Puberty Blockers

Margo Collazo

Follow this and additional works at: https://scholarship.claremont.edu/scripps_theses

Recommended Citation
Collazo, Margo, "Puberty Blockers" (2023). Scripps Senior Theses. 2048.
https://scholarship.claremont.edu/scripps_theses/2048

This Open Access Senior Thesis is brought to you for free and open access by the Scripps Student Scholarship at Scholarship @ Claremont. It has been accepted for inclusion in Scripps Senior Theses by an authorized administrator of Scholarship @ Claremont. For more information, please contact scholarship@cuc.claremont.edu.
PUBERTY BLOCKERS

A Thesis Presented

by

MARGO COLLAZO

To the Keck Science Department

of

Claremont McKenna, Scripps, and Pitzer Colleges

In Partial Fulfillment of

The Degree of Bachelor of Arts

Senior Thesis in Human Biology

1 May 2023
# Table Of Contents

- Abstract 3
- Introduction 4
- Typical Pubertal Development 5
  - Measurement 5
  - Mechanism 6
  - In Ovaries: 8
  - In Testes: 9
- Abnormal Puberty 10
  - Early puberty 10
- Puberty Blockers and Trans Youth 11
  - Gender affirming care 11
  - Mental health 12
  - Puberty blockers 12
- Conclusion 13
- Works Cited 14
Abstract

The onset of puberty initiates a period of rapid growth, the development of secondary sex characteristics and the achievement of fertility. For children with gender dysphoria (GD), puberty can be an extremely difficult period where they identify less and less with the sexual development of their body. The most common treatment for GD is puberty blockers, which can be started once puberty begins around 11 years old and have shown to reduce the risk of suicide and increase mental health in transgender and nonbinary youths (TGNB).

Puberty blockers suppress the body’s production of GnRH, delaying puberty until the individual can make the decision to progress through cisgender puberty or starts gender affirming hormone therapy (GAHT). This allows pubescent children questioning their gender to have more time to ensure that gender affirming hormones are right for them. The earliest GAHT can begin is 16-17 years old if they have parental consent and have already been on puberty blockers for one year.

While the research on the long-term impact of puberty blockers in TGNB children is lacking, the use of puberty blockers for cisgender children experiencing early puberty has been researched for decades. Using this research, we can better explore the impact puberty blockers have on the body in general.
Introduction

Puberty is defined as the period of growth characterized by the development of second sex characteristics and the achievement of fertility (Abreu & Kaiser, 2016). In people with ovaries, the first landmark of puberty is generally breast development. For those with testes, the first landmark of puberty is generally testicular enlargement (Abreu & Kaiser, 2016). As puberty progresses, both sexes see the emergence of acne, increased hair growth in the armpit and pubic area, and growth spurts (MedlinePlus, 2016). The timing of puberty varies depending on gonad type, genetics, race, and weight. For cis women, normal puberty begins around 10 years old with breast development and ends around 14 years old with menstruation being the last milestone of puberty. In cis men, puberty begins around 12 years of age with testicular enlargement and ends around 16 years of age with facial hair being the last notable pubertal landmark (Abreu & Kaiser, 2016). Puberty that begins significantly earlier than that is considered precocial puberty and is considered as such if it begins in cis girls around 8 years old or younger and in cis boys age 9 years old or younger and is treated with puberty blockers (Bradley et al., 2020). Puberty blocker have also been used in the treatment of gender dysphoria in transgender and nonbinary youth. Puberty blockers relieve some of the psychological stress that is faced these youth and reduces the rates of suicide and depression.

There has recently been a flood of anti-trans bills being passed to make puberty blockers illegal under the argument that puberty blockers cause harm to children and that they are not old enough to make life changing decisions. This thesis will look at the physiological outcomes of normal and precocious puberty in cisgender children to identify any long-term effects of puberty blockers. The goal of this thesis is to show that there are no irreversible effects of puberty blockers, making it a safe and life-saving treatment for gender dysphoria in TGNB youth.
Typical Pubertal Development

Typical pubertal development begins around 11 years old and causes secondary sex characteristics to develop, ultimately signaling the achievement of fertility. For cisgender women, these include breast growth, pubic hair growth, and an increase in fat around the hips. For cisgender men, secondary sex characteristics include facial hair, voice deepening, stronger jaw, and testicular enlargement. In transgender and nonbinary children, the development of these characteristics increases the disconnect between their gender identity and their sex.

![Tanner stages of puberty (Carel & Léger, 2008)](image)

**Figure 1**: Tanner stages of puberty (Carel & Léger, 2008).

*Measurement*

The progression of puberty can be measured using Tanner stages (**Figure 1**, (Carel & Léger, 2008)). These stages outline five pubertal developmental checkpoints for cis men – testicular
and pubic hair growth – and cis women – pubic hair growth and breast development (Carel & Léger, 2008). Puberty officially begins once an individual reaches stage 2.

**Mechanism**

The initiation of puberty is generally attributed to the increase in the pulsatile release of gonadotropin releasing hormone, GnRH (Abreu & Kaiser, 2016). GnRH is inhibited during childhood but active during the embryonic period and after the initiation of puberty. During embryonic development, GnRH causes the placenta to release hCG, human chorionic gonadotropin, which is important in maintaining pregnancy by stimulating luteinizing hormones to produce progesterone, a sex hormone important for fetal growth ("Gonadotropins," 2012). After

![Figure 2: Kisspeptin-GnRH pathway and HPG axis (Marques et al., 2022).](image)
birth, the GnRH neuronal system is present but dormant and underdeveloped as the connections don’t mature until puberty (Casteel & Singh, 2020).

GnRH is made in the hypothalamus and regulates the hypothalamic pituitary gonadal axis, HPG axis, and the downstream signaling of gonadotropes (Casteel & Singh, 2020). The HPG is known to regulate puberty, sexual maturation and reproduction in humans (Kant & Meena, 2020). The gonadotropes FSH, follicle stimulating hormone, and LH, luteinizing hormone, are responsible for stimulating gametogenesis and the production of sex steroids.

The release of GnRH is stimulated by a protein called kisspeptin that is found in the placenta, hypothalamus, ovaries, testes, pancreas, and intestines. While there are many GnRH stimulators, kisspeptin is the primary stimulator of GnRH released in response to kisspeptin (Kant & Meena, 2020). This is because kisspeptin acts as a ligand for G-protein receptor 54, GPR54, which can be found in GnRH neurons (Marques et al., 2022). Kisspeptin is part of the KNDy system along with neurokinin B and dynorphin, both of which fine tune kisspeptin signaling by acting as a stimulator and inhibitor, respectively (Kant & Meena, 2020). The KNDy system

![Figure 3: Cis female reproduction pathway (Carroll, 2007a).](image-url)
stimulates the pulsatile release of GnRH, and in turn, initiates the pulsatile release of gonadotropes from the pituitary gland (Figure 2). The pituitary gonadotropes – LH and FSH– then effect gametogenesis and the production of sex steroids: androgens (like testosterone), estrogens, and progestogens (Kant & Meena, 2020).

In Ovaries:

FSH stimulates the growth of the ovarian follicles which secrete estrogen (Figure 3). Simultaneously, LH stimulates the production of sex hormones, causing a spike in estrogens. This spike inhibits the production of FSH in the pituitary gland, but has a stimulatory effect on LH (Carroll, 2007a). LH causes the maturation of the ovarian follicles, which produce progesterone, and triggers ovulation. The mature follicle develops into a graafian follicle that comes to form the corpus luteum which produces progesterone, estrogen, and inhibin. Progesterone is linked to dynorphin, thus, when progesterone concentrations increase, so do dynorphin concentrations, inhibiting the stimulation of GnRH and in return inhibiting the production of LH and FSH in the pituitary gland (Marques et al., 2022). Days after ovulation, the corpus luteum degenerates, stopping the inhibitory feedback and allowing the production of FSH and LH to resume and the

Figure 4: Plasma FSH and LH levels throughout a cis woman's life (Carroll, 2007a).
cycle to repeat (Carroll, 2007a). Due to the fluctuation of sex hormones, GnRH pulse frequencies change depending on the menstrual cycle (Figure 4, Casteel & Singh, 2020).

Estradiol and progesterone also play an important role in the development of second sex characteristics. Estradiol is also responsible for the development of breast tissue, the closure of epiphyseal plates stopping growth spurts, and pubic hair. Progesterone is involved in the development of breast growth specific for milk secretion (Carroll, 2007a).

*In Testes:*

In the testes, LH is responsible for stimulating Leydig cells that produce testosterone from two intermediates of cholesterol: dehydroepiandosterone (DHEA) and androstenedione (Figure 5, Nassar & Leslie, 2023). DHEA can be converted into either testosterone or estrogen and androstenedione can be converted into testosterone (Nassar & Leslie, 2023). FSH stimulates Sertoli cells which produce estradiol and promotes spermatogenesis (Carroll, 2007b).
Abnormal Puberty

Early puberty

There are many components, such as gonadal type, race, weight, nutrition, etc., which determine the “normal” age of onset for puberty. Sources report the normal age for a cis girl to begin puberty at 10 years old (MedlinePlus, 2016), while others put the onset around 8 years old (Bradley et al., 2020). One reason for the variability may be due to increased rates of childhood obesity (Bradley et al., 2020). Fat cells produce leptin which stimulates GnRH neurons, however the excitation is not enough by itself to trigger the onset of puberty but it does make it easier for puberty to begin (Karapanou & Papadimitriou, 2010).

Early puberty is classified as precocious puberty when there are signs of puberty at age 7 for cis girls and 9 for cis boys (Bradley et al., 2020). Precocious puberty is divided into central precocious puberty (CPP) and peripheral precocious puberty (PPP, Fuqua, 2013). CPP is GnRH-dependent and can be caused by genetic variation, tumors, CNS conditions or idiopathic reasons. CPP can be treated using GnRH receptor analogs, GnRH-Ra, that override the natural pulsatile release of GnRH (Fuqua, 2013) causing the down regulation of GnRH by binding better to the GnRH receptors than GnRH, and thus, stopping the progression of puberty (Witchel & Topaloglu, 2019). PPP is GnRH-independent and is typically due to genetic problems affecting the ovaries or testes, and is treated depending on the cause (Fuqua, 2013).

Puberty blockers have no long-lasting effect in cis children. While there are anecdotal instances, the majority of studies have not found any changes in BMI in girls with precocious puberty (Cantas-Orsdemir & Eugster, 2019). While GnRH agonists do decrease bone mineral density, the effects are not long-lasting and returns to normal after the cessation of treatment (Cantas-Orsdemir & Eugster, 2019).
Puberty Blockers and Trans Youth

Transgender and nonbinary youth face disproportionately high rates of depression and suicide. This may be because TGNB youth experience more minority stress than their cisgender peers due to their gender identity (Allen et al., 2019). TGNB youth struggle with their safety both in and out of the home. 37% of TGNB youth report having been threatened or harmed because of their gender identity (2022 National Survey on LGBTQ Youth Mental Health, 2022). Puberty blockers allow TGNB youth to integrate into society more easily as their preferred gender by reducing the amount of gender affirming care they need.

Gender affirming care

Gender affirming care for trans women who do not use puberty blockers typically involves laser hair removal for facial hair, vocal training, and feminization. To be considered as passing, trans women go through vocal training to practice speaking in a higher and more feminine voice, since the voice drop experienced during male puberty is irreversible. Feminization surgery involves facial reconstruction to typically reshape the jawline and chin, Adam’s apple reduction, lip and cheek augmentation and forehead contouring (Facial Feminization Surgery, 2023).

If a trans woman had puberty blockers, then there would be no development of any secondary sex characteristics and they would continue with gender affirming hormones which would trigger female puberty.

Trans men that do not go through puberty suppression, have surgeries to reshape their body into a more masculine figure, typically with liposuction and the removal of breasts. For trans men, gender affirming hormones deepen the voice and causes facial hair growth making it easier for them to pass (Allen et al., 2019).
Mental health

TGNB youth face lots of discrimination from their doctors, teachers, parents, and peers. In fact, 71% of TGNB youth reported that they had experienced discrimination because of their gender identity (2022 National Survey on LGBTQ Youth Mental Health, 2022). LGBTQ youth that have been discriminated against because of their gender report higher rates of attempted suicide, 19% compared to 7% respectively (2022 National Survey on LGBTQ Youth Mental Health, 2022). In 2022, the Trevor Project found that over half of the TGNB youth that responded to their survey had seriously considered suicide and 1 in 5 TGNB youth had actually attempted suicide (2022 National Survey on LGBTQ Youth Mental Health, 2022).

They report significantly higher levels of anxiety, depression, and assault than their cisgender peers. The lack of support and active discrimination against TGNB people adds minority stressors to their lives that impact their mental health causing excess distress that presents as depression. It has been shown that treating the gender dysphoria that TGNB youth experience with puberty blockers correlates to lower rates of both depression and suicide (Green et al., 2022).

Puberty blockers

The treatment of gender dysphoria with puberty blockers has been found to be extremely effective. Stopping the development of unwanted sexual characteristics allows TGNB youth to integrate into society more easily. It also allows TGNB youth to reduce the amount of gender affirming care. Once the child is around 17 years old, they can either resume cisgender puberty or begin gender affirming hormones and go through their desired puberty. Puberty blockers may temporarily reduce bone mineral density, but once they are stopped there is no significant difference. By using puberty blockers, TGNB youth can more comfortably live their lives. There is little regret among the transgender community after transitioning and trans individuals can live their lives how they want to.
Conclusion

Puberty is a time of sexual maturation involving the development of secondary sex characteristics. Starting around age 11, there is an increase in the pulsatile release of GnRH which is ultimately responsible for the release of sex steroids that control the development of secondary sex characteristics. GnRH agonists are used as puberty blockers to postpone puberty until the individual is ready, physically, or mentally, to continue through puberty. In cisgender children, puberty blockers are used to treat precocious puberty, or puberty that begins early. GnRH agonists can cause changes in BMI and bone mineral density, but it has been found that once puberty blockers are stopped, there are no statistically significant changes.

TGNB youth face disproportionate rates of discrimination and minority stressors that affect them as depression. The psychological distress that they face is exaggerated by the fact that their body continues to develop characteristics that do not align with their identity. By taking puberty blockers, TGNB youth can have more time to safely explore their gender identity without causing harm. Pubertal suppression will also help reduce the amount of gender affirming care they may need in the future. The reduction in rates of depression and attempted suicide in TGNB youth treated with puberty blockers shows that they are an effective treatment plan.

Puberty is a very confusing time in an adolescent’s life. Transgender and nonbinary youth are faced with even more challenges as they aren’t widely accepted by society. Treating gender dysphoria with puberty blockers should continue to be one of the main forms of care in ATGNB youth as it has been shown to reduce depression and risk of suicide without any long-term effects on development.
Works Cited

https://www.thetrevorproject.org/survey-2022/

Endocrinol, 4(3), 254-264. https://doi.org/10.1016/s2213-8587(15)00418-0

transgender youth after gender-affirming hormones. Clinical Practice in Pediatric 
Psychology, 7(3), 302.

Pubertal Periosteal Bone Expansion. The Journal of Clinical Endocrinology & 
Metabolism, 89(12), 6025-6029. https://doi.org/10.1210/jc.2004-0602

l6597. https://doi.org/10.1136/bmj.l6597

https://doi.org/10.1080/17446651.2019.1575726

2366-2377. https://doi.org/10.1056/NEJMcp0800459


Copyright © 2023, StatPearls Publishing LLC.