Puberty Blocking Medications for Gender Dysphoria – Is Tapering Required During Discontinuation?

Discontinuation of Androgen Blockers and Estrogen Previously Prescribed for Males With Gender Dysphoria

Discontinuation of Testosterone Previously Prescribed for Females With Gender Dysphoria

Disclaimer

This document is meant for educational purposes only and is not to be misconstrued as medical advice. Any recommendations regarding therapeutic interventions including but not limited to changes of medication dose or type, testing, supplement suggestions, or other recommendations should only be done under the supervision of a medical professional such as a physician or other qualified licensed provider.

Puberty Blocking Medications for Gender Dysphoria – Is Tapering Required During Discontinuation?

What are Puberty Blocking Medications?

Puberty blocking medications are a type of hormone that stops the forward progression of puberty. They are typically injected at regular intervals (like every 3 months) or may be surgically implanted under the skin in which case the effects may last for a year or more.

These medications are technically referred to as GnRH analogues or agonists (GnRHa). They function by partially blocking the function of a gland in the brain called the pituitary. The pituitary controls the functions of other glands and is therefore often referred to as the “master gland”.

The pituitary produces hormones called luteinizing hormone (LH) and follicle stimulating hormone (FSH) which control sex hormone production, sex organ development, and fertility.

Puberty blockers disrupt the normal pituitary signaling of these hormones to the sex glands (ovaries or testicles). If the signaling to the sex glands is disrupted during puberty, then pubertal development will be stopped or “blocked”.

GnRH Agonists for the Treatment of Central Precocious Puberty

The FDA has approved GnRH analogues for the treatment of central precocious puberty. Precocious puberty is a condition in which a child begins pubertal development at an abnormally early age, for example, aged 4. Pediatric endocrinologists may prescribe GnRHa to halt the forward progression of early puberty. At some later time, typically around age 11 or 13 depending on the patient, the medication is stopped allowing pubertal development to continue. The adolescent will generally eventually reach full adult sexual development.

Time Course for Resumption of Pubertal Development

Studies have shown that it takes about 6-18 months for menarche to occur once puberty blockers for precocious puberty are discontinued. (Wu et al., 2021). In the male, the testes will over time resume pubertal levels of testosterone production and continue normal male sexual development. (Bertelloni, et al., 2000). For the female, cyclical production of estrogen and progesterone resumes over time, allowing further female sexual development and, eventually, monthly menstrual cycles.

Puberty Blockers Have Not Been FDA Approved for the Treatment of Gender Dysphoria

Puberty blockers have been used off label for the treatment of Gender Dysphoria. They have not received proper FDA testing for safety or efficacy for treating this mental health condition. Because they are being used to stop normally timed puberty there are additional risks to bone density and potentially other organ systems that need to be followed up by physicians over time.

There are little available data for what happens when a patient stops taking a puberty blocker to stop normal pubertal development (as opposed to stopping early pubertal development in precocious puberty). It is reasonably presumed that if a patient is receiving injections of a GnRHa like Lupron, then it will likely take approximately 6-18 months for the pituitary to recover and for normal pubertal development to resume.

There are little available data for a patient who discontinues a puberty blocker implant for Gender Dysphoria. Although an implant may have directions to be replaced each year, there is a strong possibility that the residual medication in an implant may continue to block pubertal development for an extended period of time beyond one year if not removed. Therefore, the implant should be removed by one year or sooner if the goal is to resume normal pubertal development.

Is There a Need for Tapering Puberty Blocking Medications?

Some medications require a taper (a gradual decrease in dose), if they have been used for an extended period of time, before being discontinued altogether. The goal of tapering is to prevent complications that might occur from rapid withdrawal of the medication

However, we believe that puberty blocking medications used off-label for Gender Dysphoria should not require a taper because of the prolonged time it takes for resuming normal pituitary function. In other words, it is expected that once injections are discontinued or GnRHa implants are removed then the pituitary will gradually regain normal function for both sexes. Menstrual cycles should start after 6-18 months. This is the case when GnRHa are used for precocious puberty.

However, when puberty blockers are being used off label to stop normally timed puberty, careful follow-up with the patient's pediatrician, family doctor, or endocrinologist is advised to monitor for the resumption of normal pubertal development. Additional blood hormonal tests may need to be performed if it is not clear that puberty is resuming as expected.

References

1. Bertelloni, S., Baroncelli, G. I., Ferdeghini, M., Menchini-Fabris, F., & Saggese, G. (2000). Final height, gonadal function and bone mineral density of adolescent males with central precocious puberty after therapy with gonadotropin-releasing hormone analogues. *European journal of pediatrics*, *159*(5), 369–374. https://doi.orgs/10.1007/s004310051289

2. Vickie Wu, Victoria Zhao, Rula Issa, Meredith Wilkes, Elizabeth Wallach, Robert Rapaport, Christopher Romero, Mabel Yau. Clinical findings influencing time to menarche post gonadotropin-releasing hormone agonist therapy in central precocious puberty. Ann Pediatr Endocrinol Metab. 2021;26(3):185-191. Published online May 12, 2021. DOI: https://doi.org/10.6065/apem.2040220.110

3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed., text rev.) 2022. https://doi.org/10.1176/appi.books.9780890425787

Discontinuation of Androgen Blockers and Estrogen Previously Prescribed for Males With Gender Dysphoria

Basic Principles:

There are two principal sex hormones in humans: testosterone and estrogen. Most males have a very small amount of estrogen in the blood. On the other hand, estrogen is the predominant sex hormone found in females.

There are many forms of the hormone estrogen but the main one found in both males and females is called estradiol. The normal upper level of estradiol in males is 40 pg/ml. Females, before menopause have levels more than 10 times that level found in males.

Most of the estradiol found in males is derived from conversion of testosterone to estradiol.

The testes are the principal source of testosterone in males. The testes will only produce testosterone in response to a stimulus from the pituitary gland in the brain. In normal males, two hormones, LH and FSH, turn on the testes in males. LH and FSH direct the testes to make testosterone and to produce sperm. Exogenous administration (by injections, pills, gels, etc.) of estrogen will signal the pituitary gland to turn off those stimuli to the testes. In turn, testosterone production and sperm production will decrease.

Many hormones produce their effects on the body by binding to receptors. This action is similar to a key opening up a lock. Sex hormones such as testosterone, must bind to the testosterone or androgen receptor to produce their effect.

Spironolactone is a medication that has multiple actions, one of which is to modestly block the androgen receptor. Spironolactone has been prescribed for males with Gender Dysphoria.

There is no FDA approved form of estrogen for males to treat Gender Dysphoria. Estrogen given to males as pills or injections or transdermal patches will turn off the testes as described above. Once the estrogen is discontinued the testes are likely to regain most of their function. However, the impact on testicular function is likely to depend on the duration of estrogen use and the dose of estrogen.

Discontinuation of Estrogen in Males Who Retain Their Testes

Those males who have been on estrogen long term, greater than 6-12 months, may benefit from a tapering of the dose over time. It may take time to recover normal testicular function but this will vary from person to person and will likely be related to duration of estrogen use and dosage administered. Management must be individualized. There are no rigorous data to guide discontinuation.

Some males who have been on estrogen for years may need some exogenous testosterone while their testes recover function over time. Care must be individualized and will be guided by patient response, and laboratory data.

Discontinuation symptoms may include temperature dysregulation, mood changes, and sleep disturbance. There is no evidence to indicate any serious or life-threatening consequences to rapid discontinuation of estrogen in males.

All persons require ongoing psychologic support.

Discontinuation of Spironolactone or Progesterone

Occasionally males with Gender Dysphoria are prescribed progesterone, a different female hormone. That can be rapidly discontinued. Spironolactone can also be discontinued without tapering.

Patient Follow Up:

Careful follow up should occur in the office with exam and appropriate labs coupled with the essential ongoing psychologic support for these persons. Many of these persons have ongoing psychiatric and psychologic conditions.

References

1. Matsumoto AA, B. Testicular Disorders. In: Melmed SA, R. et al., ed. Wiliams' Textbook of Endocrinology. Elsevier; 2025:660- 750.

2. Chen Z-JLRea. Androgen Excess Disorders in Women. In: DeGroot's Endocrinology Eighth Edition. Elsevier; 2023:2074.

3. Handelsman DJ, Desai R, Conway AJ, et al. Recovery of male reproductive endocrine function after ceasing prolonged testosterone undecanoate injections. Eur J Endocrinol. 2022;186(3):307-318.

4. Charlton L, Bond R. Clinical considerations and endocrinological implications in the detransition process. Best Pract. Res Clin Endocrinol Metab. 2024;38(5):101932.

Discontinuation of Testosterone Previously Prescribed for Females With Gender Dysphoria

Testosterone is the dominant sex hormone found in males. In females, the level of testosterone is normally about 20 times less than that found in males. However, females taking testosterone for Gender Dysphoria will generally have levels of testosterone in the male reference range.

For females who have used testosterone, the effects of exogenous testosterone vary based on the duration of use, stage of puberty when initiated and current stage of sexual development. Resolution of these effects may take time and may be incomplete. Some changes, such as male pattern baldness, hirsutism, clitoromegaly and voice changes, cannot be fully reversed. The outcomes will vary for everyone.

When a female discontinues testosterone, there are several factors to address:

- Plan for tapering off or immediately discontinuing testosterone
- Potential side effects of stopping testosterone
- Potential need to reintroduce estrogen with or without progesterone

We are not aware of published studies on the question of tapering testosterone doses over time in females who have been taking testosterone, but there is sound clinical logic that tapering may, in some cases, be better than abruptly stopping testosterone.

Suggestions for Testosterone Taper and Cessation

Females who have been on high-dose testosterone for less than 6-12 months, likely will not need to taper testosterone, depending on the prescribed dose. Those who have been treated for more than 6-12 months will likely benefit from a gradual decrease in dose until discontinuation. There are no rigorous data to guide discontinuation.

Discontinuation symptoms may include anxiety, depression, mood swings, psychological changes, insomnia, reduced energy, hot flashes, temperature dysregulation, and changes in libido.

Patient Follow Up:

Careful follow up should occur in the office with exams and appropriate labs coupled with the essential ongoing psychologic support for these persons.

Estrogen replacement may be necessary. Even if the female patient retains her ovaries, it may take time for the ovaries to return to normal cyclic estrogen production. Exogenous estrogen will decrease the normal function of the ovaries, so treatment should be individualized. If the patient had her ovaries removed, estrogen treatment is generally indicated for overall health.

All these persons must have ongoing psychological support.

References

1. Littman L. Individuals treated for gender dysphoria with medical and/or surgical transition who subsequently detransitioner: a survey of 100 detransitioners. *Arch Sex Behav.* 2021;50(8):3353-3369. doi: 10.1007/s10508-021-02163-w. Epub 2021 Oct 19.

2. Hembree, W.C., Cohen-Kettenis, P.T., Gooren, L., Hannema, S.E., Meyer, W.J., Murad, M.H., Rosenthal, S.M., Safer, J.D., Tangpricha, V., & T'Sjoen, G.G. (2017). Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, 102(11), 3869-3903

3. Hall RCW, Hall RCW, Chapman MJ. Psychiatric complications of anabolic steroid abuse. Psychosomatics. 2005;46(4):285-290. doi:10.1176/appi.psy.46.4.285

4. Gomez-Lumbreras A, Villa-Zapata L. Exploring safety in gender-affirming hormonal treatments: an observational study on adverse drug events using the food and drug administration adverse event reporting system database [published online ahead of print February 12, 2024]. Ann Pharmacother.doi:10.1177/10600280241231612

5. Laidlaw MK, Jorgensen S. Exploring Safety in Gender-Affirming Hormonal Treatments: An Observational Study on Adverse Drug Events Using the Food and Drug Administration Adverse Event Reporting System Database. Annals of Pharmacotherapy. 2024;0(0). doi:10.1177/10600280241278913

6. Ruuska, S. M., Tuisku, K., Holttinen, T., & Kaltiala, R. (2026). Psychiatric Morbidity Among Adolescents and Young Adults Who Contacted Specialised Gender Identity Services in Finland in 1996-2019: A Register Study. *Acta paediatrica (Oslo, Norway : 1992)*, *115*(7), 1545–1553. https://doi.org/10.1111/apa.70533