Gender Dysphoria in Children and Suppression of Debate

Michelle A. Cretella, M.D.

ABSTRACT

Gender dysphoria (GD) of childhood describes a psychological condition in which a child experiences marked incongruence between his experienced gender and the gender associated with his biological sex. When this occurs in the prepubertal child, GD resolves in the vast majority of patients by late adolescence. Currently there is a vigorous albeit suppressed debate among physicians, therapists, and academics regarding what is fast becoming the new treatment standard for GD in children. Modeled after a paradigm developed in the Netherlands, it involves pubertal suppression with gonadotropin releasing hormone (GnRH) agonists followed by the use of cross-sex hormones-a combination that will result in the sterility of minors. A review of the current literature suggests that this protocol is rooted in an unscientific gender ideology, lacks an evidence base, and violates the longstanding ethical principle of "First do no harm."

Gender Dysphoria in Children: This Debate Concerns More than Science

Gender is a term that refers to the psychological and cultural characteristics associated with biological sex.¹ It is a psychological concept and sociological term, not a biological one. Gender identity refers to an individual's awareness of being male or female. Gender dysphoria (GD) in children is used to describe a psychological condition in which a child experiences marked incongruence between his experienced gender and the gender associated with his biological sex. He will often express the belief that he is the opposite sex.²

The debate over treatment of children with GD concerns physician worldview as much as science. Medicine does not occur in a moral vacuum; every therapeutic action or inaction is the result of a moral judgment of some kind that arises from the physician's philosophical worldview. Medicine also does not occur in a political vacuum, and being on the wrong side of sexual politics can have severe consequences.

Dr. Kenneth Zucker, long acknowledged as a foremost authority on gender identity issues in children, has also been a life-long advocate for gay and transgender rights. However, much to the consternation of adult transgender activists, Zucker also believes that gender-dysphoric prepubertal children are best served by helping them align their gender identity with their anatomic sex. This view ultimately cost him his 30-year directorship of the Child Youth and Family Gender Identity Clinic (GIC) at the Center for Addiction and Mental Health in Toronto.^{3,4}

Many critics of pubertal suppression hold a modernist teleological worldview, but others, like Dr. Zucker, identify as post-modernists. What unites the two groups is a traditional interpretation of "First do no harm." For example, there is a growing online community of gay-affirming physicians, mental health professionals, and academics. Their homepage is entitled "First, do no harm: youth trans critical professionals." They write:

We are concerned about the current trend to quickly diagnose and affirm young people as transgender, often setting them down a path toward medical transition.... We feel that unnecessary surgeries and/or hormonal treatments which have not been proven safe in the long-term represent significant risks for young people. Policies that encourage—either directly or indirectly such medical treatment for young people who may not be able to evaluate the risks and benefits are highly suspect, in our opinion.⁵

Advocates of the medical interventionist paradigm, in contrast, are post-modernists who hold a subjective view of "First do no harm." Dr. Johanna Olson-Kennedy, an adolescent medicine specialist at Children's Hospital Los Angeles, for example, has stated that "[First do no harm] is really subjective. [H]istorically we come from a very paternalistic perspective...[in which] doctors are really given the purview of deciding what is going to be harmful and what isn't. And that, in the world of gender, is really problematic."⁶

Gender Fluidity: Is There a Scientific Basis?

In their "Overview of Gender Development and Gender Nonconformity in Children and Adolescents," Forcier and Olson-Kennedy dismiss the binary model of human sexuality as "ideology." They then present an "alternate perspective" of "innate gender fluidity" as established fact. Alluding to brain studies in transgender adults, they recommend that pediatricians tell families that a child's real gender is what he feels it to be because "a child's brain and body may not be on the same page."⁷

Diffusion-weighted MRI scans have demonstrated that the pubertal testosterone surge in boys increases white matter volume. A study by Rametti and colleagues found that the white matter microstructure of the brains of female-to-male (FtM) transsexual adults, who had not begun testosterone treatment, more closely resembled that of men than that of women.⁸ Other diffusion-weighted MRI studies have concluded that the white matter microstructure in both FtM and maleto-female (MtF) transsexuals falls halfway between that of genetic females and males.9 These studies, however, are of questionable clinical significance due to the small number of subjects and neuroplasticity. Neuroplasticity is the wellestablished phenomenon in which long-term behavior alters brain microstructure. There is no evidence that people are born with brain microstructures that are forever unalterable, but there is significant evidence that experience changes brain

microstructure.¹⁰ Therefore, if and when valid transgender brain differences are identified, these will be more likely the result of transgender behavior than its cause. Furthermore, infants' brains are imprinted prenatally by their own endogenous sex hormones, which are secreted from their gonads beginning at approximately eight weeks' gestation.¹¹⁻¹³

To be clear, this "alternate perspective" of an "innate gender fluidity" arising from prenatally "feminized" or "masculinized" brains trapped in the wrong body is an ideological belief that has no basis in rigorous science.

A teleological view of human sexuality is at least drawn with reference to biological reality. The norm for human design is to be conceived either male or female. Sex chromosome pairs "XY" and "XX" are genetic markers of sex, male and female, respectively. They are not genetic markers of a disordered body or birth defect. Human sexuality is binary by design with the purpose being the reproduction of our species. This principle is self-evident. Barring one of the rare disorders of sex development (DSD), no infant is "assigned" a sex at birth; rather birth sex declares itself anatomically in utero and is acknowledged at birth.

The exceedingly rare DSDs, including but not limited to testicular feminization and congenital adrenal hyperplasia, are all medically identifiable deviations from the human binary sexual norm. The 2006 consensus statement of the Intersex Society of North America does not endorse DSD as a third sex.¹⁴ The norm for human development is for one's thoughts to align with physical reality, and for one's gender identity to align with one's biologic sex. People who identify as "feeling like the opposite sex" or "somewhere in between" do not comprise a third sex. They remain biological men or biological women.

No Objective Standards for Mental Health?

Psychology has increasingly rejected the concept of norms for mental health, focusing instead on emotional distress. The American Psychiatric Association (APA), for example, explains in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) that GD is listed therein not due to the discrepancy between the individual's thoughts and physical reality, but due to the presence of emotional distress that hampers his social functioning. The DSM-V also notes that a diagnosis is required for insurance companies to pay for crosssex hormones and sex reassignment surgery (SRS) that alleviate the emotional distress of GD. Once the distress is relieved, GD is no longer considered a disorder.²

There are problems with this reasoning. Consider the following examples: a girl with anorexia nervosa has the persistent mistaken belief that she is obese; a person with body dysmorphic disorder (BDD) harbors the erroneous conviction that she is ugly; a person with body integrity identity disorder (BID) identifies as a disabled person and feels trapped in a fully functional body. Individuals with BIID are often so distressed by their fully capable bodies that they seek surgical amputation of healthy limbs or the surgical severing of their spinal cord.¹⁵ Dr. Anne Lawrence, who is transgender, has argued that BIID has many parallels with GD.¹⁶ The aforementioned false beliefs, like GD, are not merely emotionally distressing for the individuals but also life-threatening. In each case, surgery to "affirm" the

false assumption (liposuction for anorexia, cosmetic surgery for BDD, amputation or surgically induced paraplegia for BIID, sex reassignment surgery for GD) may very well alleviate the patient's emotional distress, but will do nothing to address the underlying psychological problem, and may result in the patient's death. Completely removed from physical reality, the art of psychotherapy will diminish as the field of psychology increasingly devolves into a medical interventionist specialty, with devastating results for patients.

Alternatively, a minimal standard could be sought. Normality has been defined as "that which functions according to its design."¹⁷ One of the chief functions of the brain is to perceive physical reality. Thoughts that are in accordance with physical reality are normal. Thoughts that deviate from physical reality are abnormal—as well as potentially harmful to the individual or to others. This is true whether or not the individual who possesses the abnormal thoughts feels distress. A person's belief that he is something or someone he is not is, at best, a sign of confused thinking; at worst, it is a delusion. Just because a person thinks or feels something does not make it so.

Children with GD do not have a disordered body-even though they feel as if they do. Similarly, a child's distress over developing secondary sex characteristics does not mean that puberty should be treated as a disease to be halted, because puberty is not, in fact, a disease. Likewise, although many men with GD express the belief that they are a "feminine essence" trapped in a male body, this belief has no scientific basis. Until recently, the prevailing worldview with respect to childhood GD was that it reflected abnormal thinking or confusion on the part of the child that may or may not be transient. Consequently, the standard approach was either watchful waiting or pursuit of family and individual psychotherapy.^{1,2} The goals of therapy were to address familial pathology if it was present, treat any psychosocial morbidities in the child, and aid him in aligning his gender identity with his biological sex.^{18, 19} Experts on both sides of the pubertal suppression debate agree that within this context, 80 percent to 95 percent of children with GD accepted their biological sex and achieved emotional well-being by late adolescence.²⁰

This worldview began to shift, however, as adult transgender activists increasingly promoted the "feminine essence" narrative to secure social acceptance.²¹ In 2007, the same year that Boston Children's Hospital opened the nation's first pediatric gender clinic, Dr. J. Michael Bailey wrote:

Currently the predominant cultural understanding of male-to-female transsexualism is that all maleto-female (MtF) transsexuals are, essentially, women trapped in men's bodies. This understanding has little scientific basis, however, and is inconsistent with clinical observations. Ray Blanchard has shown that there are two distinct subtypes of MtF transsexuals. Members of one subtype, homosexual transsexuals, are best understood as a type of homosexual male. The other subtype, autogynephilic transsexuals, are motivated by the erotic desire to become women. The persistence of the predominant cultural understanding, while explicable, is damaging to science and to many transsexuals.²²

As the "feminine essence" view persisted, the suffering

of transgender adults was invoked to argue for the urgent rescue of children from the same fate by early identification, affirmation, and pubertal suppression.²³ It is now alleged that discrimination, violence, psychopathology, and suicide are the direct and inevitable consequences of withholding social affirmation of a child's gender discordance and allowing a gender dysphoric child to pass through puberty in accordance with his biological sex.²³ Yet, the fact that 80 percent to 95 percent of gender-dysphoric youth emerge physically and psychologically intact after passing through puberty without social affirmation refutes this claim.¹⁰ Furthermore, more than 90 percent of people who die of suicide have a diagnosed mental disorder.²⁴ There is no evidence that gender-dysphoric children who complete suicide are any different. Therefore, the cornerstone for suicide prevention should be the same for them as for all children: early identification and treatment of psychological co-morbidities.

Nevertheless, there are now 40 gender clinics across the United States that promote the use of pubertal suppression and cross-sex hormones in children. The rationale for suppression is to allow the gender-dysphoric child time to explore his gender identity free from the emotional distress triggered by the onset of secondary sex characteristics. The standards followed in these clinics are based on "expert opinion." There is not a single large, randomized, controlled study that documents the alleged benefits and potential harms to gender-dysphoric children from pubertal suppression and decades of cross-sex hormone use. Nor is there a single long-term, large, randomized, controlled study that compares the outcomes of various psychotherapeutic interventions for childhood GD with those of pubertal suppression followed by decades of toxic synthetic steroids. In today's age of "evidence-based medicine," this should give everyone pause. Of greater concern is that pubertal suppression at Tanner Stage 2 followed by the use of cross-sex hormones will leave these children sterile and without gonadal tissue or gametes available for cryo-preservation.²⁵⁻²⁷

Neuroscience clearly documents that the adolescent brain is cognitively immature and lacks an adult capacity for risk assessment prior to the early to mid-twenties.²⁸ There is a serious ethical problem with allowing irreversible, life-changing procedures to be performed on minors who are too young to give valid consent themselves. This ethical requirement of informed consent is fundamental to the practice of medicine, as emphasized by the U.S. Department of Health & Human Services website: "The voluntary consent of the human subject is absolutely essential."²⁹ Moreover, when an individual is sterilized, even as a secondary outcome of therapy, lacking full, free, and informed consent, it is a violation of international law.³⁰

Transgender-Affirming Protocol: What Is the Evidence Base?

Over the past two decades, Hayes, Inc., has grown to become an internationally recognized research and consulting firm that evaluates a wide range of medical technologies to determine the impact on patient safety, health outcomes, and resource utilization. This corporation conducted a comprehensive review and evaluation of the scientific literature regarding the treatment of GD in adults and children in 2014. It concluded that the practice of using hormones and sex reassignment surgery to treat GD in adults is based on "very low" quality of evidence:

Statistically significant improvements have not been consistently demonstrated by multiple studies for most outcomes. Evidence regarding quality of life and function in male-to-female (MtF) adults was very sparse. Evidence for less comprehensive measures of wellbeing in adult recipients of cross-sex hormone therapy was directly applicable to GD patients but was sparse and/or conflicting. The study designs do not permit conclusions of causality and studies generally had weaknesses associated with study execution as well. There are potentially long-term safety risks associated with hormone therapy but none have been proven or conclusively ruled out.^{31,32}

Regarding treatment of children with GD using gonadotropin releasing hormone (GnRH) agonists and crosssex hormones, Hayes, Inc. awarded its lowest rating indicating that the literature is "too sparse and the studies [that exist are] too limited to suggest conclusions."³¹

Gender Clinics Proliferate across United States despite Lack of Medical Evidence

In 2007 Dr. Norman Spack, a pediatric endocrinologist and founder of the nation's first gender clinic at Boston Children's Hospital, launched the pubertal suppression paradigm in the United States.³³ It consists first of affirming the child's false belief by instituting name and pronoun changes, and facilitating the impersonation of the opposite sex within and outside of the home. Next, puberty is suppressed via GnRH agonists as early as Tanner Stage 2, and then patients may graduate to cross-sex hormones at age 16 in preparation for sex-reassignment surgery as an older adolescent or adult.³⁴ Endocrine Society guidelines currently prohibit the use of cross-sex hormones before age 16, but this prohibition is being reconsidered.³⁵ Some gender specialists are already bypassing GnRH agonists and instead putting children as young as 11 years old directly onto crosssex hormones.³⁶ The rationale is that the child will experience the pubertal development of the opposite sex he desires and thereby avoid the iatrogenic emotional distress associated with his appearance of a prepubertal child while his peers progress along their natural pubertal trajectory.

In 2014 there were 24 gender clinics clustered chiefly along the East Coast and in California; one year later there were 40 across the nation. Dr. Ximena Lopez, a pediatric endocrinologist at Children's Medical Center Dallas, and a member of that program's GENder Education and Care, Interdisciplinary Support program (Genecis) stated, "[Use of this protocol is] growing really fast. And the main reason is [that] parents are demanding it and bringing patients to the door of pediatric endocrinologists because they know this is available."³⁷

Risks of GnRH Agonists

The GnRH agonists used for pubertal suppression in GD include two of those approved for the treatment of precocious puberty: leuprolide by monthly intramuscular injection, and

histrelin, a subcutaneous implant with yearly dosing. Boys have three less expensive options: medroxyprogesterone administered either orally or intramuscularly to inhibit gonadal steroidogenesis, oral spironolactone (which inhibits testosterone), or oral finasteride (which inhibits type II 5-alpha-reductase). The only alternative available for girls is medroxyprogesterone.²⁶

In addition to preventing development of secondary sex characteristics, these medications arrest bone growth, decrease bone accretion, prevent the sex-steroid dependent organization and maturation of the adolescent brain, and inhibit fertility by preventing the development of gonadal tissue and mature gametes for the duration of treatment. If the child discontinues the GnRH agonists, puberty will ensue.^{26, 34} Consequently, the Endocrine Society maintains that GnRH agonists, as well as living socially as the opposite sex, are fully reversible interventions that carry no risk of permanent harm to children.³⁴ However, social learning theory, neuroscience, and the single long-term follow-up study of adolescents who have received pubertal suppression challenge this claim.

In a follow-up study of their first 70 eligible candidates to receive puberty suppression, de Vries and colleagues documented that all subjects went on to embrace a transgender identity and request cross-sex hormones.³⁸ This is cause for concern. There is an obvious self-fulfilling nature to encouraging a young boy with GD to socially impersonate a girl and then institute pubertal suppression. Given the wellestablished phenomenon of neuroplasticity, the repeated behavior of impersonating a girl alters the structure and function of the boy's brain in some way—potentially in a way that will make identity alignment with his biologic sex less likely. This, together with the suppression of puberty that prevents further endogenous masculinization of his brain, causes him to remain a gender non-conforming prepubertal boy disguised as a prepubertal girl. Since his peers develop into young men and young women, he is left psychosocially isolated. He will be less able to identify with being male and more likely to identify as "non-male." A protocol of impersonation and pubertal suppression that sets into motion a single inevitable outcome (transgender identification) that requires life-long use of synthetic hormones, resulting in infertility, is neither fully reversible nor harmless.

GnRH agonists, Cross-sex Hormones, and Infertility

Since GnRH agonists prevent the maturation of gonadal tissue and gametes in both sexes, youth who graduate from pubertal suppression at Tanner Stage 2 to cross-sex hormones will be rendered infertile without any possibility of having genetic offspring in the future because they will lack gonadal tissue and gametes for cryo-preservation. The same outcome will occur if prepubertal children are placed directly on cross-sex hormones. Older adolescents who declined pubertal suppression are advised to consider cryo-preservation of gametes prior to beginning cross-sex hormones. This will allow them to conceive genetic offspring in the future via artificial reproductive technology. While there are documented cases of transgendered adults who stopped their cross-sex hormones in order to allow their bodies to produce gametes there is

no absolute guarantee that this is a viable option in the long term. Moreover, transgendered individuals who undergo sex reassignment surgery and have their reproductive organs removed are rendered permanently infertile.²⁵⁻²⁷

Additional Health Risks Associated with Cross-sex Hormones

Potential risks from cross-sex hormones to children with GD are based on the adult literature. Recall that regarding the adult literature, the Hayes report states: "There are potentially long-term safety risks associated with hormone therapy but none have been proven or conclusively ruled out."³¹ For example, most experts agree that there is an increased risk of coronary heart disease among MtF adults when placed on oral ethinyl estradiol; therefore, alternative estrogen formulations are recommended. However, there is one study of MtF adults using alternative preparations that found a similar increased risk. Therefore, this risk is neither established nor ruled out.³⁹⁻⁴¹ Children who transition will require these hormones for a significantly greater length of time than their adult counterparts. Consequently, they may be more likely to experience physiologically theoretical though rarely observed morbidities in adults. With these caveats, it is most accurate to say that oral estrogen administration in boys may place them at risk for experiencing: thrombosis/thromboembolism, cardiovascular disease, weight gain, hypertrigyceridemia, elevated blood pressure, decreased glucose tolerance, gallbladder disease, prolactinoma, and breast cancer.³⁹⁻⁴¹ Similarly, girls who receive testosterone may experience an elevated risk for: low HDL and elevated triglycerides; increased homocysteine levels; hepatotoxicity; polycythemia; increased risk of sleep apnea; insulin resistance; and unknown effects on breast, endometrial and ovarian tissues.³⁹⁻⁴¹ In addition, girls may legally obtain a mastectomy as early as 16 years of age after receiving testosterone therapy for at least one year; this surgery carries its own set of irreversible risks.²⁶

Conclusion

Gender dysphoria (GD) in children is a term used to describe a psychological condition in which a child experiences marked incongruence between his experienced gender and the gender associated with his biological sex. There is no rigorous scientific evidence that GD is an innate trait. Moreover, 80 percent to 95 percent of children with GD accept the reality of their biological sex and achieve emotional health by late adolescence.

The treatment of GD in childhood with hormones effectively amounts to mass experimentation on, and sterilization of, youth who are cognitively incapable of providing informed consent. There is a serious ethical problem with allowing irreversible, life-changing procedures to be performed on minors who are too young to give valid consent themselves.

Michelle A. Cretella, M.D., is a board-certified pediatrician, and serves as president of the American College of Pediatricians. Contact: drmcretella@ gmail.com.

REFERENCES

- 1. Shechner T. Gender identity disorder: a literature review from a developmental perspective. *Isr J Psychiatry Relat Sci* 2010;47:132-138.
- 2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed; 2013:451-459.
- Singal J. How the fight over transgender kids got a leading sex researcher fired. *New York Magazine*, Feb 7, 2016. Available at: http://nymag.com/ scienceofus/2016/02/fight-over-trans-kids-got-a-researcher-fired.html. Accessed May 15, 2016.
- Bancroft J, Blanchard R, Brotto L, et al. Open Letter to the Board of Trustees of CAMH; Jan 11, 2016. Available at: www.ipetitions.com/ petition/boardoftrustees-CAMH. Accessed May 125, 2016.
- 5. Youth Trans Critical Professionals. About. Available at: https:// youthtranscriticalprofessionals.org/about/. Accessed May 11, 2016.
- GenderTrender. Skipping the puberty blockers: American "transgender children" doctors are going rogue; Nov 4, 2014. Available at: https:// gendertrender.wordpress.com/2014/11/11/skipping-the-pubertyblockers-american-transgender-children-doctors-are-going-rogue/. Accessed May 15, 2016.
- Forcier M, Olson-Kennedy J. Overview of gender development and gender nonconformity in children and adolescents. *UpToDate*; 2016. Available at: www.uptodate.com/contents/overview-of-genderdevelopment-and-clinical-presentation-of-gender-nonconformity-inchildren-and-adolescents?source=search_result&search=Overview+of+ gender+nonconformity+in+children&selectedTitle=2%7E150. Accessed May 16, 2016.
- 8. Rametti G, Carrillo B, Gomez-Gil E, et al. White matter microstructure in female to male transsexuals before cross-sex hormonal treatment. A diffusion tensor imaging study. *J Psychiatr Res* 2011;45:199-204.
- Kranz GS, Hahn A, Kaufmann U, et al. White matter microstructure in transsexuals and controls investigated by diffusion tensor imaging. J Neurosci 2014;34(46):15466-15475.
- 10. Gu J, Kanai R. What contributes to individual differences in brain structure? *Front Hum Neurosci* 2014;8:262.
- Reyes FI, Winter JS, Faiman C. Studies on human sexual development.
 I. Fetal gonadal and adrenal sex steroids. J Clin Endocrinol Metab 1973;37(1):74-78.
- 12. Lombardo M. Fetal testosterone influences sexually dimorphic gray matter in the human brain. *J Neurosci* 2012;32:674-680.
- Campano A. [ed]. Geneva Foundation for Medical Education and Research. *Human Sexual Differentiation*; 2016. Available at: www.gfmer. ch/Books/Reproductive_health/Human_sexual_differentiation.html. Accessed May 11, 2016.
- 14. Consortium on the Management of Disorders of Sex Development. *Clinical Guidelines for the Management of Disorders of Sex Development in Childhood*. Intersex Society of North America; 2006. Available at: www. dsdguidelines.org/files/clinical.pdf. Accessed Mar 20, 2016.
- 15. Blom RM, Hennekam RC, Denys D. Body integrity identity disorder. *PLoS One* 2012;7(4).
- Lawrence A. Clinical and theoretical parallels between desire for limb amputation and gender identity disorder. *Arch Sexual Behavior* 2006;35:263-278.
- 17. King CD. The meaning of normal. Yale J Biol Med 1945;18:493-501.
- Zucker KJ, Bradley SJ. Gender identity and psychosexual disorders. *Focus* 2005;3:598-617.
- 19. Zucker KJ, Bradley SJ, Ben-Dat DN, et al. Psychopathology in the parents of boys with gender identity disorder. *J Am Acad Child Adolesc Psychiatry* 2003;42:2-4.
- 20. Cohen-Kettenis PT, Delemarre-van de Waal HA, Gooren LJ. The treatment of adolescent transsexuals: changing insights. *J Sexual Med* 2008;5:1892–1897.
- 21. Jeffreys S. Gender Hurts: a Feminist Analysis of the Politics of Transgenderism. New York, N.Y.: Routledge; 2014.

- Bailey MJ, Triea K. What many transsexual activists don't want you to know and why you should know it anyway. *Perspect Biol Med* 2007;50:521-534. Available at: www.ncbi.nlm.nih.gov/pubmed/17951886. Accessed May 11, 2016.
- 23. Sadjadi S. The endocrinologist's office—puberty suppression: saving children from a natural disaster? *J. Med Humanit* 2013;34:255-260.
- 24. Bertolote JM, Fleischmann A. Suicide and psychiatric diagnosis: a worldwide perspective. *World Psychiatry* 2002;1(3):181–185.
- 25. Eyler AE, Pang SC, Clark A. LGBT assisted reproduction: current practice and future possibilities. *LGBT Health* 2014;1(3):151-156.
- 26. Schmidt L, Levine R. Psychological outcomes and reproductive issues among gender dysphoric individuals. *Endocrinol Metab Clin N Am* 2015;44:773-785.
- 27. Jeffreys, S. The transgendering of children: gender eugenics. *Women's Studies International Forum* 2012;35:384-393.
- Johnson SB, Blum RW, Giedd JN. Adolescent maturity and the brain: the promise and pitfalls of neuroscience research in adolescent health policy. J Adolesc Health 2009;45(3):216-221.
- US Department of Health and Human Services. Nuremberg Code;
 2015. Available at: www.stat.ncsu.edu/people/tsiatis/courses/st520/ references/nuremberg-code.pdf. Accessed 5/15/16.
- World Health Organization. Eliminating forced, coercive and otherwise involuntary sterilization. Interagency Statement; 2014. Available at: www.unaids.org/sites/default/files/media_asset/201405_sterilization_ en.pdf. Accessed May 16, 2016.
- Hayes, Inc. Hormone therapy for the treatment of gender dysphoria. *Hayes Medical Technology Directory*. Lansdale, Pa: Winifred Hayes; May 19, 2014.
- Hayes, Inc. Sex reassignment surgery for the treatment of gender dysphoria. *Hayes Medical Technology Directory*. Lansdale, Pa.: Winifred Hayes; May 15, 2014.
- 33. Kennedy P. Q & A with Norman Spack: a doctor helps children change their gender. Boston Globe, Mar 30, 2008. Available at http://archive. boston.com/bostonglobe/ideas/articles/2008/03/30/qa_with_ norman_spack/. Accessed May 16, 2016.
- Hembree WC, Cohen-Kettenis PT, Delemarre-van de Wall HA, et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2009;94:3132-3154.
- 35. Reardon S. Transgender youth study kicks off: scientists will track psychological and medical outcomes of controversial therapies to help transgender teens to transition. *Nature* 2016;531:560. Available at: www. nature.com/news/largest-ever-study-of-transgender-teenagers-set-to-kick-off-1.19637. Accessed May 16, 2016.
- 36. Keleman M. What do transgender children need? *Houstonian Magazine*, Nov 3, 2014. Available at: www.houstoniamag.com/articles/2014/11/3/ what-do-transgender-children-need-november-2014. Accessed May 16, 2016.
- 37. Farwell S. Free to be themselves: Children's Medical Center Dallas opens clinic for transgender children and teenagers, the only pediatric center of its type in the Southwest. *Dallas Morning News*, Jun 4, 2015. Available at: http://interactives.dallasnews.com/2015/gender/. Accessed May 16, 2016.
- De Vries ALC, Steensma TD, Doreleijers TAH, Cohen-Kettenis, PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. J Sex Med 2011;8:2276-2283.
- 39. Feldman J, Brown GR, Deutsch MB, et al. Priorities for transgender medical and healthcare research. *Curr Opin Endocrinol Diabetes Obes* 2016;23:180-187.
- 40. Tangpricha V. Treatment of transsexualism. UpToDate 2015. Available at: www. uptodate.com/contents/treatment-of-transsexualism?source=search_result& search=treatment+of+transsexualism&selectedTitle=1%7E8. Accessed May 14, 2016.
- 41. Moore E, Wisniewski A, Dobs A. Endocrine treatment of transsexual people: a review of treatment regimens, outcomes, and adverse effects. *J Clin Endocrinol Metab* 2003;88:3467-3473.