

# The Feasibility of Endocrine Interventions in Juvenile Transsexuals

Journal of Psychology & Human Sexuality, Vol. 8(4) 1996 ©1996 by The Haworth Press, Inc. All rights reserved.

Louis Gooren is Endocrinologist and Professor of Transsexuality, and Henriette Delamarre-van de Waal is Professor of Pediatric Endocrinology, both affiliated with the Hospital of the Vrije Universiteit in Amsterdam, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands.

Louis Gooren, PhD  
Henriette Delamarre-van de Waal, PhD

## INTRODUCTION

A large number of adult transsexuals recall that their gender dysphoria started early in life, well before puberty. They remember puberty with abhorrence, since the hormones of puberty precisely induced the body characteristics they perceived as improper in relation to their gender identity. The latter often reinforced their determination to rid themselves from the primary and secondary sex characteristics. For most of them, the time and period they grew up in provided not much room for the expression of their gender dysphoria; they themselves often would not even know how to label themselves until they learned about the phenomenon of transsexuality. They all agree that this period in their lives has been a vexation.

An incongruence between gender identity/role can indeed be observed at an early age, as young as four years of age. Zucker, Kuksis, and Bradley (1988) have reported that there are young children who, from the moment they can talk, show their dissatisfaction with the sex they are being raised in and behave as a child of the opposite sex. These children are aware of their genital sex and often hope that a "magical" solution for their problem will happen one day.

With an expanding public information about transsexualism, parents and caretakers seek professional advice for these gender atypical children. Not all children with gender atypicality will turn out to be transsexuals later in life. Several prospective studies of gender atypical boys show that this childhood behavior correlates considerably stronger with future homosexuality than with transsexualism (Green 1987; Money and Russo 1979; Zuger 1984).

Now that juvenile persons with gender problems come more frequently to the attention of the psychomedical care system, some of the youngsters will turn out to be genuinely transsexual in their mid-teen years; that is, there is no reasonable expectation that their cross-sexed gender identity will evermore change (Cohen-Kettenis 1994, 1995). The interests of such adolescents could be served with an early start of (cross-sex) hormone treatment to spare them the torments of developing the secondary sexual characteristics of a sex they view as not their own. It goes without saying that eligibility for hormone treatment of transgendered juvenile persons can only be the outcome of long-term observation by experts in the field. It obviously requires parental involvement in the decision until the age that they can legally make their own decision on medical interventions.

The aim of this contribution is to describe methods of hormonal treatment that might be of use in the above situation. The psychological indications for this treatment, as well as the legal implications of cross-sex (hormone) treatment of minors, is left aside. It is understood that the approach should be careful and cautious. It is to be remembered that giving, but also withholding endocrine treatment is a momentous and responsible decision from the side of the therapist with important implications for the person in question.

In the first instance, it may be preferable to halt the own hormonal pubertal development rather than induce hormonally a cross-sex development. There are endocrine tools available to achieve this; for the purpose we describe them, they have been mainly developed in the care of children with precocious puberty. Another approach is to suppress some expressions of pubertal development of the child in question, such as menstrual periods in young female-to-male transsexuals, leaving the female development as such for the time being intact.

## ENDOCRINE METHODS TO HALT THE OWN PUBERTAL DEVELOPMENT

There are several hormonal methods available, but luteinizing hormone-releasing hormone (LHRH) agonists are the drugs of choice. Both the testis and the ovary are for their sex hormone production dependent upon stimulation with the pituitary hormones, luteinizing hormone (LH) and follicle stimulation hormone (FSH); the latter hormones are in turn dependent on stimulation by a hypothalamic hormone (LHRH). The latter hormone can synthetically be manufactured and several chemical modifications have become available. Some of these modifications exert biologically an effect opposite to that of native LHRH: they bind so strongly to the pituitary that endogenous LHRH can no longer exert its effects, and therewith, the pituitary secretions of LH and FSH discontinues and subsequently the gonadal production of sex steroids. Such LHRH agonists induce therewith, so to say, again a prepubertal state of the

subject, so that the own puberty does not progress or even regresses. Or if given early enough, before the first sign of puberty, the own puberty will not come forth.

Several forms of LHRH agonists are available; they differ in their biopotency, their duration of action, and their route of administration. Their use is now widespread in the treatment of a number of conditions of adulthood, such as prostatic cancer in men, and of uterine myomas, polycystic ovarian syndrome, endometriosis, or fine-tuned ovulation induction in women. A number must be administered on a daily basis, either by subcutaneous injection or as a nasal administration. For the purpose mentioned above, the long-acting, depot-intramuscular preparations of LHRH analogues, such as depot leuprolide (Lucrin depot®, Abbot) or depot triptorelin (Decapeptyl®, Ferring), are probably the most suitable. The usual frequency of administration is every four weeks. The effects must be sustained and, therefore, excellent compliance is critical for success. But young transsexuals are usually keenly motivated to cooperate. LHRH agonists are efficacious. Their effects are present already after two weeks and after 4-12 weeks, sex steroid production is essentially stopped. During the first year of treatment, growth velocity and the rate of skeletal maturation decreases greatly if the subject was already going through puberty. The initial expectation was that, as a consequence of halting puberty with its eventual closure of the epiphyses, the final adult height will increase. This has not come true in clinical studies. The latter might have an advantage for juvenile female-to-male transsexuals who, when undergoing sex reassignment in adulthood, tend to be small men. The average woman in the Netherlands is 12 cm smaller than the average man.

The effects of LHRH analogues are fully reversible; in other words, no lasting undesired effects are to be expected. Upon discontinuation of the LHRH analogues, the hormonal activity of the own puberty is resumed within three months. Side effects are few, particularly when there is usage only for a limited period of 3-18 months, as will be the case with adolescent gender dysphoric persons. In their case, the issue is often that they themselves are highly motivated to start with cross-sex hormones, but the psychotherapist sometimes needs more time to work with this person, or parental approval is pending or the personal educational situation of the youngster makes it undesirable to start on cross-sex hormones now or legal regulations prevent a start on cross-sex hormones at this age. Treatment with LHRH agonists buys time for all parties in the decision whether or not to start cross-sex hormones while the person in question does not have the feeling that while this decision is weighed, the irrevocable and irremediable of the undesired own pubertal development speeds on. It follows that this process of decision making is limited in time, and therefore, side effects such as insufficient formation of bone mass (which occurs in cases of long-term sex steroid deficiency) are of no great concern in this type of patient.

As stated above, LHRH analogues are the drugs of choice for adolescents in this predicament, but if they are not available, two other compounds, both also used with some merits in the treatment of precocious puberty, can be considered: medroxyprogesterone acetate in both boys and girls and cyproterone acetate in boys. Medroxyprogesterone acetate is a progestational agent that can suppress LH and FSH, the pituitary hormones that stimulate the ovary and the testis. It is effective in halting the advancement of secondary sex characteristics in both sexes and in preventing menstrual periods in girls. This drug is available as an oral and an injectable preparation.

Medroxyprogesterone has weak androgenic effects on bone maturation and is a weak glucocorticoid. Side effects of long-term use of this compound are related to these pharmacological properties: adrenal suppression and cushingoid features with high doses and salt and water retention.

In juvenile male-to-female transsexuals, treatment with cyproterone acetate (Androcur®, Schering Pharma) may be considered. It is a progestational compound with strong antiandrogenic properties; it suppresses LH and FSH and counteracts the effects of testosterone on peripheral organs. It is not available in the USA. Its antiandrogenic properties give it an advantage over medroxyprogesterone. Side effects are similar. A degree of gynecomastia may develop with this treatment.

Other drugs that might be considered are ketoconazole; it is an antifungal agent that inhibits testosterone synthesis at the 17-20 lyase step, blocking the formation of androstenedione. Testolactone is an inhibitor of the enzyme aromatase that converts androgens to estrogens. Serum estradiol levels fall upon administration of this drug and skeletal maturation is slowed, which may be an advantage in juvenile female-to-male transsexuals. Spironolactone is an aldosterone antagonist but it also has potent antiandrogenic properties by inhibiting the binding of androgens to their receptors in the target organs. The clinical experience with the latter drugs is not so extensive as with medroxyprogesterone and of late LHRH agonists.

## SUPPRESSION OF SOME ASPECTS OF THE OWN PUBERTAL DEVELOPMENT

Teenage transsexuals may be helped if some expression of belonging to the loathed sex can be suppressed. For young female-to-male transsexuals, menstrual periods can be upsetting. This can be achieved by low dose progestins. They are also used as progestin only minipills in female contraception, but must in the case of transsexuals be given without interruptions. The dose is so fine-tuned low that the tablet must be taken each day at the same time. Examples are lynestrenol 0,5 mg (Exluton®) and levonorgestrol 0.030 mg. Older preparations with a higher progestin content are lynestrol 5mg (Orgametril®, Organon) and norethisterone 5mg (Primolut N®, Schering Pharma). For young male-to-female transsexuals, erections and nocturnal emissions may be a painful reminder of unwanted boyhood. These can be suppressed with cyproterone acetate (Androcur®, Schering Pharma) in a dose of 1/2 to 1 tablet of 50 mg. Gynecomastia may be a side effect and this may not be wholly irreversible. Recently its safety has been questioned on the basis of animal experimentation, but in its long-term clinical use it has been found to be safe.

## CONCLUSION

Teenagers with gender problems come to the attention of the psychomedical profession. Reversible hormonal treatment of juvenile transsexuals is breaking new ground, but the accounts of their impossible and distressing situation are realistic. Professionals dealing with this category cannot ignore their plight. Modern endocrinology can help to create a frame where in the juvenile transsexual and the therapist can work on the problem under less pressure of time rendering the gender problem more amenable to the right type of treatment.

## REFERENCES

Cohen-Kettenis, P.T. (1994). Die Behandlung von Kindern und Jugendlichen mit Geschlechtsidentitätsstörungen an der Universiteit Utrecht. *Zeitschrift fuer Sexualforschung*, 7, 231-239.

Cohen-Kettenis, P.T. (1995). Replik auf Bernd Meyenburgs Kritik der hormonellen Behandlung Jugendlicher mit Geschlechtsidentitätsstörungen. *Zeitschrift fuer Sexualforschung*, 8, 165-167.

Green, R. (1987). *The "sissy boy syndrome" and the development of homosexuality*. New Haven: Yale University Press.

Money, J. and Russo, A.J. (1979). Homosexual outcome of discordant gender identity/role: Longitudinal follow-up. *Journal of Pediatric Psychology*, 4, 29-41.

Zucker, K.S., Kuksis, M., and Bradley, S.J. (1988). Gender constancy judgements in cross-gender identified children. Paper at the 14th annual meeting of the International Academy of Sex Research, Minneapolis, MN.

Zuger, B. (1984). Early effeminate behavior in boys: Outcome and significance for homosexuality. *Journal of Nervous and Mental Disease*, 172, 90-97.