality: Transsexual and transgender rights*. London: Cavendish Publishing Company; 2002.