

EDUCATIONAL OBJECTIVES

After completing the continuing education activity, pharmacists will be able to

- Use inclusive language that respects the gender identity of patients during communication and/or interactions
- Review masculinizing and feminizing therapy in adults and adolescents
- Provide recommendations for inclusive and stigma-free care practices
- Discuss the components of a gender-affirming treatment plan

After completing the continuing education activity, pharmacy technicians will be able to

- Use inclusive language that respects the gender identity of patients during communication and/or interactions
- Review masculinizing and feminizing therapy in adults and adolescents
- Identify best practices for inclusive, stigma-free care for patients undergoing gender-affirming care
- Discuss the components of a gender-affirming treatment plan



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What You've GAHT to Know About Gender-Affirming Care

ABSTRACT: This continuing education activity focuses on key aspects of transgender healthcare, encompassing language inclusivity, physiologic considerations, and pharmacologic interventions across different life stages. The activity begins with an exploration of gender-inclusive language, highlighting the importance of respectful communication in healthcare settings. It discusses puberty's physiology, highlighting the role of the hypothalamic-pituitary-gonadal axis in the development of secondary sexual characteristics. The activity then delves into feminizing and masculinizing pharmacology, detailing hormone therapies, their mechanisms of action, and associated outcomes. It outlines special considerations for adults, adolescents, and children, along with guidelines for puberty suppression and hormone therapy initiation. It also addresses non-pharmacologic interventions such as chest binding, tucking, and voice therapy, stressing the importance of holistic care. Last, the activity examines other healthcare areas impacted by gender-affirming hormone therapy (GAHT), such as anticoagulation, kidney function assessment, and fertility preservation. It provides recommendations for clinical practice and the need for individualized care with shared decision-making. Overall, this activity aims to enhance understanding and promote inclusive and affirming healthcare practices for transgender individuals.

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INTRODUCTION

Practitioners in all healthcare settings need to understand and respect gender diversity. Pharmacists and pharmacy technicians can play a pivotal role in gender-affirming care by using inclusive language and developing comprehensive knowledge of pharmacologic interventions. The scope of gender affirming care ranges from puberty suppression to gender-affirming surgeries to align physical appearance with gender identity. Gender dysphoria is a very serious condition among

transgender individuals that can lead to depression and suicide. Gender dysphoria is not solely internally driven and can be exacerbated by external stressors/stigma. This includes external aspects of experience such as distress associated with misgendering and social norms, social isolation, transphobia, etc.^{1,2} It may be treated with hormone therapy and can require lifelong treatment. Healthcare professionals in the pharmacy setting can help these patients by creating a supportive environment that promotes adherence to their treatment. The **SIDEBAR** (to the right) provides definitions for frequently used terms in transgender care.

Guidelines

The World Professional Association for Transgender Health (WPATH) publishes the *Standards of Care for the Health of Transgender and Gender Diverse People* (SOC),⁷ which is the main guideline used internationally for transgender health. This continuing education activity is based on SOC Version 8.

The Endocrine Society develops the *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline*.³ These guidelines establish a framework for the appropriate treatment of individuals and standardize terminology to be used by healthcare professionals. This activity cites these guidelines as well.

Inclusive Language

Everyday language often revolves around the concept of two genders and one sexuality, potentially overlooking diverse identities. Using gender-inclusive language demonstrates respect and acknowledgment of all gender identities while eliminating assumptions. Using they/them pronouns instead of he/his or she/her when unsure of someone's pronouns is best.⁶ Healthcare professionals can demonstrate inclusivity by introducing themselves with their own pronouns and asking patients how they prefer to be addressed. Common pronouns include she/her/hers, he/him/his, and they/them/theirs.⁶ Healthcare professionals should avoid stating that a person is transgender to others unless that is how the person identifies and is comfortable with sharing that information.⁶ Another suggestion is saying "feel free to bring your spouse or partner" instead of "feel free to bring your husband or wife."⁶

PAUSE AND PONDER: A fellow colleague consistently misgenders a transgender patient despite being corrected. How would you address this behavior while promoting inclusivity and respect in the pharmacy setting?

Physiology

Puberty is the process of an adolescent becoming capable of reproduction. This process involves the hypothalamic-pituitary-gonadal axis. The first biologic sign of puberty is an increase in endogenous gonadotropin hormone-releasing hormone

SIDEBAR: Terminology¹⁻⁶

- **Gender expression:** External manifestations of gender, expressed through one's behavior, body characteristics, clothing, haircut, name, pronouns, or voice. Typically, transgender people seek to make their gender expression align with their gender identity, rather than their assigned gender.
- **Gender role:** Behaviors, attitudes, and personality traits that a society (in a given culture and historical period) assigns as masculine or feminine and/or that society associates with or considers typical of the social role of men or women
- **Gender identity/experienced gender:** One's internal, deeply held sense of gender. For transgender people, gender identity does not match their sex assigned at birth. Most people have a gender identity of male or female. For some people, gender identity does not fit neatly into one of those two choices (e.g., nonbinary). Unlike gender expression, gender identity is invisible to others.
- **Sex:** The best-known attributes include sex-determining genes, sex chromosomes, gonads, sex hormones, internal and external genitalia, and secondary sex characteristics.
- **Sex assigned at birth:** Sex assigned at birth, usually based on genital anatomy. AFAB refers to "assigned female at birth," and AMAB to "assigned male at birth."
- **Transgender** (also TGD, trans): An umbrella term for people whose gender identity and/or gender expression differs from what is typically associated with their sex assigned at birth. Not all transgender individuals seek treatment.
- **Cisgender:** A term for people whose gender identity and/or gender expression is aligned with what is typically associated with their sex assigned at birth.
- **Gender dysphoria:** The distress experienced when one's gender identity and assigned gender are incongruent, often worsened by external factors like misgendering, social norms, isolation, and transphobia. Not all transgender people experience gender dysphoria; being transgender on its own is not a medical condition.
- **Transition:** The process during which transgender people change their physical, social, and/or legal characteristics consistent with their affirmed gender identity. Transgender individuals may initially transition socially and postpone medical transition. This is especially true for prepubertal children.
- **Transgender male** (also: trans man, female-to-male): Individuals assigned female at birth but who identify and live as men.
- **Transgender woman** (also: trans woman, male-to-female, transgender female): Individuals assigned male at birth but who identify and live as women.
- **Non-binary:** An adjective describing a person who does not identify exclusively as a male or a female. Non-binary people may identify as being both male and female, somewhere in between, or as falling completely outside these categories. While many also identify as transgender, not all non-binary people do.
- **Embodiment goals:** Body qualities/characteristics that a patient wishes to have (e.g. shape, feeling, behavior of body).

Table 1. Patterns of Typical Puberty⁷

About	Ovaries	Testes
Puberty	Onset: 7 to 13 years old Hormone effects: The ovaries produce estrogen, stimulating mammary gland budding.	Onset: 9 to 14 years old Hormone effects: LH and FSH lead to increased testicular volume (>4 mL), which allows the testes to produce enough testosterone for masculinization.
Cisgender Adult Hormone Levels	Estradiol: 30 to 400 pg/mL (pre-menopause) Testosterone: 15 to 70 ng/dL Progesterone: 1 to 90 ng/mL	Estradiol: 10 to 40 pg/mL Testosterone: 300 to 1000 ng/dL Progesterone: < 1 ng/mL

ABBREVIATIONS: FSH = follicle stimulating hormone; LH = luteinizing hormone

(GnRH).⁷ GnRH produced by the hypothalamus causes the pituitary gland to secrete gonadotropins: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH stimulate gonads to produce sex hormones.⁸ **Table 1** (above) compares puberty in individuals with ovaries and those with testes.

ADULTS

Feminizing Pharmacology

The goals of feminizing pharmacology care are the development of female secondary sex characteristics and the minimization of male secondary sex characteristics. Treatments include externally dosed estrogens and antiandrogens. The selection of therapy should include a patient-specific evaluation of patient goals, medical conditions, medication risk/benefit, and economics.⁷

Estrogen promotes feminine features such as breast growth. Antiandrogens diminish masculine features by reducing endogenous testosterone. Examples of antiandrogens include spironolactone, cyproterone acetate, GnRH agonists, and 5-alpha reductase inhibitors.

Estrogen

In gender-affirming care, estrogen (or 17-beta estradiol) used for feminizing treatment is chemically identical to estrogen produced by human ovaries.^{3,7} Multiple dosing formulations exist including oral tablets, topical patches, intramuscular injections, and topical gels/sprays. A major safety concern for anyone using exogenous estrogen is the increased risk of thromboembolic events. 17-beta estradiol is generally preferred over synthetic estrogens for the ease of monitoring serum levels and its lower risk of thromboembolic events. For those older than 45 years and those at a higher risk of venous thromboembolism (VTE), the guidelines recommend transdermal formulations. Cardiovascular screening is essential to identify patients at higher VTE risk. Due to multiple Boxed Warnings in the product labeling and potentially significant adverse events, providers should use caution and consider the risks and benefits of estrogen therapy.^{3,7}

The desired effects of exogenous estrogen include breast development, redistribution of facial and subcutaneous fat, reduction of muscle mass, reduction of body hair, and reversal of scalp hair loss. Exogenous estrogen will not alter voice or height in adults. **Table 2** (on the next page) describes available estrogens used in gender-affirming care.^{3,7}

Antiandrogens

Antiandrogens, listed in **Table 3** (on page 5), can reduce endogenous testosterone levels or its activity and are usually used in combination with estrogen for feminizing effects. While antiandrogens may be employed as monotherapy, combination treatment can help minimize the amount of estrogen necessary for gender-affirming effects and therefore reduce the estrogen-associated risks. General adverse effects of antiandrogen monotherapy may include hot flashes, low mood or energy, and bone loss when used long term.⁷

Spironolactone is a potassium-sparing diuretic that has many therapeutic uses including in heart failure and hypertension. Spironolactone is also an aldosterone receptor antagonist that can cause positive effects, such as gynecomastia (an increase in breast gland tissue) for transgender women. Gynecomastia is dose and duration dependent, occurring in approximately 10% of patients. The diuretic and antihypertensive effects may become apparent within two to three weeks potentially resulting in excess urination and low blood pressure.^{3,14}

GnRH agonists (histrelin, leuprolide) work by continuously activating the pituitary gland to make more LH and FSH. This overactivation eventually suppresses sex steroid production. Out of pocket costs for these medications can range anywhere from \$10,000 to \$50,000 for three months, thereby significantly limiting their use.¹⁶

WPATH does not regularly recommend other drugs like 5-alpha reductase inhibitors, finasteride or dutasteride, as data supporting use in the transgender population is sparse.⁷

Table 2. Estradiol for GAHT⁹

Doses and Formulations	Safety	Monitoring
<p>Tablet : 2-6 mg/day PO or SL</p> <p>Patch: 0.025-0.2 mg/day TD, change every 3-5 days or weekly</p> <p>Injection: estradiol valerate or cypionate 2-10 mg IM weekly or 5-30 mg IM every 2 weeks</p> <p>Transdermal gel or spray may not reach blood levels of cisgender female range</p>	<p>Boxed Warnings</p> <ul style="list-style-type: none"> - Endometrial cancer - Cardiovascular disease - Breast cancer - Dementia <p>Contraindications</p> <ul style="list-style-type: none"> - History of estrogen-sensitive neoplasm - Previous VTE related to underlying hypercoagulation - End-stage chronic liver impairment or disease - Thrombophilic disorders - Angioedema - Anaphylactic reaction <p>Adverse Events</p> <ul style="list-style-type: none"> - Infertility, hypertriglyceridemia, weight gain, cerebrovascular disease, cholelithiasis, hypertension, erectile dysfunction, type 2 diabetes mellitus, low bone mineral density, hyperprolactinemia, migraines, hot flashes 	<ul style="list-style-type: none"> - Baseline risk for breast cancer and cardiovascular disease - Serum triglycerides (2 weeks after initiation in patients with baseline > 200mg/dL) - Thyroid stimulating hormone - Bone mineral density - Serum estradiol levels (goal <100 to 200 pg/mL) and serum testosterone every 3 months in first year, then annually or biannually - Prolactin levels

Cyproterone acetate is a synthetic progestin that inhibits testosterone synthesis and action. This medication is not approved in the United States but may be used elsewhere.³

PAUSE AND PONDER: A transgender patient presents with concerns about the different formulations of estrogen available for feminizing treatment. How would you explain the advantages and disadvantages of each formulation?

Masculinizing Pharmacology

The goals of masculinizing treatment are the development of male secondary sex characteristics and the minimization of female secondary sex characteristics. Masculinizing GAHT typically consists of testosterone.

Testosterone

Testosterone treatment in transgender patients is used in the same way that it is used for hypogonadism in cisgender male patients. **Table 4** (on page 6) illustrates the various testosterone formulations in transgender care, including intramuscular, transdermal, and implantable options. Intramuscular injections may be preferred due to available clinical data, efficacy, patient satisfaction, and low levels of injection pain and local irritation relative to subcutaneous injections. Prescribers and patients should not interchange products without considering pharmacodynamic differences.^{7,16}

Positive effects of masculinizing hormones include irreversible deepening of voice, increased body/facial hair, and increased

lean muscle mass. Patients and care teams should know that masculine hormone therapy will not reverse previous feminine features such as breast tissue. Achieving physiological testosterone levels will usually suppress menses. If testosterone monotherapy doesn't suppress menses, additional therapies can be used including progestins, GnRH agonists, and aromatase inhibitors. Patients may continue testosterone therapy for life unless medically contraindicated.¹⁶

CHILDREN

GAHT is not recommended in children who have not begun endogenous puberty. Healthcare providers should take a non-pharmacologic approach instead for pre-pubertal individuals, including psychosocial gender-affirming care. Patients should continue gender exploration regardless of social transition.⁷

ADOLESCENTS

GAHT's goal in adolescents is pubertal suppression. Halting progression of puberty allows adolescents to explore gender identity and embodiment goals. Although suppression is reversible, the treatment team should discuss fertility preservation before starting suppression.⁷ Current timing and readiness estimates are as follows: pubertal suppression at 12 years old, GAHT at 16 years old, and surgery at 18 years old.

Pubertal Suppression Pharmacology

Healthcare providers employ Tanner staging to track children's development during puberty. It outlines five specific stages for the physical changes during this period, including genital, breast,

and pubic hair development. Patients should reach Tanner Stage 2 before initiating pubertal suppression. In Tanner Stage 2, individuals who are assigned female at birth would experience breast budding while those who are assigned male at birth would experience external genitalia enlargement.⁶ Menstrual suppression is recommended for patients assigned female at birth with gender incongruence, regardless of testosterone therapy.⁷

Pharmacologic Agents

Gonadotropin-Releasing Hormone (GnRH) Agonists

GnRH agonists cause partial regression of secondary sex characteristics and inhibit physical functions, such as menses and erections, by decreasing concentrations of gonadotropin and sex steroid hormones. Supraphysiological doses of sex steroids are not needed with GnRH agonists.⁷

Short-term hypertension is an important counseling point. Individuals who are older than 14 years also have a long-term risk of poor bone health because of the lack of exposure to adequate levels of sex steroid hormone levels. Sex steroid hormone therapy, however, induces rapid recovery of bone mineralization rate.⁶

For feminizing therapy, patients should continue puberty blocking until gonadectomy. Masculinizing pharmacology is covered in the following *Hormone Therapy* section. If patients have functioning uterus and ovaries, health care providers should counsel on potential breakthrough menstrual bleeding two to three weeks after GnRH agonist initiation.

Progestins

Oral or injection depot progestins are recommended if GnRH agonists are unavailable or cost-prohibitive.⁷

Patients can also receive these progestins if they seek menstrual suppression only⁷:

- Oral progestin-only pills (contraceptive and non-contraceptive options)
- Medroxyprogesterone injection (e.g. Depo-Provera)
- Levonorgestrel intrauterine device (e.g. Mirena, Liletta, Kyleena, Skyla)
- Etonogestrel implant (e.g. Nexplanon)

If a patient continues to have menstrual bleeding after taking progestin and/or is seeking a contraceptive, healthcare providers

Table 3. Antiandrogens for GAHT¹⁰⁻¹³

Doses and Formulations	Safety	Monitoring
Spirolactone - directly inhibits testosterone synthesis and activity Positive effects: gynecomastia		
Tablet Starting: 25 mg once or twice daily in combination Therapeutic: Increase at one-week intervals based on response and tolerability to a usual dose of 100-300 mg/day in 2 divided doses Max: 400 mg/day	Contraindications - Hyperkalemia - Addison's Disease Adverse Events - Hyperkalemia (uncommon if avoided with renal insufficiency), polyuria, polydipsia, orthostasis	- Serum testosterone levels (goal <50 ng/dL) every 3 months in first year, then annually or biannually - BP, serum electrolytes (potassium), glucose, kidney function, volume status, uric acid
GnRH agonists - suppress testosterone synthesis Positive effects: gynecomastia		
Leuprolide: IM/subcutaneous: 3.75 mg every month IM/subcutaneous depot: 11.25 mg every 3 months or 22.5 mg every 6 months Histrelin: subcutaneous depot: 50 mg every 12 months	Contraindications - Hypersensitivity Adverse Events - Hyperglycemia, asthma related exacerbation, decreased BMD, increased risk of CV events, psychiatric symptoms (mania, depression), QTc prolongation (rare), seizures (with long acting)	- BMD - Mood and depression screening - Serum testosterone every 3 months for first year, then annually or biannually - LH, FSH, and prolactin baseline and annually - Routine cancer screenings
ABBREVIATIONS: BMD = bone mineral density; BP = blood pressure; CVD = cardiovascular; FSH = follicle stimulating hormone; LH = luteinizing hormone		

can consider a combination progestin-estrogen product for amenorrhea and counsel on possible breast development. Combined formulations include oral contraceptive pills, transdermal patches, and vaginal rings. Note that increased breakthrough bleeding is associated with lower dose ethinyl estradiol in combined oral contraceptives.⁷

Hormone Therapy (HT)

The patient’s health care professionals will need to measure hormone levels during gender-affirming treatment. The purpose is to ensure that endogenous sex steroids are falling and the sex steroids administered to the patient stay at appropriate levels. Appropriate levels are determined by (1) the patient’s treatment goals and (2) the patient’s Tanner stage. Timing of pubertal suppression determines sex steroid HT regimen, as shown in **Table 5** (on the next page).⁷

WPATH suggests 12 months as sufficient time for psychological adaptations to physical changes due to GAHT. Healthcare providers should monitor sex steroid levels every three months during the first year of HT or with dose changes. Once the prescriber titrates the patient’s dose to the adult maintenance dose, monitoring one to two times annually is sufficient. As GAHT can activate the hypothalamic-pituitary-gonadal axis, prescribers may need to add a GnRH agonist as adjunctive therapy after GAHT initiation to avoid development of characteristics associated with the patient’s sex assigned at birth.⁷

For masculinizing GAHT, testosterone monotherapy at physiologic doses is typically sufficient to decrease estrogen secretion by the ovaries. Injection, transdermal, and subcutaneous pellets are available androgen formulations. Key counseling points include

Table 4. Testosterone Formulations for GAHT¹⁷

Doses and Formulations	Safety	Monitoring
Testosterone - endogenous testosterone androgen mimic		
<p>Cypionate (IM), Enanthate (IM or SC) initial: 50-100 mg IM/SUBCUTANEOUSLY every week or 100-200 mg IM every 2 weeks max: 400 mg every 2 weeks IM Titrate every 3-12 months</p> <p>Topical Gel <i>AndroGel</i> 1%: start 50mg every morning (max 100 mg) 1.62%: start 40.5mg every morning (max 81 mg) Titrate: based on pump/packet size</p> <p>TD Patch <i>Androderm</i> 2.5 to 7.5 mg/d initial: apply 4 mg every night max: 6 mg (4 mg + 2 mg) every night</p> <p>Axillary topical solution/gel 2% <i>Axiron</i> initial: 30 mg (1 actuation) every morning to each armpit max: 120 mg</p> <p>Undecanoate (deep IM; gluteus maximus) initial: 750mg, repeat in 4 weeks for 2 total doses maintenance: 750 mg every 10 weeks or 1000 mg every 12 weeks</p>	<p>Contraindications</p> <ul style="list-style-type: none"> - Pregnancy - Severe hypertension - Sleep apnea - Polycythemia <p>Boxed Warning: subcutaneous enanthate & PO undecanoate: hypertension and major adverse cardiovascular events</p> <p>Secondary exposure to topical products can cause virilization in children</p> <p>Adverse Events</p> <ul style="list-style-type: none"> - Urge to cough, dyspnea, throat tightening, chest pain, dizziness, syncope - IM undecanoate: pulmonary oil microembolism reactions 	<ul style="list-style-type: none"> - Baseline risk for breast cancer and CVD - Serum triglycerides - TSH - BMD - Serum estradiol levels and testosterone - Prolactin levels
ABBREVIATIONS: BMD = bone marrow density; CVD = cardiovascular disease; IM = intramuscularly; TSH = thyroid stimulating Hormone		

the possibility of developing androgenic acne or sexual dysfunction.

Patients on GnRH agonists should continue them until they reach maintenance testosterone level. If the patient was not on a GnRH agonist as an adolescent, then no concomitant GnRH agonist is needed. While testosterone usually suppresses menstruation in the first six months of therapy, healthcare providers should make sure to counsel adolescents on possible pregnancy despite amenorrhea because they can still ovulate.⁷

NON-PHARMACOLOGIC INTERVENTIONS

Chest Binders

Chest binding refers to compressing breast tissue to achieve a flatter chest appearance. Research indicates that up to 87% of individuals identifying as transgender males have tried chest binding.⁶ Various methods used for binding include commercial binders, sports bras, layering clothes, elastics, and bandages.⁷

Healthcare providers play a crucial role by making patients aware of chest binding's potential advantages and risks. Transgender men who bind often report benefits such as increased comfort, enhanced safety, and reduced instances of misgendering.⁷

Negative physical impacts of chest binding include back or chest pain, difficulty breathing, and feeling overheated.⁷ Severe health issues like skin or respiratory infections and rib fractures, which are rare, have been linked to adult chest binding.⁶ Providers can lower the risk by counseling patients on safe binding methods, like binders specifically designed for gender-diverse individuals, to lessen the likelihood of serious health complications. Meanwhile, patients should avoid unsafe methods like duct tape, ace wraps, or plastic wrap due to their potential to constrict blood flow, harm the skin, and restrict breathing.⁶ If negative health effects occur, seeking guidance from medical professionals experienced with transgender and gender-diverse patients is sensible.⁷

Tucking

Genital tucking involves positioning the penis and testes to minimize the visibility of genital bulges.⁷ This can be done by tucking the penis and testes between the legs or placing the testes inside the inguinal canal while pulling the penis back between the legs.⁷

Underwear or specialized garments called gaffs are commonly used to keep the genitals in place.⁷

Research on the risks and advantages of tucking in adults is limited, and no studies conducted specifically address youth.⁶ Previous research has highlighted that snug undergarments might lead to reduced sperm concentration and motility. Moreover, higher scrotal temperatures due to tucking might theoretically impact sperm production and fertility.⁷ However, no conclusive evidence confirms these negative effects. More data is needed to understand the risks and benefits of tucking.

Voice Therapy

Hormone treatment for transgender and gender diverse (TGD) individuals has potential effects on voice and communication. While estrogen treatment does not usually cause measurable voice changes, testosterone treatment can lead to desired shifts in voice pitch and male attributions but may also result in undesired outcomes.⁷

Research indicates that some TGD individuals experience positive effects from testosterone, such as lowered voice pitch and increased satisfaction, aligning with their gender identity. However, a significant portion may face challenges like insufficient pitch changes, vocal quality issues, limitations in singing range, and vocal instability post-treatment.^{7,18} A meta-analysis examined about 600 patients across 19 studies to determine the effects of at least one year of testosterone therapy. The patients were all at least 18 years old, with an average age of 35 years. According to the results, approximately 21% of participants did not reach the expected normative frequencies associated with cisgender males. Additionally, a similar percentage reported incomplete alignment between their voice and gender identity, experiencing voice-related challenges or incongruence. Furthermore, 16% of individuals undergoing testosterone therapy expressed dissatisfaction with the changes in their voice.¹⁸

It's essential to provide accurate counseling beforehand to establish realistic expectations and avoid potential disappointment. Referral to voice and communication specialists can address concerns through tailored voice training and assisting those dissatisfied with outcomes or lacking access to hormone treatment.⁷

Table 5. Sex Steroid Hormone Therapy Regimen Based on GnRH Agonist Treatment Timing⁷

Pubertal Suppression	Sex Steroid Dose	Time To Goal Levels	Growth Spurt?
Early	Similar to peripubertal hypogonadal adolescents	Adult doses usually reached over 2 years	Yes
Late/Post-Pubertal	Higher starting dose	More rapid titration until maintenance dose is achieved	No

Electrolysis And Laser Hair Removal

Hair removal is a significant part of transitioning for many transgender women (or females), particularly for those seeking a more stereotypical feminine appearance. The process helps alleviate dysphoria, boosts self-confidence, and enhances overall quality of life.¹⁹ The U.S. Food and Drug Administration recognizes laser hair removal as a permanent hair removal method.¹⁷ It targets melanin in hair follicles using laser light waves.¹⁹ An alternative, electrolysis, also removes hair permanently using a small probe inserted into individual hair follicles to administer an electric current.¹⁷

For individuals undergoing GAHT, healthcare providers need to keep specific considerations in mind. Among transgender women taking estrogen¹⁹

- Estrogen hormone therapy often results in an overall reduction in body hair, except for minimal effects on facial and genital hair.
- The extent of hair removal (complete hairlessness or retaining some hair) depends on personal preference and comfort levels.
- Many transgender women find facial and neck hair removal crucial for increased self-confidence, reduced dysphoria, and a sense of safety in public spaces.
- Those prioritizing gender-affirming lower surgeries like vaginoplasty (vagina construction surgery) require completely hair-free areas for surgery preparation, as hair growth within transformed tissue can cause complications.

For transgender men taking testosterone¹⁹

- Testosterone hormone therapy generally leads to increased body hair growth.
- Preparing for surgeries like phalloplasty (penis construction surgery) often requires completely hair-free skin areas for successful procedures, the specific area depending on the type of surgery planned.
- It is important to note that electrolysis doesn't prevent the growth of new hair follicles activated by testosterone. Therefore, new hair growth might occur in areas previously treated with electrolysis due to testosterone's effects on stimulating hair follicles.

The adverse effects of hormone therapy may be beneficial for some patients, while being detrimental to others. It is critical for healthcare providers to educate patients on hair removal methods and their impact within the context of hormone therapy, so that patients understand what to expect.

Gender-Affirming Surgery

Gender-affirming surgery is often a crucial milestone for many, but not all transgender adults.³ Broadly classified into two categories, surgeries (1) directly impact fertility or (2) have no effect on fertility.³ Surgeries that alter fertility involve procedures like the removal of male genitalia (penis and gonads) for transgender



women or the removal of female reproductive organs (uterus and ovaries) for transgender men.³ Surgeries that do not affect fertility include chest masculinization or breast augmentation, facial feminization, or facial masculinization surgeries.³

There is a lack of evidence supporting the routine discontinuation of hormone therapy before planned surgeries.²⁰ The majority of evidence advocating for estrogen cessation before surgery is derived from studies involving oral synthetic estrogen regimens (ethinyl estradiol), which are uncommon in transgender patients.¹⁹ WPATH advises maintaining estrogen therapy both before and after surgical procedures in transgender women, particularly in those without specific risk factors such as smoking, family history of VTE, or the use of synthetic estrogens.⁷ If the patient has the previously mentioned risk factors, the prescribing endocrinologist should discuss estrogen therapy cessation in the perioperative setting openly with the patient and make decisions collaboratively.²⁰ Typically, an acceptable timeframe for estrogen discontinuation is two to four weeks before the procedure.²⁰ Anticipated physiological and psychological withdrawal symptoms may include anxiety, autonomic hyperactivity, depression, decreased seizure threshold, and fatigue.²⁰ This comprehensive approach ensures a thoughtful consideration of hormonal factors in the surgical process for transgender women.

Evidence suggests that there is generally no need to discontinue testosterone treatment routinely in transgender men before scheduled or elective surgery despite the concern that testosterone can be aromatized to estradiol, which theoretically could increase the clotting risk.²⁰ A recent systematic review found no association of increased VTE complications after surgery with perioperative testosterone use.^{21,22}

The decision to undergo these surgeries is deeply personal and varies based on individual needs, preferences, financial access, and dysphoria. Access to comprehensive information, counsel-

ing, and support from healthcare professionals helps patients make informed decisions aligned with their gender identity and long-term goals while understanding the potential impact on fertility.³

PAUSE AND PONDER: A transgender patient would like to undergo breast augmentation but has only been on hormone therapy for six months. Is she eligible for the surgery?

Chest or “Top” Surgery

“Top” surgery is either removing breast tissue for a more masculine appearance or enhancing breast size and shape for a more feminine appearance. Breast surgery is a type of gender-affirming surgery with no impact on fertility.³ Since breast size varies among females, it is advisable for transgender women to postpone breast augmentation surgery until they have undergone at least two years of estrogen therapy.³ This is recommended because the breasts continue to grow during this period of hormone therapy.³

Meanwhile, the primary masculinizing surgery for transgender men is a mastectomy, which also has no impact on fertility.³ While breast size only partially regresses with androgen therapy, discussions about mastectomy in adults typically occur after androgen therapy starts.³ However, in some cases where trans-masculine adolescents present after significant breast development, a mastectomy may be considered approximately two years after starting androgen therapy and before the age of 18.³ Treatment decisions should be individualized based on the individual’s physical and mental health status.³

Genital or “Bottom” Surgery

Genital or “bottom” surgery involves transforming and reconstructing the genitalia. According to The Endocrine Society Clinical Practice Guideline Criteria for Gender-Affirming Surgery, the following factors may influence decisions related to fertility preservation³:

1. Persistent and well-documented gender dysphoria
2. Meets the legal age requirement in the relevant country
3. Use of gender-affirming hormones for a continuous 12-month period, unless there is a medical contraindication
4. Successful in living full-time as a new gender role for the duration of 12 months
5. Well-controlled management of any significant medical or mental health conditions, if present
6. Demonstrated knowledge of practical aspects related to surgery, including cost, required lengths of hospitalizations, likely complications, and postsurgical rehabilitation.

Gender-affirming surgeries for transgender women that affect fertility include procedures like gonadectomy (orchiectomy), penectomy, and the creation of a neovagina.³ In the case of transgender men, surgeries that affect fertility include an oophorectomy, vaginectomy, complete hysterectomy, and the cre-

ation of a neopenis.³ Infertility can occur from both the temporary consequences of gender-affirming hormone therapy and permanent effects of gender-affirming surgeries (GAS).⁶ It is crucial to engage in ongoing discussions about infertility risks and fertility preservation options with transgender individuals and their families before and after initiation of therapies and surgeries.⁶

OTHER CARE IMPACTED BY GAHT **Anticoagulation**

When assessing the risk of VTE associated with GAHT, it is crucial to consider the alternative—the risk of not providing GAHT.²² Withholding GAHT could lead to adverse mental health consequences that might outweigh the risk of VTE.²⁰ Some individuals may seek hormone therapy outside clinical care settings (that is, from unreliable sources) if healthcare providers refuse to provide it.²²

For transgender individuals experiencing VTE while on GAHT, treatment should align with current therapeutic anticoagulation recommendations for cisgender individuals.²⁰ The American Society of Hematology guidelines recommend direct oral anticoagulants (DOACs) over other options due to a lower risk of bleeding.²² Despite limited data in transgender people, recent case reports suggest DOACs are effective in those with VTE during GAHT. In severe cases threatening limbs, clinicians can consider thrombolysis and recommend it as they would in cisgender individuals.²² GAHT discontinuation during an acute VTE episode is often recommended, especially with above normal hormone levels, but this recommendation lacks extensive data.²² Clinicians and patients should discuss the potential risks and benefits of continuing GAHT during an episode.

Following acute VTE treatment, the decision to resume GAHT becomes complex. Many clinicians continue GAHT, even in patients with previous VTE, along with full-intensity anticoagulation to prevent recurrence.²² Although researchers have not





conducted systematic evaluation in transgender patients, this approach was effective in cisgender women on hormone therapy.²² While cisgender patients may reduce anticoagulation dose after initial therapy, it is uncertain if dose reduction is prudent with GAHT. Shared decision-making, emphasizing the risks and benefits, remains crucial in determining the course of GAHT post-VTE treatment.

Estimating Kidney Function

Many healthcare providers are accustomed to using the Cockcroft-Gault equation to estimate kidney function.²³ This formula factors in sex, causing uncertainty as to how to calculate creatinine clearance in transgender patients. Although GAHT affects muscle mass and creatinine, using the duration of therapy is unreliable because the timing and magnitude of effect differ by individual. As such, cystatin C is often more accurate than creatinine. Acknowledging that cystatin C levels are not accessible at all practice sites, some experts suggest using the Cockcroft-Gault-calculated male and female creatinine clearance estimates as a range. Other methods include using vancomycin clearance calculations.²³

Fertility Preservation

Individuals who have transitioned may wish to have biological children for personal reasons, to maintain a genetic connection with their offspring, or to conform with cultural expectations.²² While many transgender individuals may not initially consider having children, their desires can change over time.²⁴ In a survey of 50 transgender men who had undergone gender-affirmation surgery, the majority (77%) had not contemplated fertility preservation before GAHT. An average of 9.9 years after starting testosterone therapy, 54% of participants wanted to have children.²⁵ The study also found that participants with children had a higher quality of life than those who did not have children.²⁵

Fertility preservation through the cryopreservation of sperm and oocytes is a well-established technique, available for prepubertal, late pubertal, and adult individuals assigned male or female at birth.⁶ Ideally, clinicians should present this option before ini-

tiating GAHT.⁷ Clinicians can offer embryo cryopreservation to adult transgender individuals, particularly those who have completed puberty, express a desire to have a child, and have a willing partner.⁷

While research has shown semen parameters may be compromised after the initiation of GAHT, a small study indicated that when treatment was discontinued, semen parameters were minimally altered.²⁶ In regards to oocyte preservation, there is no expectation that assisted reproductive technology (ART) treatments would be different for TGD patients compared to cisgender patients.⁷ The only potential variations are individuals with confounding factors related to infertility.⁷

Barriers to fertility preservation include financial constraints, invasiveness of procedures, and concerns about mistreatment or bias from healthcare providers.²⁴ Some fertility preservation procedures, such as sperm or egg collection, can serve as reminders of their sex assigned at birth and may trigger gender dysphoria.²⁴ Transgender individuals who pursued ART reported mixed experiences. Some have positive encounters with supportive providers who use gender-neutral language. Others experienced misgendering in clinical documentation.²⁴ Patients should be provided with options for future family planning whether they desire biological children or not.

BARRIERS IN PRACTICE

Laws and Legislation

When the Supreme Court tackled the Conservative challenge to the Affordable Care Act (ACA), the focus was on whether it was constitutional to mandate health insurance purchase.²⁷ This overshadowed Section 1557's anti-discrimination provisions protecting transgender individuals. The 2016 Rule, finalized by Health and Human Services, extended Title IX's anti-sex discrimination coverage to include "gender identity," ensuring equitable access to healthcare for transgender patients. The Trump administration attempted to reverse these protections but faced legal obstacles. This led to the Supreme Court's ruling in *Bostock v. Clayton County*, which affirmed protections for transgender individuals under existing civil rights statutes. Despite the Trump administration's efforts, subsequent legal challenges and judicial actions further emphasized protections for transgender individuals, leading to ongoing debates and policy shifts under the Biden administration.²⁷

The *Bostock* ruling, initially about employment, now impacts transgender minors' access to gender-affirming care.²⁷ Federal courts often interpret Title VII and Title IX together, meaning they see both statutes as prohibiting sex-based discrimination similarly.²⁵ This means that the Biden Administration can confidently enforce protections for gender identity under Title IX, following *Bostock*'s reasoning.²⁷ Since *Bostock*'s ruling was made under a majority conservative Supreme Court, it's unlikely to be reversed. This leaves opponents of gender-affirming care to ex-

plore other tactics, like raising religious objections or labeling such care as "experimental" or "medically dangerous."²⁷ These viewpoints circumvent many physicians' clinical judgement, thus restricting how they practice medicine.

Over the past 18 months, the number of states implementing laws that restrict or prohibit minors' access to gender affirming care has increased dramatically.²⁸ Currently, the count of states with restrictions increased from just four states in June 2022 to 23 states by January 2024. Among these states, 17 have fully enacted their restrictions, while four face temporary injunctions, and one is permanently blocked pending appeal. The laws vary in complexity, with some focusing on specific aspects of gender affirming care, such as GAHT or gender affirming surgery. Additionally, while these laws primarily target minors' access to care, they often include provisions affecting other groups, such as parents, medical providers, and teachers.²⁸ These laws and policies cause potential harm to the wellbeing of young TGD, thus emphasizing the need for continued advocacy and support for inclusive and affirming practices.

Insurance Coverage

Ensuring comprehensive healthcare for transgender individuals requires access to both gender-affirming care and a wide range of inclusive services. However, numerous barriers have historically hindered access, with lack of health insurance coverage being shaped by intersecting factors at the individual, interpersonal, and structural levels.

Many state Medicaid programs exclude coverage for gender-affirming care, posing a significant concern given the elevated prevalence of poverty among transgender people. In a study utilizing Behavioral Risk Factor Surveillance System (BRFSS) data, gender non-conforming individuals were nearly twice as likely as cisgender women to report unmet care needs due to financial issues.²⁹ According to the 2015 United States Transgender Survey, 25% of insured respondents encountered insurance discrimination.²⁹ Experiences included denial of coverage for gender-specific services, such as cancer screenings (13%), for care unrelated to gender affirmation (7%), and for gender-affirming surgery (55%) or hormone therapy (25%).²⁹ TGD individuals (33%) reported negative experiences related to being transgender when seeing a healthcare provider in the previous year, which includes verbal harassment, physical assault, or treatment refusal.²⁹ Additionally, 23% refrained from seeking care when needed in the previous year due to fear of mistreatment.²⁹

A 2019 systematic review revealed that 27% (range, 19% to 40%) of transgender individuals reported outright denial of healthcare.²³⁰ Assessments of provider readiness indicate that many clinicians lack training in transgender clinical and cultural competency, potentially contributing to interpersonal discrimination in healthcare settings.

Assessing Implicit Bias, Addressing Bad Behavior

1. Respect Gender Identity: TGD individuals deserve the same respect as cisgender patients. Address patients by their chosen name and pronouns, reflecting their gender identity. Avoid gossiping or making jokes about patients and treat them with the same respect you would want at work.³¹

2. Recognize Workplace Values: Understand the difference between your personal beliefs and the workplace values of dignity and respect for everyone. While you are entitled to your opinions, professionalism requires setting aside personal views and treating everyone with fairness and courtesy in the workplace.³¹

3. Seek Feedback and Learn from Mistakes: Don't be afraid to ask for feedback from TGD individuals about how you can better support them or avoid inadvertently causing harm. Be open to learning from your mistakes and apologize if you unintentionally offend someone. Additionally, take the initiative to stay updated on evolving terminology and practice recommendations, as ideas/norms about gender are fluid and change over time. Learning from reputable sources, such as *The Trevor Project's Guide to Being an Ally to Transgender and Nonbinary Youth*, shows a genuine commitment to fostering inclusivity and respect in the workplace.^{31,32}

4. Support Colleagues with Challenges: If you notice co-workers struggling to adjust to interactions with TGD individuals, offer gentle reminders about using the correct name and pronouns. Help them understand the impact of their behavior on both the TGD individual and the workplace environment. Encourage empathy and understanding to foster a more inclusive workplace culture.³¹

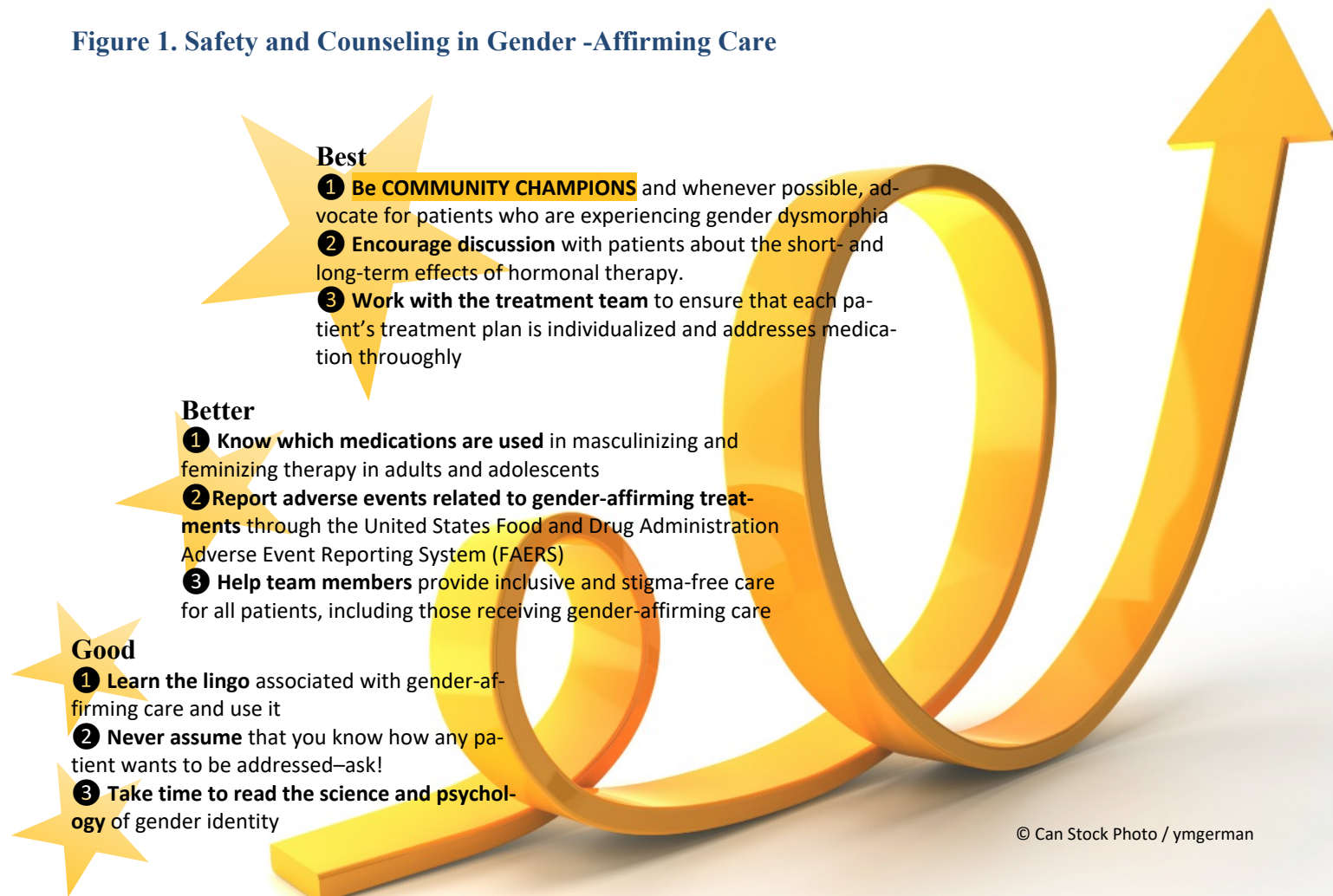
5. Intervene When Appropriate: If you witness blatant inappropriate behavior or discriminatory actions with no remorse towards a TGD individual in the workplace, don't remain silent. Find appropriate ways to intervene, whether it's addressing the behavior directly, reporting it to management, or offering support to the affected individual. Standing up against prejudice and discrimination helps create a safer and more inclusive work environment for everyone.³¹



CONCLUSION

Embracing gender diversity and providing gender-affirming care is essential in healthcare settings, including pharmacies. Pharmacists and pharmacy technicians who employ inclusive language and possess a thorough understanding of pharmacological interventions play a critical role for transgender individuals. Pharmacists can help tailor GAHT regimens to individual patient needs, promoting safety and helping patients achieve their goals towards gender affirmation. Pharmacists and pharmacy technicians can create a more inclusive and safer environment when interacting with patients. As healthcare workers in the pharmacy setting, we can provide patients with the resources they need without judgement. **Figure 1** summarizes key points when providing gender-affirming care.

Figure 1. Safety and Counseling in Gender -Affirming Care



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