

13

But Doc, Is It Safe? Effects of Pubertal Suppression and Trans Hormone Therapy for Youth

Irene N. Sills, MD

Reports of medical and psychological interventions that support transition of gender dysphoric children and transgender adolescents are being published, the results of which show clear benefits to mental health. Providing cross-gender hormones to youth in later adolescence who have been carefully evaluated is likewise proving to be optimal for future adult life.

Despite overwhelmingly positive outcomes, parents and guardians remain concerned about the potential ill effects of stopping puberty in their young adolescents and/or giving older adolescents gender-affirming hormone therapy.

Positive Effects of Medical Interventions

There are two kinds of medical interventions I will discuss: (1) treating gender dysphoric adolescents in early puberty with puberty suppression, and (2) treating older adolescents with cross-gender hormone therapy. Note that no medical interventions are provided for children before the onset of puberty.

The positive effects of early puberty suppression include buying time for youth to explore their evolving gender identity and to assess whether eventual gender reassignment is appropriate. Research has shown that the development of puberty in the direction of their natal body often causes great emotional distress and potential long-term psychological harm that can frequently be alleviated by the suppression of biological puberty (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2011). Additionally, for those adolescents who do transition, delay in the growth of secondary sex characteristics will assist them in passing better in their chosen gender expression (deVries & Cohen-Kettenis, 2012). Beginning

Medical knowledge is continuously growing in this field and readers should be certain to seek out the most recent studies.

REFERENCES

- American Society of Health System Pharmacists. (2014). *AHFS drug information*.
- Asscheman, H., Giltay, E. J., Megens, J. A. J., de Ronde W., van Trotsenburg, M. A. A., & Gooren, L. J. G. (2011). A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. *European Journal of Endocrinology*, 164, 635–642.
- Asscheman, H., T'Sjoen, G., Lemaire, A., Mas, M., Meriggiola, M. C., Mueller, A., Kuhn, A., . . . & Gooren, L. J. (2014). Venous thrombo-embolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: A review. *Andrologia*, 46, 791–795.
- Blakemore, S., Burnett, S., & Dahl, R. E. (2010). The role of puberty in the developing adolescent brain. *Human Brain Mapping*, 31, 926–933.
- Burcombe, R. J., Makris, A., Pittam, M., & Finer, N. (2003). Breast cancer after bilateral subcutaneous mastectomy in a female-to-male trans-sexual. *Breast*, 12, 290–293.
- Carel, J. C., Eugster, E., Rogol, A., Ghizzoni, L., & Palmert, M. (2009). Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*, 123 (4), e752–762.
- Chlebowski, R. T., Hendrix, S. L., Langer, R. D., Stefanick, M. L., Gass, M., Lane, D., . . . & McTiernan, A. (2003). Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: The Women's Health Initiative randomized trial. *Journal of the American Medical Association*, 289, 3243–3253.
- Cohen-Kettenis, P. T., Delemarre-van de Waal, H. A., & Gooren, L. J. G. (2008). The treatment of adolescent transsexuals: Changing insights. *Journal of Sexual Medicine*, 5, 1892–1897.
- Cohen-Kettenis, P. T., Schagen, S.E.E., Steensma, T. D., de Vries, A.L.C., & Delemarre-van de Waal, H. A. (2011). Puberty suppression in a gender-dysphoric adolescent: A 22-year follow-up. *Archives of Sexual Behavior*, 40, 843–847.
- Coleman, E., Bockting, W., Botzem, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., . . . & Zucker, K. (2012). Standards of Care for the health of transsexual, transgender, and gender-nonconforming people, Version 7. *International Journal of Transgenderism*, 13 (4), 165–232.
- Delemarre-van de Waal, H. A., & Cohen-Kettenis, P. T. (2006). Clinical management of gender identity disorder in adolescents: A protocol on psychological and paediatric endocrinology aspects. *European Journal of Endocrinology*, 155, S131–S137.
- de Vries, A. L. C., & Cohen-Kettenis, P. T. (2012). Clinical management of gender dysphoria in children and adolescents: The Dutch approach. *Journal of Homosexuality*, 59, 301–320.
- de Vries, A. L., Steensma, T. D., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *Journal of Sexual Medicine*, 8, 2276–2283.
- Dizon, D. S., Tejada-Berges, T., Koelliker, S., Steinhoff, M., & Granai, C. O. (2006). Ovarian cancer associated with testosterone supplementation in a female-to-male transsexual patient. *Gynecologic and Obstetric Investigation*, 62 (4), 226–228.
- Dorff, T. B., Shazer, R. L., Nepomuceno, E. M., & Tucker, S. J. (2007). Successful treatment of metastatic androgen-independent prostate carcinoma in a transsexual patient. *Clinical Genitourinary Cancer*, 5, 344–346.

- Elbers, J. M., Giltay, E. J., Teerlink, T., Scheffer, P. G., Asscheman, H., Seidell, J. C., & Gooren, L. J. (2003). Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. *Clinical Endocrinology (Oxf)*, 58, 562–571.
- Futterweit, W., & Deligdisch, L. (1986). Histopathological effects of exogenously administered testosterone in 19 female to male transsexuals. *Journal of Clinical Endocrinology and Metabolism*, 62, 16–21.
- Ganly, I., & Taylor, E. W. (1995). Breast cancer in a trans-sexual man receiving hormone replacement therapy. *British Journal of Surgery*, 82, 341.
- Giltay, E. J., Lambert, J., Gooren, L. J., Elbers, J. M., Steyn, M., & Stehouwer, C. D. (1999). Sex steroids, insulin, and arterial stiffness in women and men. *Hypertension*, 34, 590–597.
- Gooren, L. J., Assies, J., Asscheman, H., de Slegte, R., & van Kessel, H. (1988). Estrogen-induced prolactinoma in a man. *Journal of Clinical Endocrinology and Metabolism*, 66, 444–446.
- Gooren, L. J., Bowers, M., Lips, P., & Konigs, I. R. (2015). Five new cases of breast cancer in transsexual persons. *Andrologia*, 47, 1202–1205.
- Gooren, L., & Delemarre-van de Waal, H. (1996). The feasibility of endocrine interventions in juvenile transsexuals. *Journal of Psychology & Human Sexuality*, 8, 69–74.
- Gooren, L. J. G., & Giltay, E. J. (2008). Review of studies of androgen treatment of female-to-male transsexuals: Effects and risks of administration of androgens to females. *Journal of Sexual Medicine*, 5, 765–776.
- Gooren L. J., Giltay, E. J., & Bunck, M. C. (2008). Long-term treatment of transsexuals with cross-sex hormones: Extensive personal experience. *Journal of Clinical Endocrinology and Metabolism*, 93, 19–25.
- Hage, J. J., Dekker, J. J., Karim, R. B., Verheijen, R. H., & Bloemena, E. (2000). Ovarian cancer in female-to-male transsexuals: Report of two cases. *Gynecologic Oncology*, 76, 413–415.
- Hembree, W. C., Cohen-Kettenis, P., Delemarre-van de Waal, H. A., Gooren, L. J., Meyer, W. J., Spack, N. P., Tangpricha, V., & Montori, V. M. (2009). Endocrine treatment of transsexual persons: An Endocrine Society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism*, 94, 3132–3154.
- Kaunitz, A. M., Arias, R., & McClung, M. (2008). Bone density recovery after depot medroxyprogesterone acetate injectable contraception use. *Contraception*, 77, 67–76.
- Knight, E. J., & McDonald, M. J. (2013). Recurrence and progression of meningioma in male-to-female transgender individuals during exogenous hormone use. *International Journal of Transgenderism*, 14, 18–23.
- Lev, A. I. (2004). *Transgender emergence: Therapeutic guidelines for working with gender-variant people and their families*. Binghamton, N.Y.: Haworth Press.
- Meyer, W. J., Webb, A., Stuart, C. A., Finkelstein, J. W., Lawrence, B., & Walker, P. A. (1986). Physical and hormonal evaluation of transsexual patients: A longitudinal study. *Archives of Sexual Behavior*, 15, 121–138.
- Mueller, A., & Gooren, L. (2008). Hormone-related tumors in transsexuals receiving treatment with cross-sex hormones. *European Journal of Endocrinology*, 159, 197–202.

- Nota, N. M., Dekker, M. J. H. J., Klaver, M., Wiepjes, C. M., van Trotsenburg, M. A., Heijboer, A. C., & den Heijer, M. (2017). Prolactin levels during short- and long-term cross-sex hormone treatment: An observational study in transgender persons. *Andrologia*, 49 (6).
- Nuttbrock, L., Hwahng, S., Bocking, W., Rosenblum, A., Mason, M., Macri, M., & Becker, J. (2010). Psychiatric impact of gender-related abuse across the life course of male-to-female transgender persons. *Journal of Sex Research*, 41 (1), 12–23.
- Pritchard, T. J., Pankowsky, D. A., Crowe, J. P., & Abdul-Karim, F. W. (1988). Breast cancer in a male-to-female transsexual. A case report. *Journal of the American Medical Association*, 259, 2278–2280.
- Serri, O., Noiseux, D., Robert, F., & Hardy, J. (1996). Lactotroph hyperplasia in an estrogen treated male-to-female transsexual patient. *Journal of Clinical Endocrinology and Metabolism*, 81, 3177–3179.
- Tangpricha, V., Ducharme, S. H., Barber, T. W., & Chipkin, S. R. (2003). Endocrinologic treatment of gender identity disorders. *Endocrine Practice*, 9, 12–21.
- Toorians, A. W., Thomassen, M. C., Zweegman, S., Magdeleyns, E. J., Tans, G., Gooren, L. J. G., & Rosing, J. (2003). Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. *Journal of Clinical Endocrinology & Metabolism*, 88, 5723–5729.
- Turo, R., Jallad S., Prescott S., & Cross, W. R. (2013). Metastatic prostate cancer in transsexual diagnosed after three decades of estrogen therapy. *Canadian Urological Association Journal*, 7, e544–546.
- Van Haarst, E. P., Newling, D. W., Gooren, L. J., Asscheman, H., & Prenger, D. M. (1998). Metastatic prostatic carcinoma in a male-to-female transsexual. *British Journal of Urology*, 81, 776.
- Van Kesteren, P. J. M., Asscheman, H., Megens, J. A., & Gooren, L. J. G. (1997). Mortality and morbidity in transsexual subjects treated with cross-sex hormones. *Clinical Endocrinology (Oxf)*, 47, 337–342.
- Van Kesteren, P. J. M., Meinhardt, W., van der Valk, P., Geldof, A., Megens, J. A., & Gooren, L. J. G. (1996). Effects of estrogens only on the prostates of aging men. *Journal of Urology*, 156, 1349–1353.
- Viallard, J. F., Marit, G., Mercié, P., Leng, B., Reiffers, J., & Pellegrin, J. L. (2000). Polycythaemia as a complication of transdermal testosterone therapy. *British Journal of Haematology*, 110, 237–238.
- Wierckx, K., Elaut, E., Declercq, E., Heylens, G., De Cuypere, G., Taes, Y., Kaufman, J., & T'Sjoen, G. (2013). Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: A case-control study. *European Journal of Endocrinology*, 169, 471–478.
- Wierckx, K., van Caenegem, E., Schreiner, T., Haraldsen, I., Fisher, A., Toye, K., Kaufman, J. M., & T'Sjoen, G. (2014). Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: Results from the European Network for the Investigation of Gender Incongruence. *Journal of Sexual Medicine*, 11, 1999–2011.