



Rostrum

## Buying time or arresting development? The dilemma of administering hormone blockers in trans children and adolescents

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ABSTRACT

In recent years, the use of gonadotropin-releasing hormone (GnRH) analogues in adolescents with gender dysphoria (GD) to suppress puberty has been adopted by an increasing number of gender clinics, generating controversial debate. This short essay provides an overview of the difficulties associated with this heterogeneous group of adolescents and discusses arguments for and against the suspension of puberty. Further, it reviews the main follow-up studies conducted in some of the world's largest clinical centres for gender-variant children and adolescents.

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*How long have I been here, what a question, I've often wondered.  
And often I could answer, An hour, a month, a year, a century,  
depending on what I meant by here, and me, and being.*

-Samuel Beckett

Gender-variant children and adolescents compose a heterogeneous group of persons who present an incongruence between their perceived gender identity and the gender to which they were assigned at birth. This incongruence can cause significant distress (gender dysphoria) and may require clinical intervention. The complex phenomenon of gender dysphoria (GD) is described in detail in the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*.<sup>1</sup>

Over the last 20 years, youth referrals to gender clinics have dramatically increased. In Europe, the two largest gender clinics for children and adolescents are the Gender Identity Development Service (GIDS) in London and the VU University Medical Center in Amsterdam. Both centres have witnessed a significant increase in referrals over the past 10 years (e.g. in London, referrals increased from 97 to more than 2000 between 2009/2010 and 2016/2017<sup>a</sup>), along with an impressive decrease in the mean age of referred clients and an inversion in the sex ratio of referrals to favour natal females.<sup>2,3</sup> Research on children and adolescents with GD or gender variance (GV) is sparse. However, some findings are emerging.<sup>4,5</sup> It

is now acknowledged, for instance, that children's GD/GV persists after puberty in only 10–30 per cent of all cases; when it does not, the children are referred to as 'desisters'.<sup>1,5</sup> At present, there is no way to predict which individuals will or will not suffer from GD into adolescence or adulthood. However, 'persisters', whose GD continues into adolescence, are more likely to experience GD in adulthood (to a degree of almost 80 per cent).<sup>6,7</sup>

Whether or not GD persists, gender-variant children are at risk of suffering many psychological adversities, mostly linked to body dissatisfaction (e.g.<sup>8</sup>) and a lack of acceptance within the family and social environment (e.g.<sup>9</sup>). Children with GD have been shown to be more psychologically vulnerable in comparison to the general population (e.g.<sup>10–12</sup>). Their psychological problems seem to be of a more internalised nature (e.g. depression, anxiety, eating disorders) than an externalising nature.<sup>10,12,13</sup> However, there is considerable variability across studies (for an overview, see<sup>14</sup>). For these children, family and peer relations are generally poorer than for non-referred children (e.g.<sup>10,15</sup>). As Bandini and colleagues<sup>16</sup> point out, it has been demonstrated that children showing gender variance are at higher risk for maltreatment and abuse.<sup>17,18</sup> Moreover, some studies have reported a high frequency in trans persons of childhood sexual and physical abuse, perpetrated by parents and caregivers (e.g.<sup>19–21</sup>). Finally, research has shown that trans youth are at higher risk of self-harm, suicidal ideation and suicidal attempts (e.g.<sup>22–24</sup>).

To address the clinical needs of such a complex population and to reduce their risk, specialised centres have developed various models of intervention. One of those, on which this short essay focuses, is the use of hormone blockers to suppress puberty.

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<sup>a</sup> Data presented by Bernadette Wren at the conference 'Hot Topics in Child Health: Transgender and Gender Diverse Children and Adolescents' held at the Royal College of Paediatrics and Child Health, London, June 2017.

This methodology is becoming increasingly common in several specialised centres. The intervention was developed by Dutch clinicians in the framework of a combined approach, including medical therapies as well as psychotherapy, social intervention and family work.<sup>25-28</sup> It consists of a fully reversible medical therapy that suspends pubertal development. Individuals who have reached Tanner stage 2 or 3<sup>29</sup> and are considered eligible for treatment<sup>b</sup> are administered gonadotropin-releasing hormone (GnRH) analogues, which temporarily suspend pubertal development. These analogues act on the pituitary gland, inhibiting hormone secretion and temporarily suppressing the endogenous production of oestrogen in girls and testosterone in boys. These hormones are sometimes called 'blockers', because they prevent the development of secondary sex characteristics. During this stage of treatment, in the absence of pubertal physical changes, the child is guided through an exploration of other gender roles, in order to experience congruence with the presumed innate gender identity. As Steensma and colleagues<sup>30</sup> point out, the suspension provides adolescents with GD 'time and rest before making definite decisions on gender reassignment without the distress of developing secondary sex characteristics'. Cohen-Kettenis and colleagues<sup>27</sup> consider it an extended diagnostic phase, in which the distress that the physical feminisation or masculinisation was producing is significantly reduced. For these authors, the early suppression entails great advantages for transitioning to the desired role throughout one's life, and thus minimises the harm to youth and maximises their opportunity for good social and sexual relationships. The process of passing to the other gender is made significantly easier.

The child normally also receives psychological assistance in determining whether or not to proceed to hormone therapy – specifically, the administration of cross-sex hormones, which is the first step in irreversible gender reassignment. Alternatively, she or he may interrupt therapy and revert to the assigned gender. Once endogenous sex hormone production is resumed, the pubertal development is thought to restart normally.<sup>31,32</sup>

Although the use of puberty suppressants is described in international guidelines, there is no consensus in the Endocrine Society Guidelines and the Standards of Care of the World Professional Association of Transgender Health.<sup>33,34</sup> The primary risks of pubertal suppression include adverse effects on bone mineralisation (which can theoretically be reversed with cross-sex hormone treatment) and compromised fertility; data on the effects on brain development are still limited.<sup>26,35</sup>

Several studies have proven the effectiveness of early medical interventions and the safety of these interventions with regard to physical and psychological harm. Overall, research has shown improved psychological functioning during suppression, no change of mind in terms of gender identity and the reduction or disappearance of distress related to GD; in addition, several studies have reported an increase in GD and harmful behaviour when blockers are not used.<sup>34,36</sup>

In their longitudinal study on the first 70 adolescents to receive puberty blockers, de Vries and colleagues<sup>37</sup> reported an improvement in general functioning after two years, along with a decrease in depression and behavioural and emotional difficulties. Fifty-five of these 70 individuals were assessed later in early adulthood, after cross-sex hormones had been administered and gender

reassignment surgery had been performed. Depressive symptoms had decreased, general mental health functioning had improved and no regret about transitioning was found. Many (about 70 per cent) reported that their social transition had been 'easy'. Cohen-Kettenis and colleagues,<sup>38</sup> in a 22-year follow-up of the first described adolescent treated with GnRH analogues and cross-sex hormones, reported overall improved psychological well-being and no clinical signs of adverse effects on the brain. An improvement in global functioning following puberty suppression was also found in the UK study of Costa and colleagues<sup>39</sup> in their follow-up of adolescents at the GIDS centre in London.

Consistent with the Dutch and British studies was Spack and colleagues' report<sup>40</sup> about their sample of 97 patients at a clinic in Boston, MA, in which no adolescents showed regrets regarding puberty blocking or subsequent cross-sex hormone use.

However, use of this intervention has only recently begun, so no other follow-up studies are available and many questions are still unanswered. Thus, many professionals remain critical about the puberty-blocking treatment (e.g.<sup>25,41,42</sup>). The primary counter-arguments are as follows:

1. At Tanner stage 2 or 3, the individual is not sufficiently mature or authentically free to take such a decision.<sup>25,41</sup>
2. It is not possible to make a certain diagnosis of GD in adolescence, because in this phase, gender identity is still fluctuating.<sup>25,41,42</sup>
3. Moreover, puberty suppression may inhibit a 'spontaneous formation of a consistent gender identity, which sometimes develops through the "crisis of gender"' (p. 375).<sup>43</sup>
4. Considering the high percentage of desisters, early somatic treatment may be premature and inappropriate.<sup>25</sup>
5. Research about the effects of early interventions on the development of bone mass and growth – typical events of hormonal puberty – and on brain development is still limited,<sup>7</sup> so we cannot know the long-term effects on a large number of cases.
6. Although current research suggests that there are no effects on social, emotional and school functioning, 'potential effects may be too subtle to observe during the follow-up sessions by clinical assessment alone' (p. 1895).<sup>25</sup>
7. The impact on sexuality has not yet been studied, but the restriction of sexual appetite brought about by blockers may prevent the adolescent from having age-appropriate socio-sexual experiences.<sup>41</sup>
8. In light of this fact, early interventions may interfere with the patient's development of a free sexuality and may limit her or his exploration of sexual orientation.<sup>41,42</sup>
9. Finally, for trans girls (natal boys with a female gender identification), the blockage of phallic growth may result in less genital tissue available for an optimal vaginoplasty.<sup>44</sup>

Vrouenraets and colleagues<sup>45</sup> conducted a remarkable study interviewing various professionals of 17 treatment teams of children and adolescents worldwide, finding that the majority of professionals recognised the distress of teens with GD/GV and felt that early intervention was urgently needed. At the same time, though many teams embraced the so-called 'Dutch approach', a general feeling of unease was expressed, due to the lack of long-term physical and psychological outcome studies. One of the main arguments in support of early intervention was limiting suicidal risk. Subsequently, the same group<sup>46</sup> interviewed trans adolescents. Surprisingly, the adolescents also seemed cautious. Many had doubts about the ability of a person so young to make such a significant decision, but they also emphasised the capital importance of preventing the development of secondary sexual characteristics. The adolescents seriously weighed the short- and long-term consequences of treatment, but this awareness did not stop them from wanting to suspend puberty.

<sup>b</sup> Eligibility criteria for hormone blockers 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' (Cohen-Kettenis et al., 2008, p. 1894).

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