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THE TECHNOLOGY OF PUBERTY SUPPRESSION

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The theory and practice of transsexualism were institutionalised in the mid-twentieth century by men like Harry Benjamin and John Money, who helped males who wished to become women. Transgenderism, as it emerged in the 1990s, was created primarily by women and eventually recruited more young females than young males wanting to change sex. One of the progenitors of transgenderism was Judith Butler, the famous American academic theorist of gender. Her books articulated the negative axiom that gender bears no relation to sex and the positive axiom that gender is essential to the self (see Jones, this volume). Just as important, but less renowned, was a Dutch psychologist, Peggy Cohen-Kettenis. She was largely responsible for inventing a technology that promised to transform boys into women and girls into men. While the discursive theory of transgenderism was formulated at Berkeley, the endocrinological practice was assembled in Utrecht and Amsterdam. This chapter examines the origin of puberty suppression in the Netherlands in the 1990s, scrutinising the rationale for this intervention. It then traces the subsequent adoption of this Dutch protocol in the United States and Britain down to the 2010s. The chapter concludes by evaluating recent evidence for the outcomes of puberty suppression.

Gender dysphoria is used here to describe a persistent desire to escape one's natal sex. Medical terminology has changed over time, from 'gender identity disorder' and 'transsexualism' (both introduced in the *Diagnostic and Statistical Manual of Mental Disorders III*; American Psychiatric Association 1980) to 'gender dysphoria' (as renamed in *DSM-5*; American Psychiatric Association 2013) and 'gender incongruence' (as renamed in the *International Classification of Diseases–11*; World Health Organization 2019). In the nomenclature of transgender medicine, 'puberty blockers' refers to a class of drugs which stop the production of sex hormones: gonadotropin-releasing hormone agonists (GnRHa), alternatively known as luteinising hormone-releasing

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hormone (LHRH) agonists. (The literature sometimes refers to GnRH [or LHRH] analogues, which is a broader classification comprising antagonists as well as agonists.) Drugs in this class include triptorelin, which is used in the Netherlands and Britain, and leuprorelin (branded Lupron) in North America. GnRHa drugs are licensed to treat several medical conditions including precocious puberty in children, endometriosis and uterine fibroids in women, and advanced prostate cancer and sexual deviance in men. The drugs have never been licensed as a treatment for gender dysphoria. The justification comes by analogy with treatment for precocious puberty—when puberty commences before the age of 7 in girls or 9 in boys. But that treatment involves delaying a puberty that arrives abnormally early so that the child can undergo puberty at the normal age. Puberty suppression for gender dysphoria means stopping normal puberty in order to prepare the child for taking hormones of the opposite sex, typically at the age of 16. If GnRHa is started early enough, the child will barely experience puberty in their natal sex (on the importance of puberty, see Hilton and Wright, this volume). It is even possible for an adolescent who identifies as 'agender' to refuse the transition to cross-sex hormones, thus remaining in effect prepubescent for the rest of their life (Pang et al. 2020).

Only a tiny minority of those who identify as transgender have undergone early puberty suppression. The great majority who seek clinical treatment do so well after puberty. Even those who are referred to gender clinics early in adolescence often fail to obtain GnRHa due to lengthy waiting lists (in the United Kingdom) or high costs (in the United States). And those who do access GnRHa will often commence treatment towards the end of puberty (at the age of 15 for instance) and so will not undergo complete puberty suppression. Nevertheless, puberty blockers occupy a central place in the transgender imaginary. Cross-sex hormones and surgeries in adulthood have limited effects in transforming physical appearance, especially for males. Puberty blockers enable a fantasy of truly changing sex. That is why transgender youth celebrated in the media invariably have taken GnRHa from early puberty.

Creating the Dutch protocol

Cross-sex hormones and plastic surgery created the phenomenon of transsexualism in the mid-twentieth century (Hausman 1995). These novel physical interventions had their counterpart in the new theoretical constructs formulated by American psychologists and psychiatrists. It is telling that the first recorded use of the term *gender identity* was in the name of the Gender Identity Clinic at Johns Hopkins University, which pioneered physical treatments for intersex and transsexual patients. This name for the unit, previously known informally as the 'sex change clinic', was suggested by psychologist John Money (1994). Although gender identity was conceived as developing in infancy (e.g. Green 1968), physical treatment was confined to adults. It is worth quoting the Standards of Care formulated by the Harry Benjamin International Gender Dysphoria Association (HBIGDA), which had been created by clinicians and academics to professionalise the new field. 'Hormonal

and surgical sex reassignment is extensive in its effects, is invasive to the integrity of the human body, has effects and consequences which are not, or are not readily, reversible' (HBIGDA 1985, 83). The standards did not specify a minimum age, and in practice, some clinicians were willing to give cross-sex hormones under the age of 18. Money advised a doctor to prescribe testosterone to a 15-year-old girl and even to consider mastectomy—but he was unusually reckless, and there is no evidence that his advice was followed (Gill-Peterson 2018, 163–64). Specialist clinics for children and adolescents with gender identity problems were founded in Toronto in 1975, in Utrecht in 1987, and in London in 1989. They provided counselling. Cross-sex hormones had to wait until the patient was referred to an adult clinic, at an age ranging from 16 to 18 (Bradley and Zucker 1990). Surgeries were never performed under the age of 18 (Petersen and Dickey 1995). Referrals to these clinics were rare. The Gender Identity Development Unit in London—the only one in the United Kingdom—over its first decade accepted an annual average of 14 patients (Di Ceglie 2018). In its first seven years, the Utrecht clinic averaged nine per year (Cohen-Kettenis 1994).

The age barrier was broken in the Netherlands. The innovator was Peggy Cohen-Kettenis, professor of psychology in the Department of Child and Adolescent Psychiatry at University Medical Centre Utrecht (Everaerd et al. 2014). She established herself in the field of gender medicine in the 1980s, presenting her research to the HBIGDA's international conferences and founding Europe's first clinic for children with gender dysphoria. She was closely connected to clinicians at VU Medical Centre Amsterdam (affiliated with the Free University), which housed the country's clinic for adult transsexuals.

Cohen-Kettenis believed that transsexuals would experience better outcomes if they started treatment before adulthood. By the mid-1990s, she was referring some patients aged 16 and 17 to the Amsterdam clinic for endocrinological treatment prior to cross-sex hormones (Cohen-Kettenis 1994). Males were given an antiandrogen, cyproterone acetate, which prevented erections and caused breast tissue to grow; females were given progestin to stop menstruation (Gooren and Delemarre-van de Waal 1996). Johanna, for example, 'fulfilled all necessary requirements for early treatment': she did not favour girly things (although neither did her sisters), she was fond of soccer, she never dated in school (hardly surprising given that she was evidently homosexual), and her parents discovered her wearing a tight T-shirt to conceal her breasts (Cohen-Kettenis et al. 1998, 124). Brought to the clinic at 17, she was prescribed progestin for four months and then testosterone. Within two years, Jaap (as Johanna had become) underwent a mastectomy, hysterectomy, and oophorectomy and obtained a new birth certificate. Evidence to support such early treatment came from the first 22 patients from Cohen-Kettenis's clinic, interviewed in their early 20s, no more than a year after surgery (Cohen-Kettenis and van Goozen 1997). They were compared to a larger group of transsexuals who had transitioned later in adulthood in previous decades (Kuiper and Cohen-Kettenis 1988). Her former patients showed better psychological functioning and 'more easily pass in

the desired gender role' (Cohen-Kettenis and van Goozen 1997, 270). One problem with the comparison is that they had transitioned in a more tolerant era. Another is the fact that they were still young; most did not yet have a sexual partner. Moreover, they had not reached an age at which they might regret their inability to conceive children. (This group has not since been followed up.) Naturally her experiment was praised by Money (1998, xviii): he singled out her contribution to a conference in London as 'the bravest'.

Cohen-Kettenis had two collaborators at the Free University Amsterdam. One was Louis Gooren, an older endocrinologist who was installed as the world's first professor of transsexuality in 1989. His inaugural professorial lecture was addressed by Cohen-Kettenis and by Money, who flew over from Johns Hopkins University (Nederlands Tijdschrift voor Geneeskunde 1989). Like the pioneering generation who created transsexualism, Gooren saw gender dysphoria as an intersex condition: 'there is a contradiction between the genetic, gonadal and genital sex on the one hand, and the brain sex on the other', and therefore, 'we must provide them with reassignment treatment which meets their needs' (Gooren 1993, 238). The last of the triumvirate was a paediatric endocrinologist, Henriette Delemarre-van de Waal. She had expertise using the new GnRHa drugs—developed in the 1980s—to treat precocious puberty and other conditions (e.g. Schroor et al. 1995).

GnRHa was introduced as a treatment for gender dysphoria in two articles. Gooren and Delemarre-van der Waal (1996) proposed the 'Feasibility of Endocrine Interventions in Juvenile Transsexuals'. More influential was a case study of the first 'adolescent transsexual' treated with GnRHa (Cohen-Kettenis and van Goozen 1998). From the age of 5, FG 'had made it very clear that I was supposed to be a boy' (Bakker 2021, 131). It later transpired that FG was sexually attracted to women. FG's father, a very traditional Italian, disapproved of her masculinity, and serious conflict ensued. Extensive psychotherapy did not improve matters; FG even wrote a suicide note at the age of 12. When FG was 13, Delemarre-van der Waal prescribed triptorelin. The paediatric endocrinologist was not named in the original article, but her identity is clear from later sources (e.g. Delemarre-van de Waal 2014). FG is known as 'B' in the published literature. Three years later, around 1990, FG came to the Utrecht gender clinic, and Cohen-Kettenis was impressed by FG's 'boyish appearance' (Bakker 2021, 115). The clinic provided therapy and introduced FG to other adolescent girls who identified as transsexual. (Whether FG was introduced to any girls who identified as lesbian is not recorded.) Puberty suppression continued for five years until FG was 18, when testosterone commenced, followed by multiple surgeries: mastectomy, oophorectomy and hysterectomy, and metoidioplasty. Awaiting the last surgery, FG was 'happy with his life' and 'never felt any regrets'; the gender dysphoria was apparently cured (Cohen-Kettenis and van Goozen 1998, 247).

Puberty suppression for some years remained exceptional. By 2000, GnRHa had been administered to only seven children under the age of 16 (Cohen-Kettenis et al. 2000). A new treatment regime was codified at VU Medical Centre, where Cohen-Kettenis was appointed professor of medical psychology in 2002, moving with her

clinic. This regime became known as the Dutch protocol; Ferring Pharmaceuticals, the manufacturer of triptorelin, provided financial support (Delemarre-van de Waal and Cohen-Kettenis 2006, S137). GnRHa could be administered to transsexuals as young as Tanner Stage Two—marked by the first growth of pubic hair and for girls by budding breasts and for boys by growing testicles—as long as they had reached the age of 12. The child would usually then begin 'to live permanently in the role of their desired sex' (Delemarre-van de Waal and Cohen-Kettenis 2006, S132). After some years of puberty suppression, the adolescent would start cross-sex hormones at the age of 16 and then surgeries at the age of 18. These were the key elements of the Dutch protocol adopted in other countries, albeit without the minimum age of 12—to which the Dutch did not strictly adhere anyway (de Vries 2010, 104). Less often adopted were the apparently strict eligibility criteria for puberty suppression. First, gender dysphoria should have begun early in childhood and worsened with the onset of puberty. Second, the patient should be psychologically stable and not suffer from other mental health problems. Third, the patient should have support from their family. The last criterion could be violated in practice. GnRHa was administered to a 14-year-old—who was institutionalised due to a physical handicap—against the parents' objections (Cohen-Kettenis and Pfäfflin 2003).

As the protocol was formalized, puberty suppression became routine rather than exceptional. Between 2000 and 2008, GnRHa was prescribed to 111 children, which is about one per month (de Vries et al. 2011). One of them was Valentijn de Hingh. After a teacher was disconcerted by the boy's passion for dolls, Cohen-Kettenis diagnosed de Hingh with gender dysphoria at the age of 5 (Bakker 2021). GnRHa was administered from the age of 12 in 2002. De Hingh's transition was celebrated in a television documentary broadcast in 2007.

The Dutch protocol scrutinised

The Dutch protocol comprised not just a drug (GnRHa) and a treatment regime (from 12 or Tanner Stage Two) but also two rhetorical devices. The first was the notion of reversibility. The initial article confidently declared GnRHa to be 'fully reversible; in other words, no lasting undesired effects are to be expected' (Gooren and Delemarre-van de Waal 1996, 72). The peculiar phrasing tacitly acknowledged the lack of actual evidence. Suppressing puberty for just one month would have a negligible effect on a child's development, of course. Yet the Dutch protocol entailed suppression for up to four years (from age 12 to 16), and for FG the duration was at least five years (from 13 to 18). It was simply incredible to claim that suppressing puberty for so many years would have no lasting effect if the child were to stop GnRHa and restart their natal sex hormones. Indeed, the final paragraph of Delemarre-van de Waal and Cohen-Kettenis's (2006, S137) manifesto admits as much: 'It is not clear yet how pubertal suppression will influence brain development'. The postulate of reversibility, however implausible, was crucial for circumventing the question of whether a child aged 12 could give consent to this endocrinological experiment.

Recall that the HBIGDA Standards of Care warned that cross-sex hormones 'are not, or are not readily, reversible'. By pronouncing GnRHa to be reversible, the Dutch clinicians created an imaginary boundary between one endocrinological intervention and another.

The second rhetorical device was the notion of puberty suppression as a diagnostic tool. FG's case study described GnRHa as an 'aid in diagnosis and treatment' (Cohen-Kettenis and van Goozen 1998). This echoed the prior conception of cross-sex hormones as 'both therapeutic and diagnostic in that the patient requesting such therapy either reports satisfaction or dissatisfaction regarding the results' (HBIGDA 1985, 85). GnRHa was posited to provide space for therapeutic exploration of gender identity without the pressure of the physical changes accompanying puberty (Delemarre-van de Waal and Cohen-Kettenis 2006). This claim was plausible, although it was also plausible that stopping normal sexual and intellectual development would impede such exploration. In the event, the Dutch clinicians found that the diagnostic test invariably turned up the same result: 'none of the [54] patients who were selected for pubertal suppression has decided to stop taking GnRHa' (Delemarre-van de Waal and Cohen-Kettenis 2006, S136). This might be explained by a rigorous selection process, as described by Dutch clinicians. An alternative explanation is that puberty suppression becomes a self-fulfilling prophecy. Subsequent experience in other countries confirms the fact that 96 percent or 98 percent of children who undergo puberty suppression continue to cross-sex hormones (Brik et al. 2020; Carmichael et al. 2021; Wiepjes et al. 2018). Does any other diagnostic test in medicine yield such singular results?

The fiction of diagnosis enabled the Dutch to escape a problem recognised in the earliest articles. 'Not all children with GID [gender-identity disorder] will turn out to be transsexuals after puberty', acknowledged Cohen-Kettenis and Gooren (1999, 319). 'Prospective studies of GID boys show that this phenomenon is more closely related to later homosexuality than to later transsexualism'. They cited four longitudinal studies of boys with gender dysphoria. The most famous was by Richard Green, who selected a group of 'sissy boys' to understand the psychology of 'pre-transsexuals'. To his surprise, after 15 years, two thirds of the 44 had become bisexual or homosexual men and only one was contemplating transsexuality (Green 1987). Given such studies, Cohen-Kettenis concluded that 'most GID children under 12 will not grow up to become transsexuals' (Cohen-Kettenis and van Goozen 1998, 246).

These findings were downplayed in their subsequent publications; the manifestos for the Dutch protocol did not mention homosexuality and did not cite any study of feminine boys (Cohen-Kettenis et al. 2008; Delemarre-van de Waal and Cohen-Kettenis 2006). The assertion that 'GID persisting into early puberty appears to be highly persistent' rested on slender evidence (Cohen-Kettenis et al. 2008, 1895). The only relevant cited source described adolescents who had been first assessed at ages ranging from 13 to 18, a range extending well beyond early puberty (Smith et al. 2001). This source did not support the hypothesis that the probability of

gender dysphoria persisting to adulthood jumped suddenly on the cusp of age 12, from under 50 percent to virtually 100 percent. What is known is that most adolescents subjected to puberty suppression were homosexual. Of the first 70 adolescents referred to the Amsterdam clinic from 2000 to 2008 and given GnRHa, 62 were homosexual while only one was heterosexual (de Vries et al., 2011). The Dutch clinicians never questioned whether some of those homosexual adolescents might have developed naturally into butch lesbians or queeny gays, with their sexuality and fertility intact.

The crucial advantage of puberty suppression was creating 'individuals who more easily pass into the opposite gender role' (Delemarre-van de Waal and Cohen-Kettenis 2006, 155). The emphasis was on external appearance, as is revealed by an almost obsessive concern with height. Paediatric endocrinology's obsession with height has motivated the use of artificial oestrogen to accelerate puberty in girls judged as too tall (Cohen and Cosgrove 2009) and the use of GnRHa to delay puberty in girls judged as too short (Hayes 2016). The word *height* appears 23 times in Delemarre-van de Waal's (2014) review of puberty suppression. There is one cursory reference to 'loss of fertility'. The words *orgasm*, *libido*, and *sexuality* do not appear. This is curious because it was well known that men taking GnRHa for prostate cancer completely lose erotic interest (Marumo et al. 1999). This effect was exploited to treat men with sexual obsessions. Gooren himself cautiously advocated GnRHa as a treatment for paraphilias, though warning that the side effects 'may be very uncomfortable' (Gijs and Gooren 1996, 279). Curiously, the Dutch clinicians did not ask whether blocking the normal development of erotic desire would affect their patients' understanding of their own bodies and their interest in future romantic relationships.

One significant disadvantage of puberty suppression for males was not mentioned in the 2006 manifesto for the Dutch protocol, although it had been raised at a conference in the previous year (Gender Identity Research and Education Society [GIRES] 2005). Stopping sexual development meant the penis did not grow, and so 'the genital tissue available for vaginoplasty may be less than optimal' (Cohen-Kettenis et al. 2008, 1895). This made it more likely that the orifice would need to be lined with a portion of the patient's intestine rather than the inverted penis (van de Grift et al. 2020). This procedure is more invasive, requiring a second surgical site, and it entails a greater risk of complications such as rectal fistula. Surgical techniques have been refined so that the 'possible occurrence of intestinal discharge could be kept under control' (Bakker 2021, 141), but one quarter of the patients need further corrective surgeries (Bouman et al. 2016).

International adoption of the Dutch protocol

The Dutch protocol immediately attracted interest in other countries. Cohen-Kettenis and Gooren were already prominent in the field of transgender medicine, exemplified by their election to the board of directors of HBIGDA (the former

served two 4-year terms from 1995 and 2003, while the latter served one term from 1999). Puberty suppression quickly entered HBIGDA's Standards of Care in the Sixth Version, approved in 2001. It closely followed the Dutch protocol but did not specify a minimum age. It was 'recommended that the adolescent experience the onset of puberty in his or her biologic sex, at least to Tanner Stage Two' while also allowing even earlier intervention on the recommendation of more than one psychiatrist (HBIGDA 2001, 10). Note that by then, the published evidence for the benefits of puberty suppression was a single case study of one patient—FG—at the age of 20.

The United States provides an example of adoption led by an enthusiast clinician: Norman Spack, a paediatric endocrinologist. He recalls 'salivating' at the prospect of treating patients with GnRHa (Hartocollis 2015; Spack 2008). In 2007, Spack co-founded the Gender Management Service at Boston Children's Hospital, which was the first dedicated clinic for transgender children in America. Its programme was based on the Dutch model; the hospital sent a psychologist to Amsterdam to be trained by Cohen-Kettenis (Tishelman et al. 2015). From the outset, the Boston clinic offered GnRHa at Tanner Stage Two or Three with no minimum age (Spack et al. 2012). The drug was not covered by health insurance and so patients paid an annual cost of $6,000–$12,000. Spack joined Cohen-Kettenis, Gooren, and Delemarre-van der Waal on the Endocrine Society's committee tasked with writing their first clinical guidelines for 'transsexual persons', which naturally recommended GnRHa for children at Tanner Stage Two or Three (Hembree et al. 2009). 'There was an attitudinal shift to be able to say that the Endocrine Society supports this', he later recalled (Ruttimann 2013, 19).

Puberty suppression was first advertised to an American audience in 2011 when Oprah Winfrey Television broadcast *I Am Jazz: A Family in Transition*. 'My heart and soul are female', declared Jazz Jennings. 'I just happen to have been born with male genitalia' (Jennings and Jennings 2016, 99; see Matthews, this volume, for further discussion of the case). Diagnosed with gender dysphoria at the age of 3, Jennings had already appeared on national television when 7 years old. The 2011 documentary focused on the threat of puberty as Jazz reached the age of 11. It showed the family consulting a paediatric endocrinologist, who confirmed that Tanner Stage Two had been reached. Jennings commenced puberty suppression some months later. Within a few years, there were 32 clinics for 'gender-nonconforming children and adolescents' which offered puberty blockers (Hsieh and Leininger 2014).

England provides an example of adoption driven by patients. The advantages of the Dutch approach were broadcast in a television documentary in 1996, watched by 3 million viewers (Morse 1996; Nataf 1999). Three transgender females from England—trapped in *The Wrong Body*, according to the title of the documentary—were taken to meet Gooren, Cohen-Kettenis, and their patients who had started cross-sex hormones at 16. The narrative was driven by the looming threat of puberty for the youngest, aged 13, Fredd Foley. It contrasted the compassion of the

Dutch clinicians with the complacency of the Gender Identity Development Unit in London, which refused to prescribe the desired drugs. At the end of the documentary, Foley's mother telephoned Gooren, who immediately agreed to provide a three-month prescription of triptorelin. 'If your child knows for sure he is transsexual', he said, 'I would not let puberty happen'. His willingness to prescribe drugs for a child in another country who he had met only briefly—and against the wishes of the child's own clinicians—suggests that the assessment process was less rigorous than was portrayed in the medical literature. As Cohen-Kettenis said in the documentary, 'it's very difficult to give exact criteria, in some cases you have the feeling that the adolescent has thought about it and knows pretty well what she or he is doing'.

Dissatisfaction at the cautious policy of the Gender Identity Development Unit—still headed by its founder, Domenico Di Ceglie—became increasingly vocal. Stephen Whittle, a seasoned transgender activist and law lecturer, argued that doctors who failed to provide GnRHa could be vulnerable to litigation (Downs and Whittle 2000). Sustained pressure came from the parents of children who identified as transgender, organised by GIRES and Mermaids. GIRES obtained funding from medical charities to organise an international symposium in London in 2005 to develop consensus guidelines for endocrinological intervention. Cohen-Kettenis and Delemarre-van der Waal extolled the virtues of the Dutch approach and found a receptive audience among the American clinicians, including Spack. Di Ceglie and the other local clinicians were evidently less impressed; a paediatric endocrinologist at Great Ormond Street Hospital observed sharply that 'current treatment is based upon theoretical or anecdotal considerations rather than evidence obtained from the outcomes of controlled research trials' (GIRES 2005). GIRES (2006) then warned that 'those who can in any way afford to do so have to consider taking their children to the USA'. The first was Susie Green, later the chief executive of Mermaids. In 2007, she took her son Jackie, aged 12, to Boston, to obtain GnRHa from Spack (Sloan 2011). A presentation at Mermaids (2007), presumably by Green, instructed parents in this medical tourism. Spack treated seven more British children over the next few years (Glass 2012).

The conflict between parents and clinicians climaxed in 2008, with two clashing conferences. The Royal Society of Medicine organised a meeting on adolescent gender dysphoria, which drew criticism for the lack of overseas speakers advocating for puberty blockers, even though it had invited Delemarre-van der Waal. The co-founder of GIRES, whose child transitioned in their late teens two decades earlier, used the new epithet 'transphobic' to describe the cautious clinicians. 'What we do know is what happens if you don't offer hormone blockers. You are stuck with unwanted secondary sex characteristics in the long term and in the short term these teenagers end up suicidal' (Groskop 2008). Green—the author of *Sissy Boys*, then a visiting professor at Imperial College—quickly organised a rival conference to demand puberty suppression (Green 2008). Speakers comprised the usual cast of clinicians, including Spack, and also patients and their parents,

including two Dutch transgender adolescents. The demand for puberty suppression was becoming irresistible.

Di Ceglie was soon replaced as Director of the (renamed) Gender Identity Development Service (GIDS) by Polly Carmichael, a clinical psychologist. The GIDS in 2011 began to offer GnRHa from the age of 12, initially as part of an experimental study (Biggs 2019b, 2019c). Before any outcomes were published, Carmichael declared success: 'Now we've done the study and the results thus far have been positive we've decided to continue with it' (Manning and Adams 2014). She even appeared on BBC children's television to promote puberty suppression, in a documentary about a 13-year-old girl who wanted to be a boy, Leo. Carmichael reassured Leo about GnRHa: 'the good thing about it is, if you stop the injections, it's like pressing a start button and the body just carries on developing as it would if you hadn't taken the injection' (Niland 2014). England's National Health Service adopted a policy of offering GnRHa for adolescents at Tanner Stage Two, without age restriction (NHS England 2015).

Subsequent evidence

By the mid-2010s, then, the Dutch protocol was established as the standard for transgender medicine. Even sceptical clinicians could not resist the demand from patients, fuelled by increasing representations of transgender children in the media. The Dutch protocol was apparently vindicated when longitudinal data on the first cohort of 70 adolescents subjected to puberty suppression was published; the lead author was Cohen-Kettenis's student, Annelou de Vries (de Vries et al. 2011, 2014). Ultimate outcomes were measured at least one year after final surgery (vaginoplasty or mastectomy and hysterectomy with oophorectomy), at age 19–22. According to the authors, 'gender dysphoria had resolved, psychological functioning had steadily improved, and well-being was comparable to same-age peers' (de Vries et al. 2014, 696). When scrutinised, however, the evidence was less persuasive. The sample was quite small: the cohort began with 70 patients, but outcome measures were available for 32 to 55 patients, depending on the measure. The results omitted the outcomes for the eight patients who refused to participate in the follow-up or were ineligible for surgery and the one patient killed by necrotising fasciitis immediately after vaginoplasty. Unable to complete the post-surgery questionnaire, the dead patient counted for nothing. The authors withheld the fact that this death was caused by puberty suppression: having been prevented from developing normally, the patient's penis was too small for the normal vaginoplasty, and so surgery was attempted with a portion of the intestine, which became infected (Negenborn et al. 2017). A fatality rate exceeding 1 percent would surely halt any other experimental treatment on healthy teenagers. One inevitable limitation of the study was the measurement of results soon after surgery, which repeated the problem with the first study of adolescent transsexuals (Cohen-Kettenis and van Goozen 1997). No further follow-up of this cohort, now in their late 20s, has been published.

There is information on the very first patient, FG, who was followed up again at the age of 35. FG did not regret transitioning but scored high on the measure for depression. Owing to 'shame about his genital appearance and his feelings of inadequacy in sexual matters', he could not sustain a romantic relationship with a girlfriend (Cohen-Kettenis et al. 2011, 845). Ironically, a 'strong dislike of one's sexual anatomy' is one of the diagnostic criteria for gender dysphoria in children (according to *DSM*-5). But the clinicians were more interested in FG's height: although FG was much shorter than the average Dutch man, they also provided the Italian height distribution as a reference. Cohen-Kettenis concluded that 'the negative side effects are limited' (Cohen-Kettenis et al. 2011, 843). Delemarre-van der Waal's (2014, 194) summary was even more optimistic: 'He was functioning well psychologically, intellectually, and socially'. Now aged 48, FG has given two recent interviews. FG's situation seems to have improved, and he now has a girlfriend. He describes puberty suppression as 'life-saving' in his case (Bakker 2021, 132) but also recommends that children 'go through a significant assessment process' before intervention (Bazelon 2022). Another early Dutch patient, de Hingh, at the age of 31 now identifies as non-binary. Emphasising that 'diagnosis and treatment at a young age [5 years] were not wrong', de Hingh also observes that 'a diagnosis says you've got a problem that needs to be treated as well as possible. The medical process, with pills and protocols, takes over the normal process of identification formation' (Bakker 2021, 182–83).

As clinicians in other countries adopted the Dutch protocol, they did not collect any systematic data on outcomes. An exception was the GIDS in London. One article claimed to show a positive effect of puberty suppression after 12 months (Costa et al. 2015). In fact, the data showed that there was no significant difference between the group given GnRHa and counselling and the group given counselling only (Biggs 2019a). Full outcomes from the initial experiment—comprising 44 children aged 12 to 15—were withheld for years and presumably would have never appeared without my protracted campaign for disclosure (e.g. Health Research Authority 2019; Tominey and Walsh 2019; Biggs 2019d). The reluctance to publish became understandable when the article appeared: puberty suppression for two years produced no positive effects, contradicting Carmichael's (Carmichael et al. 2021) statements to the media. These results were significantly inferior to the Dutch results after puberty suppression and before cross-sex hormones (Biggs 2020). This comparison demonstrates that outcomes from the Netherlands cannot be extrapolated to other countries. Before treatment, adolescents referred to the Dutch clinic have fewer psychological problems and better peer relationships than those referred to the Belgian and Swiss clinics and especially to the GIDS (de Graaf et al. 2018).

Significantly more evidence has emerged on the side effects of puberty suppression. The fact that GnRHa could cause 'an insufficient formation of bone mass' was initially dismissed 'of no great concern' (Gooren and Delemarre-van de Waal 1996). Then it was recognised that patients could 'end with a decreased bone density, which is associated with a high risk of osteoporosis' (Delemarre-van de Waal and Cohen-Kettenis 2006, S134). According to my analysis of data from the GIDS

experiment, one third of the adolescents who had taken GnRHa ended with bone density so low (two standard deviations below the norm for their sex and age) that they are at risk for osteoporosis (Biggs 2021). The hope was that bone density would improve following cross-sex hormones. A recent study, however, shows that some females taking testosterone do recover, but males taking oestrogen do not (Schagen et al. 2020). How many patients will eventually develop osteoporosis will not be known for some decades. A female who was given GnRHa from age 11 to 15 by the Karolinska University Hospital in Stockholm now suffers from severe osteoporosis, including continual skeletal pain (SVT 2022). This case—along with two others whose puberty suppression was terminated after concerns about bone density—led Sweden to curb the use of GnRHa.

The effects of puberty suppression on emotional and cognitive development are the hardest to ascertain but the most disturbing, because they affect the adolescent's ability to consent to cross-sex hormones and surgery. Evidence is now emerging from randomized control trials on non-human animals. GnRHa impairs spatial memory in sheep, and this effect remains after the treatment is stopped—in other words, puberty suppression is irreversible (Hough et al. 2017a, 2017b). Mice treated with GnRHa manifest significant differences: males develop a stronger preference for other males and an increased stress response; females exhibit increased anxiety and despair-like behaviour (Anacker et al. 2021). One wonders why Delemarre-van der Waal, whose research group worked with rats, did not undertake similar controlled experiments to test puberty suppression before choosing FG as her guinea pig.

Conclusion

The technology of puberty suppression has been more successful than Cohen-Kettenis could have imagined in the mid-1990s, becoming the international standard for treating gender dysphoria and attracting increasing numbers of patients. The GIDS, for example, from 2012 to 2020 administered GnRHa to 344 children under the age of 15. The total number of patients subjected to this experimental treatment, worldwide, must run to several thousand. What is striking is that the proponents of puberty suppression never reassessed the rationale for the intervention as the numbers multiplied. It is one thing to assert that in very rare cases of extreme gender dysphoria, the child is predestined to become transsexual—rare as in one per year in the Netherlands in the late 1990s. It is another to make this claim for numerous children—currently about two hundred a year in the Netherlands. A recent survey in one American school district found 7 percent of students identifying as 'gender diverse'; the authors urge that all receive 'access to gender affirming care', which in effect means giving GnRHa on request (Kidd et al. 2021, 3). Aside from increasing numbers, the logic of puberty suppression tends towards escalated intervention. The availability of GnRHa encourages parents to pretend their child is the opposite sex before puberty, which makes the onset of puberty more traumatic and thus endocrinological intervention more urgent. Logically enough, Delemarre-van der Waal

(2014) eventually advocated for GnRHa to be administered at the commencement of puberty, followed soon thereafter by cross-sex hormones.

The apparently inexorable rise of puberty suppression has recently been challenged. A handful of clinicians have publicly expressed doubts in the last few years (e.g. Levine et al. 2022; Malone et al. 2021), and they founded the Society for Evidence-Based Gender Medicine (I am on its advisory board). In England, Keira Bell—who took GnRHa at 16, followed by testosterone and then underwent mastectomy—won a surprising legal victory against the GIDS in 2020. The High Court ruled that consent to puberty suppression for a child under 16 was so problematic that it should require a court order. The judgment was overturned on appeal, but it spurred the National Health Service to commission a review of gender identity services for children and young people, led by Hilary Cass. The review is ongoing but has already underlined the lack of evidence for puberty suppression and prompted the closure of the GIDS (announced just as this chapter was submitted for publication). In the United States, Florida and several other states controlled by Republicans are attempting to prohibit endocrinological and surgical interventions for minors.

The ultimate outcome of such shifts in policy is uncertain. For one thing, many children and parents still seek puberty suppression. Unsatisfied demand provides an opportunity for profiteering. A company registered in Singapore and owned by a Welsh doctor will diagnose a 9-year-old with gender dysphoria over video and prescribe GnRHa on the same day (Biggs 2022). More generally, puberty suppression is still protected from scientific scrutiny by the prestige of transgenderism as a social and cultural movement; Butler's queer theory shores up Cohen-Kettenis's endocrinology (see Jones, this volume). Faith in gender among the professional and managerial classes is not shaken even by the tragic televised spectacle of Jazz Jennings—the inability to orgasm and the botched intestinal vaginoplasty which required multiple corrective surgeries, both consequences of early puberty suppression; and the depression which prevented Jennings from starting university. It is too soon to tell whether puberty suppression will go the way of lobotomy or whether it will be one step towards a transhumanist future of self-fabrication through biotechnology.

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