

Letter to the Editor: “Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline”

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Childhood gender dysphoria (GD) is not an endocrine condition, but it becomes one through iatrogenic puberty blockade (PB) and high-dose cross-sex (HDCS) hormones. The consequences of this gender-affirmative therapy (GAT) are not trivial and include potential sterility, sexual dysfunction, thromboembolic and cardiovascular disease, and malignancy (1, 2).

There are no laboratory, imaging, or other objective tests to diagnose a “true transgender” child. Children with GD will outgrow this condition in 61% to 98% of cases by adulthood (3). There is currently no way to predict who will desist and who will remain dysphoric. The degree to which GAT has contributed to the rapidly increasing prevalence of GD in children is unknown. The recent phenomenon of teenage girls suddenly developing GD (rapid onset GD) without prior history through social contagion is particularly concerning (4).

GnRH agonists are used in precocious puberty to delay the abnormally early onset of puberty to a physiologically normal age. The goal of PB in the healthy child, however, is to induce hypogonadotropic hypogonadism to “buy time” to confirm gender incongruence. In a study of PB in adolescents aged 11 to 17 years, 100% desired to continue GAT. They simply “bought” themselves lower bone density and the need for lifelong medical therapy (5).

Studies show that <5% of adolescents receiving GAT even attempt fertility preservation (6). Those started on PB at

Tanner stage II, as recommended by current guidelines, will be blocked prior to sperm maturation and ovum release. They will have no prospect of biological offspring while on HDCS hormones and continuing on to gonadectomy.

The Endocrine Society’s guidelines recommend elevating females’ testosterone levels from a normal of 10 to 50 ng/dL to 300 to 1000 ng/dL, values typically found with androgen-secreting tumors. The ovaries of women given testosterone correspond to those found in PCOS, which itself is associated with increased ovarian cancer risk and metabolic abnormalities (1). Venous thromboembolism risk is elevated fivefold in males taking estrogen (2).

The health consequences of GAT are highly detrimental, the stated quality of evidence in the guidelines is low, and diagnostic certainty is poor. Furthermore, limited long-term outcome data fail to demonstrate long-term success in suicide prevention (7). How can a child, adolescent, or even parent provide genuine consent to such a treatment? How can the physician ethically administer GAT knowing that a significant number of patients will be irreversibly harmed?

Hypothesis-driven randomized controlled clinical trials are needed to establish and validate the safety and efficacy of alternate treatment approaches for this vulnerable patient population. Existing care models based on

psychological therapy have been shown to alleviate GD in children, thus avoiding the radical changes and health risks of GAT (8). This is an obvious and preferred therapy, as it does the least harm with the most benefit.

In our opinion, physicians need to start examining GAT through the objective eye of the scientist-clinician rather than the ideological lens of the social activist. Far more children with gender dysphoria will ultimately be helped by this approach.

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References

- Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;**102**(11):3869–3903.
- Irwig MS. Cardiovascular health in transgender people. *Rev Endocr Metab Disord.* 2018;**19**(3):243–251.
- Ristori J, Steensma TD. Gender dysphoria in childhood. *Int Rev Psychiatry.* 2016;**28**(1):13–20.
- Littman L. Rapid-onset gender dysphoria in adolescents and young adults: a study of parental reports. *PLoS One.* 2018;**13**(8):e0202330.
- 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**(8):2276–2283.
- Nahata L, Tishelman AC, Caltabellotta NM, Quinn GP. Low fertility preservation utilization among transgender youth. *J Adolesc Health.* 2017;**61**(1):40–44.
- Dhejne C, Lichtenstein P, Boman M, Johansson AL, Långström N, Landén M. Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PLoS One.* 2011;**6**(2):e16885.
- Zucker KJ, Wood H, Singh D, Bradley SJA. A developmental, biopsychosocial model for the treatment of children with gender identity disorder. *J Homosex.* 2012;**59**(3):369–397.