Masculinizing Hormone Therapy

Protocol for Care of Transgender and Non-Binary Patients Assigned Female at Birth

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Cedar River Clinics Model

The Cedar River Clinics model is a method of providing gender affirming care that incorporates the best available evidence, respect for patient autonomy, comprehensive patient education, shared decision making, harm reduction, and informed consent.

The following recommendations for managing gender affirming hormone therapy have been cultivated and modified based on the efficacy, safety, and patient satisfaction verified during an ongoing analysis of the Cedar River Clinics model and in conjunction with the most recently published information on transgender and non-binary (TNB) health. Information will be provided on both binary and non-binary gender affirmation. References are available at the end of this module.

Patient Education for Informed Consent

Patient education is critical for informed consent and to ensure patient safety while undergoing masculinizing hormone therapy. The contents of this module can serve as a guide for patient education. In addition, it is particularly important for the providers and patient to understand the following:

- Responses to hormone therapy are individualized.

  Hormone therapy impacts different people in different ways and every TNB person has their own unique medical history; this means that patients could end up having a different hormone therapy regimen than they have learned about from friends and community resources. Shared decision making must be used to ensure that patients are able to feel comfortable with and adherent to their plan of care. An environment of trust helps patients feel comfortable communicating with their provider if they are unhappy with their course of masculinization

- Continuing care and routine visits with a healthcare provider are required when on hormone therapy. Patients must understand and agree that:

  In the first year of hormone therapy, frequent visits are necessary for monitoring hormone therapy responses, dosage, and side effects. After the first year of hormone therapy, annual visits are necessary for preventive care and ongoing management of hormone therapy.

- Good communication is required when on hormone therapy.

  It is important that patients communicate honestly with providers about their goals and complete health history, including all substance use and current or past use of self-managed hormones or masculinizing supplements. Conversely, it is important for providers to give patients assurance that they will not be denied treatment based on their unique gender experience or based on revelations of self-managed hormone use or substance use.

Providers must ensure that the patient has ample opportunity to ask clarifying questions and that all questions and concerns have been addressed. During the course of hormone therapy, patients should be encouraged to alert you promptly about:

- Side effects or adverse reactions
- Dissatisfaction with the testosterone therapy
- Concerns or questions about the therapy
- Any supplement, drug, or medication use
- Any self-managed adjustments to their hormone therapy plan
- Acute mental health concerns including suicidal ideation

Advise patients that the body may convert excess testosterone into estrogen if taking a higher than recommended dose; as such, taking more than the prescribed amount of testosterone can be counter-productive to the masculinization process.

- Pace and extent of therapy may be longer than expected or desired

Patients need to understand that it may take several months before the masculinizing effects of testosterone start to become noticeable and that it can take many years to reach a desired degree of masculinization. Some desired aspects of masculinization might not occur at all. Additionally, hormone therapy is driven by the patient's goals, and those goals may sometimes feel in contradiction to their desired pace of masculinization.

Relative and Absolute Contraindications for Hormone Therapy

The presence of risk factors does not mean that hormone therapy is contraindicated. Proper monitoring and an emphasis on patient education should be employed to minimize risks without denying treatment for most conditions.

There are few absolute contraindications for testosterone therapy. These contraindications are:

- Inability to give informed consent
- Active hormone-sensitive cancer
- Current pregnancy

The presence of any of the comorbid conditions listed below does not automatically rule out hormone therapy as an option but may require further evaluation and management to ensure patient safety. In the presence of risk factors listed below, referral to an appropriate mental health provider or other specialist may be necessary prior to, or concurrent with, starting hormone therapy.

Risk factors associated with adverse events while on hormone therapy include:

- Liver disease
- Uncontrolled hyperlipidemias
- Uncontrolled hypertension
- History of venous thrombosis
- Smoking
- Family history of heart disease
- Personal or family history of hormone-sensitive cancer
- Polycythemia

Providers should not deny access to hormone therapy based on the presence of any of these comorbid conditions. The Hormone Administration section below includes guidance on decreasing risk of adverse effects with certain comorbid conditions.

Moving Towards Evidence Based Practice

Both providers and patients should be aware that there is a limited evidence base for TNB health generally, and hormone therapy specifically. While this is frustrating, we are fortunate to have standards of care and best practices that have been built on at least 60 years of clinical practice in the United States (and even longer in Europe). These best practices provide excellent guidance for care.

The guidelines and recommendations in this module are based, in part, on this legacy of cumulative knowledge and rely heavily on the efforts of University of California – San Francisco Center for Excellence in Transgender Health, which has culled available evidence into easily accessible practice documents. These recommendations are also based on clinical experience providing care to a large panel of TNB patients at Cedar River Clinics.

Given the lack of Level 1 (highest level) evidence for initiation and management of hormone therapy, it should be understood that:

- Hormone therapy for gender affirmation has not been well studied.
- The effects of hormone therapy may be beneficial, damaging, or both.
- Individualized responses to hormone therapy are difficult to predict.

Effects of Hormone Therapy

Physical Changes

Hormone therapy causes many physical changes, some of which may be desired and some of which may be very much undesired. Certain changes will be permanent, and others will be reversible if hormone therapy is discontinued.

The Endocrine Society's table below provides a quick overview of changes associated with masculinizing hormone therapy.

TABLE 13. Masculinizing effects in FTM transsexual persons

Effect	Onset (months)[1]	Maximum (yr)[1]
Skin oiliness/acne	1–6	1–2
Facial/body hair growth	6–12	4–5
Scalp hair loss	6–12	[2]
Increased muscle mass/strength	6–12	2–5
Fat redistribution	1–6	2–5
Cessation of menses	2–6	[3]
Clitoral enlargement	3–6	1–2
Vaginal atrophy	3–6	1–2
Deepening of voice	6–12	1–2

[1]Estimates represent clinical observations.
[2]Prevention and treatment as recommended for biological men.
[3]Menorrhagia requires diagnosis and treatment by a gynecologist.

Table credit: Hembree WC et al (2009). Guidelines on the Endocrine Treatment of Transsexuals. *J Clin Endocrinol Metab*, 94(9):3145: Table 13

Permanent effects of hormone therapy include:

- Significant enlargement of the clitoris (although note that clitoral size may reduce somewhat if hormone therapy is discontinued)
- Male pattern scalp hair loss
- Facial hair growth
- Deepening of the voice (although vocal tone may become somewhat higher if hormone therapy is discontinued)
- Increased body hair growth
- Changes to fertility (limited data suggest that these changes may be reversible; until additional data are available all patients should be advised these changes could be permanent)

Non-permanent effects that will not persist if hormone therapy is discontinued include:

- Redistribution of body fat
- Increased muscle development

- Increased energy levels
- Increased acne
- Increased red blood cells
- Amenorrhea
- Anovulation (if this does occur during hormone therapy)
- Vaginal atrophy

Limitations of Masculinizing Hormone Therapy

- Overall masculinization

  Patient goals for masculinization vary. Many patients desire to be consistently perceived as male in all contexts. For some patients, this will be possible. For others, hormone therapy alone will not allow for this degree of masculinization. It is important to help patients explore and set realistic expectations for the outcomes of their hormone therapy

- Height

  Hormone therapy does not cause significant changes in height.

- Breast size

  Testosterone will not have a significant impact on breast size or composition.

- Clitoral growth

  Significant clitoral growth will occur with hormone therapy. Some patients will be satisfied with the growth achieved; others will want to consider metoidioplasty or phalloplasty.

Emotional Changes

Masculinizing hormone therapy can have an impact on one's "emotional landscape," including greater extroversion, less somatization, decrease in affective intensity (i.e. mood swings), increased libido, heightened anxiety, and greater contentment.

- It is difficult to separate which emotional responses are attributable to testosterone and which are associated with increased comfort with one's body.
- Mood appears to be most affected at the beginning and end of dosing for injected testosterone.
- Although increased aggression has been historically associated with testosterone use at supraphysiologic levels (i.e. by cisgender body builders), this does not appear to be a common side effect when testosterone levels remain at a physiologically normal level.

Throughout the course of hormone therapy providers should:

- Screen and offer treatment for pre-existing mood disorders or mental health issues.

- Assist patients in finding coping strategies as needed.
- Ensure access to mental health provider and support services as needed.

Fertility and Sexual Health

Hormone therapy causes significant changes to fertility, sexual function, and libido.

Changes that may impact sexuality and sexual function include:

- Vulvovaginal atrophy, which may cause discomfort. Some patients may require artificial lubrication with penetrative sex, or medication management for general comfort and well-being. Atrophy may also cause increased risk for STIs and barrier methods should be encouraged.
- Increased libido and sex drive.
- Changes in sexual interest and orientation are possible.

Fertility should be discussed in detail, including the following:

- Fertility changes related to hormone therapy have not been well studied.
- Hormone therapy may lead to permanent infertility, although significant anecdotal data and limited research suggest that changes to fertility could be reversible with discontinuation of hormone therapy.
- Hormone therapy is not a guaranteed form of birth control; barrier methods and hormonal contraceptive methods can be utilized to protect against unintended pregnancy.
- Egg storage should be offered to all patients, although it is often considered prohibitively expensive and invasive.
- Patients who desire to conceive may stop testosterone at any time to attempt to conceive. There is minimal research to guide expectations on 1) if or when normal menses will resume, 2) if or when conception will occur, or 3) if a certain hormone-free interval is advisable before trying to conceive. Limited research and anecdotal data suggest that ovulation and menstruation may return between three and six months after testosterone cessation.

Additionally, hormone therapy does not protect against HIV and other STIs. Barrier methods and proper sex toy hygiene are important for reducing risk of infections.

Health Risks and Side Effects of Hormone Therapy

Testosterone therapy may increase risks for certain diseases, conditions, and cancers or exacerbate existing diseases and conditions; it may also cause unpleasant side effects. Discuss this with patients in detail and ensure that all questions regarding level of risk, anticipated schedule for monitoring those risks, and prevention strategies are answered. More detailed explanation and discussion regarding the health risks and side effects of masculinization hormone therapy can be found at here. Below is an overview of these risks. As noted above, the risk of cardiovascular disease or risk factors increase the risk of adverse events with hormone therapy.

Health Risks

Potential health risks of testosterone hormone therapy are described below; it is important to note that no increase in long-term morbidity or mortality has been seen in research.

Cancer

Cancer risks with testosterone therapy are uncertain at this time. Based on limited research, it is unlikely that rates of breast/chest, cervical, or ovarian cancer are increased in individuals undergoing gender affirming hormone therapy, although detection may be delayed due to lower screening rates compared to cisgender women, and breast cancer may occur earlier in the lifespan. Additionally, inadequate pap smear samples and abnormal cytology results are common – this is likely related to both atrophic vulvovaginal changes, and increased difficulty of pelvic exams due to atrophy, gender dysphoria, and provider discomfort. As such, providers should:

- Encourage appropriate breast/chest and pelvic health maintenance
- Obtain a thorough family and personal health history.
- Discuss potential increased cancer risk with patients.
- Advise patients that any spotting or menstrual bleeding after the onset of amenorrhea should be reported immediately to the healthcare provider.
- Advise patients that taking higher than recommended doses of testosterone can increase risks for cancer and decrease the masculinizing effects of hormone therapy.
- Consult with an oncologist in cases where the patient has a history of hormone-sensitive cancer

Liver Disease

Testosterone therapy can cause transient elevations in liver enzymes with a slight increased risk for liver disease. Monitoring liver enzymes prior to or during testosterone use is not necessary for young, healthy individuals without a history of or significant behavioral risks for liver disease.

Hypertension

Taking testosterone may increase blood pressure but does not appear to increase risk for hypertension in the absence of other predisposing factors such as family history of hypertension or personal history of PCOS. If preexisting hypertension is present, care should be taken to ensure that it is well controlled with medications and/or diet and exercise, and closer monitoring may be required in order to take testosterone safely. Healthy diet and exercise can decrease these risks.

Dyslipidemias

Testosterone therapy can alter cholesterol levels to those of a cisgender male. Healthy diet and exercise are important for deceasing risks associated with dyslipidemias.

Polycythemia

An increase in the rate of blood cell production is a very common side effect of testosterone therapy. When RBC count is above that of the upper limit of the cisgender male reference range, risk for thromboembolic events, heart attack, and stroke is increased. It is important to routinely screen hemoglobin or hematocrit; elevated levels should be followed with CBC to monitor RBC levels. When polycythemia is present, this can usually be managed by decreasing testosterone dose, increasing injection frequency without changing total dose, or changing to a transdermal testosterone formulation. Blood donation to decrease total RBC count can also be an effective management strategy for testosterone-induced polycythemia. Many barriers exist to transgender patients desiring to donate blood; in cases where donation is refused, therapeutic phlebotomy in the lab setting is appropriate. Polycythemia in the setting of physiologically normal testosterone levels should prompt assessment for obstructive sleep disorders, including sleep study if indicated.

Common Side Effects

Body Composition

Testosterone therapy may cause an increase in weight and visceral fat if not accompanied by changes in diet and exercise. However, research has demonstrated that weight, adiposity and BMI alone are not adequate measures of health status. As with all patients, a health at every size approach should be used in patients undergoing hormone therapy, and health status while on hormone therapy should be based on appropriate assessments such as lipid status and glucose control.

Patients may need to increase their protein intake during the first several months of testosterone therapy to accommodate muscle development.

Acne

Acne is increased with testosterone therapy and may be severe enough to cause scarring and require medical intervention. Standard treatment approaches can be used.

Vulvovaginal Atrophy

Testosterone therapy may cause vulvovaginal dryness and thinning that results in pain or bleeding with vaginal penetration, or bothersome daily dryness. This may require use of lubricants or topical estradiol. In patients who are not bothered by atrophy symptoms but have inadequate pap smear results, a short course of topical estradiol should be considered prior to repeat pap sampling.

Informed Consent Process

Cedar River Clinics recognizes that informed consent is the basis of the healthcare process for all care, including gender affirming hormone therapy. Informed consent is a rigorous and patient-centered process

that requires an assessment of the patient's mental capacity and their ability to make complex medical decisions. Informed consent is achieved when the patient understands and can verbalize the limitations, side effects, permanency, and health risks associated with hormone therapy, and is able to make informed decisions about their care. There are several approaches to utilizing an informed consent model.

- Two-Visit Protocol

  This protocol involves an initial one-hour visit to establish care, complete patient education, and assess the patient's ability to give consent. This is followed by a second 30-minute visit to review labs and complete a basic physical exam before providing prescriptions for gender affirming hormones. This protocol requires that the primary provider have an ability to assess for mental capacity and co-occurring mental health conditions. The two-visit protocol falls within the World Professional Association of Transgender Health (WPATH) standards of care. The following criteria should be met prior to initiating hormone therapy:

  - Persistent, well-documented gender dysphoria
  - Capacity to make a fully informed decision and to give consent for treatment
  - Age of majority or consent of all legal guardians
  - Any co-occurring mental health conditions are reasonably well controlled

  It is important to note that the diagnostic criteria for gender dysphoria presented by the American Psychiatric Association are flawed in that they 1) assume that gender dysphoria must be present in order for gender affirming therapy to be indicated, and 2) are based on a binary concept of gender identity. These criteria may be hard to apply to non-binary individuals or individuals we choose to initiate hormone therapy not because they feel an internal inflict with their bodies but because they wish to mitigate distress, safety concerns, economic concerns or other complex social phenomenon associated with being transgender or non-binary in a culture of strict gender roles. As such, Cedar River Clinics endorses an approach of trusting patients to understand their own gender affirming needs. This is supported by WPATH standards of care which state that it is appropriate to initiate gender affirming hormone therapy in the absence of meeting criteria for gender dysphoria if this is supported by the specific "anatomic, social or psychosocial" needs and realities of the patient.

- Expedited Therapy Protocol

  This protocol uses the two-visit protocol above, with the addition of the patient providing an "ICATH" letter at the time of first visit. This letter results from an in-depth one-time visit with a mental health professional competent in gender identity issues. This protocol allows for expedient access to gender affirming care and accommodates the variable levels of comfort each primary provider has with mental health and mental capacity assessments. This protocol falls within the WPATH standards of care.

  Informed Consent for Access to Trans Health (ICATH) is a website that offers an explanation of the informed consent model and a letter templates for providers. This letter stipulates that the patient has been deemed mentally competent to make medical decisions and has expressed an informed desire to

seek gender affirming care. This template was created in response to the WPATH Standards of Care recommendation for a letter to be provided by a mental health provider prior to initiating gender affirming hormone or surgical care.

- Harm Reduction Protocol

The harm reduction protocol states that patients actively undergoing self-managed gender affirming hormone therapy at time of intake should be managed differently than patients naïve to hormone therapy and should not be subject to the two-visit protocol or provision of a therapy letter. The rationale behind this protocol is that 1) the patient has already had the opportunity to see if hormone therapy is right for them and has accepted that there are risks associated with treatment, 2) the patient may currently be using unregulated medications and it would promote safety to provide immediate access to pharmacy-obtained medications, and 3) non-consensual cessation of hormone therapy may cause emotional harm or increase the risk of suicide. Harm reduction standards for this protocol are as follows:

- Complete all screening, patient teaching, and lab draws with initial visit
- Complete basic physical exam with initial visit
- Obtain informed consent with initial visit
- Continue current hormone treatment at safe doses at time of initial visit
- Further assess need for subsequent dosage adjustments based on clinical, medical, and lab findings
- Closely monitor for possible harmful effects of self-dosing

Cedar River Clinics recommends the two-visit protocol or the expedited therapy model based on provider experience and comfort. Extended therapy models may be an acceptable alternative as long as they do not place “real life experience” demands; however, delays in accessing gender-affirming care may be socially or emotionally detrimental to many patients.

Initiation of Hormone Therapy

The following is based on a two-visit protocol and can be tailored as needed to other models of care. Addition customization may be required for providers outside of the United States.

Initial Visit

Patient Interview

Complete personal and family medical history with special attention to:

- Hyperlipidemia
- Cardiovascular disease
- PCOS

- Diabetes
- Liver disease
- Personal or family history of hormone-sensitive cancers
- Health habits including diet, exercise, substance use and smoking
- Past gender affirming treatments and surgeries

Complete psychosocial assessment including:

- Gender experience
- Goals of hormone therapy
- Mental health concerns
- Support system
- Family system and intimate relationships
- Housing and economic stability
- Parenting desire

Physical Examination

- Vital signs
- Height and weight

Lab Screenings

Baseline lab work:

- Hematocrit and hemoglobin
- STI screening per current CDC guidelines (see recommendations for screening in Preventive Care section below)

PRN lab work:

- Total testosterone
- Lipid panel PRN per USPSTF guidelines
- A1C PRN per USPSTF guidelines

Patient Education

- Elicit patient goals and expectations for physical and emotional changes.
- Effects of hormone therapy, both desired and undesired, including review of pace and degree of masculinization
  - Older patients should be advised that pace of changes will be slower for them than with younger patients, and they may ultimately experience less masculinization overall.
- Potential impacts on health and wellness tailored to patient's medical history:
  - Worsening hyperlipidemia

  - Worsening snoring or obstructive sleep disorders
  - Worsening acne
  - Increased risk for cardiovascular disease
- Discuss potential impacts on fertility and options for becoming a parent, including discussion of fertility preservation options
- Smoking cessation counseling if applicable.
- Anticipated schedule for well-person and gender affirming care during hormone therapy.
- Potential social consequences.
- Potential occupational consequences.
- Potential impact on familial relationships.
- Potential impact on romantic relationships.
- Anticipated medical and non-medical expenses.
- Potential impact on emotional health and review of available resources.

Documentation

- Complete comprehensive chart note including findings of mental health assessment.
- Name and pronouns used in your chart notes should be patient-directed. It is completely acceptable to use gender-neutral pronouns such as they/them in your chart note. The patient's name and pronoun should be documented prominently in an easy-to-see area of their chart, if different than those on file.

Billing

- In the past, it was strategic to use the ICD-10 Gender Identity Disorder code (F64.1), after obtaining patient consent with a prior discussion that you do not consider their gender identity pathological. However, we have found that code is very rarely accepted for non-psychiatric providers. The code for Endocrine Disorder (E34.9) is most often used. Please note that this code is more generic and may require you to have a clinical discussion and/or advocate for coverage on behalf your patients with insurance companies.
- Bill by time

Second Visit

Patient Interview

- Review lab results.
- Discuss impact of findings on health status.
- Discuss initial hormone therapy regimen and plan for titration over time

Physical Examination

- Vital signs
- Height and weight
- Palpate thyroid
- Auscultate heart and lungs
- Assess extremities for signs of circulatory compromise
- Assess gait as a component of mental health screening
- Additional assessments as appropriate to the patient's medical history and wellness needs

Patient Education

- Reinforce healthy diet and regular physical exercise.
- Create plan for management of health conditions and health risks as needed.
- Reinforce smoking cessation and provide resources as needed.
- Review medication doses and plan for titration.
- Provide injection training
- Provide written materials about safe testosterone injection.
- Review routine well-person healthcare visit expectations and scheduling for patients on hormone therapy.

Documentation

- Comprehensive chart note
- Findings of physical exam
- Signed consent form
- Coding same as for visit one, with addition of general physical exam Z00.00

Injection Training

Injection training can be done during the second visit or scheduled separately once the patient has medication and supplies "in-hand" from the pharmacy. The patient should be taught and be able to demonstrate safe self-injection technique. Provide a visual aid demonstrating appropriate dose, written information on self-injection technique, and education on the importance of not sharing needles and safe sharps disposal.

Hormone Administration

Routes of Testosterone Administration

There are a number of routes by which patients can take testosterone, including intramuscular or subcutaneous injections, gels, patches, and implants.

Injectable Testosterone

Injection is the most common and least expensive route of hormone administration. Intramuscular injection has historically been recommended. However, at least one study on testosterone treatment of hypogonadal cisgender men have shown that it is safe, effective, more comfortable, and more convenient to use subcutaneous injections. Many providers now recommend this route. Other providers avoid the subcutaneous route secondary to frequent complaints of local site reactions. For subcutaneous injection, needles should be 25 gauge - a smaller gauge can cause unnecessary trauma to tissues by injecting the preparation with too much pressure. Needle length varies based on body habitus, but an average length would be a 5/8 tuberculin needle. Eighteen-gauge needles are ideal for drawing up medication from the bottle.

Careful patient teaching is required for patients who are self-injecting because the dose may be confusing. Express doses to patients as mL to inject, with injection amount based on the specific concentration of the preparation prescribed. Providing visual aids (such as an image of a syringe with the correct dose marked and shaded in) can help patients be successful in administering their medication correctly. Patients should also be advised that it is normal for a very small amount of medication to be left in the syringe after injection, and that their dose does not need to be increased to account for this.

Transdermal

Gels and patches are an effective but sometimes more expensive route of hormone administration. They also result in a slower onset of physical changes. Individuals may be sensitive or allergic to patch adhesive or they may not stick well if the person sweats heavily. Additionally, testosterone levels may fluctuate more with the transdermal route than with injections. Patients using transdermal testosterone require careful patient teaching to prevent the accidental transfer of testosterone to others. It is especially important to prevent transfer to children. Testosterone gel should be applied in the morning and to the upper arms and shoulders only, and the site of application should be kept dry for at least 2 hours after administration. The site should be cleaned with soap and water before children or cisgender women have direct skin-to-skin contact with the area.

Implants

Implants offer a long-term and slow-release route of hormone administration with less abrupt hormonal shifts. However, implants are quite expensive and require a minor in-office surgical procedure approximately every 3 months. Additionally, there is very limited data available to guide testosterone therapy using this route of administration. For these reasons, implants are much less commonly used than other forms of testosterone administration.

Common Regimens

Binary Gender Affirmation

Injectable Route

- Testosterone cypionate 200 mg/mL in sesame or cottonseed oil. Prescribe alternative oil for suspension if patient has an allergy.
- Administer via intramuscular or subcutaneous route
- Dosing:
  - Some patients appreciate a slow process of dose titration, while others prefer a more rapid titration. In most cases it is safe to titrate rapidly.
  - For most patients, it is appropriate to start at an initial dose of 50 mg every week; after one month or sooner PRN, increase dose to 80-100 mg every week. For patients experiencing frequent breakthrough bleeding after initiation of testosterone therapy, earlier titration may be helpful.
- Post oophorectomy, tailor dose to lab values and patient satisfaction. Many patients will have the same testosterone requirement as before oophorectomy, since removal of the gonads does not increase endogenous testosterone production.

Transdermal

There are several options for transdermal therapy.

- 1% Gel
  - Initiate at one 50 mg packet per day; titrate to two 50 mg packets per day after 1 month.
  - Apply to shoulder or uppers arms once daily in the morning.
  - Wash hands carefully after application and cover the skin on which gel was applied to prevent transfer to others.
  - Keep application site dry for at least two hours.
  - Clean application site with soap and water before children or cisgender women have direct skin-to-skin contact with the area.
  - Keep packets as well as empty packet wrappers away from children and pets.

- 4 mg patch
  - Initiate at 1 patch each evening (remove before placement of next patch); titrate to 2 patches each evening after 1 month. It is safe to cut the patch to tailor dosing.
  - Apply patch to upper arms, back, stomach or thighs once daily in the evening.
  - Site must be rotated, with 7 days between using a patch at the same site.
  - Avoid showering, baths, and swimming for 3 hours after application.

  - Children and cisgender women should not have direct contact with the patch.
  - Keep new and used patches away from children and pets.

- Compounding pharmacies can prepare tailored creams or gels.
  - Sample dosing: initiate at 1 g/day of 5% formulation (50 mg); titrate to 1 g/day of 10% formulation (100 mg) after one month.
  - Can tailor dosing to individual needs.
  - Compounding pharmacies are not subject to the same regulations and oversight as traditional pharmacies.
  - Use strategies noted above to reduce risk of exposure to children and cisgender women.

Medication for Management of Male Pattern Scalp Hair Loss

Finasteride can be used if needed for management of significant scalp hair loss. Finasteride can be initiated at 1 to 2.5 mg daily and titrated to a maximum of 5 mg daily. If using a 5 mg dose, monitor for signs of excessive androgen blockade.

Non-Binary Gender Affirmation

Goals for gender affirmation vary broadly, and patients with non-binary gender identities may not desire the same degree of masculinization as their binary-identified peers. Non-binary gender identity is quite common, although this community of TNB individuals has historically been poorly served and often denied access to care. To a greater degree than with binary gender affirmation, non-binary gender affirmation is highly customized and may or may not include the use of hormones. Gender affirmation may be adequately achieved with social strategies such as name and pronoun change and/or changes in gender presentation. Additional common gender affirmation strategies are discussed below.

Hormone Therapy for Non-Binary Individuals

- Low-dose testosterone may be administered by any route

- Risks of low-dose hormone therapy have not been adequately explored in research, but may include:
  - Balding
  - Acne
  - Permanent deepening of voice
  - Permanent hair growth
  - Irregular menses
  - Unknown effect on uterine lining (could consider progestin IUD for endometrial protection as a precaution, if acceptable to patient)

- Weight gain
- Mood issues
- Hypogonadal side effects such as hot flashes, fatigue
- Osteoporosis
- Impact on fertility

Surgical and Cosmetic Gender Affirmation for Non-Binary Individuals

While also used by patients desiring binary transition, the treatments below may be used by non-binary patients as stand-alone treatments or in conjunction with modified or low-dose hormone therapy regimens.

- Removal of unwanted hair growth on the face or body
- Gender affirming chest surgery such as double mastectomy or breast reduction
- Hysterectomy/oophorectomy
- Metoidioplasty/phalloplasty

Patients who are considering breast reduction vs. double mastectomy should be cautioned against approaching this an “interim” step – i.e., starting with reduction and then proceeding to mastectomy in the future if desired. Breast reduction technique and scar tissue/adhesion formation may make this surgical progression difficult or impossible. Desired outcomes and technical considerations should be discussed in detail with a surgeon before making a plan.

Monitoring and Follow Up

It is important to monitor response to hormone therapy through regularly scheduled follow-up visits to:

- Assess patient satisfaction with therapy.
- Assess efficacy.
- Address any questions or concerns.
- Monitor lab work.
- Provide preventive screenings.
- Provide continued support and referrals as needed.

Hormone Level Monitoring

Serum hormone levels are a useful quantitative tool for assessing masculinization, and many patients find these lab values reassuring. Overall, hormone levels should fall in the normal physiologic range for a male of the patient’s age. If the patient is happy with masculinization without reaching what is considered to be

an optimal or physiologic range, this is not concerning, and the dose should not be titrated up solely to increase serum levels. Patient satisfaction and safety (i.e. avoiding supraphysiologic testosterone levels and subsequent polycythemia) are the primary goals of treatment. Guidelines for evaluating hormone levels are as follows:

- Total testosterone: There is no clear consensus on exact reference range for serum testosterone in individuals undergoing masculinizing hormone therapy. Many providers use 350-700 ng/dL (at mid cycle if using injectable testosterone), while some labs set the upper limit at 900 ng/dL.
  - If testosterone level is significantly above a normal physiologic range, the patient's dose should be reduced, and a CBC should be draw to assess for polycythemia.
- It is not typically useful to evaluate estradiol level in masculinizing patients. This should be referred to complex cases, such as persistent menses at therapeutic testosterone dose. SHBG and albumin can also be drawn to guide management in complex cases.

Choosing Reference Ranges for Other Labs

There are no strict guidelines for determining when to use a male reference range or a female reference range when evaluating laboratory findings in masculinizing patients. Knowledge of physiology and using a gestalt approach will guide decision-making. For example, when testosterone is in a cisgender male range, hematocrit and hemoglobin will be elevated above a cisgender female range and cisgender male reference ranges should be used to assess for polycythemia.

Follow Up Schedule

The schedule below provides a general guide for hormone therapy management, but some patients will benefit from additional monitoring and problem visits may be required between routine follow up visits. While in-person follow up visits are suggested below, it may be appropriate to complete many of these visits using e-medicine modalities. It is helpful to have labs drawn prior to appointments so that results can be reviewed with the patient and taken into account when dosage adjustments are made.

Testosterone levels should be drawn mid-cycle (on day 3 or 4 after injection) in patients who are using injectable testosterone. Occasionally a peak or trough draw may be useful in evaluating symptoms.

One month after initiation of hormone therapy

- Increase dose if appropriate
- PRN labs: testosterone, hemoglobin & hematocrit
- STI screening if indicated

Three months after initiation of hormone therapy:

- Increase dose if appropriate

- Recommended labs: testosterone, hemoglobin & hematocrit
- STI screening if indicated
- PRN labs reserved for complex cases: SHBG, albumin, estradiol

Six months after initiation of hormone therapy:

- Increase dose if appropriate
- Recommended labs: testosterone, hemoglobin & hematocrit
- STI screening if indicated
- PRN labs reserved for complex cases: SHBG, albumin, estradiol

One year after initiation of hormone therapy:

- Annual wellness exam
- Recommended labs: testosterone, hemoglobin & hematocrit
- STI screening if indicated
- PRN labs based on USPSTF guidelines: lipids, A1C
- PRN labs reserved for complex cases: SHBG, albumin, estradiol

After one year of therapy – annual visits:

- Annual wellness exam
- Recommended labs: Hemoglobin & hematocrit
- STI screening if indicated
- HPV testing/Pap smear if indicated
- PRN if concerns about masculinization or dosing: Testosterone
- PRN labs based on USPSTF guidelines: lipids, A1C
- PRN labs reserved for complex cases: SHBG, albumin, estradiol
- See Masculinizing Annual Exam module

Preventive Care While on Hormone Therapy

Preventive care should be tailored to anatomy present, hormonal status, sexual behavior, and overall context.

HPV Testing/Pap Smears

HPV testing/Pap smears will continue to be necessary after initiation of testosterone therapy, if a cervix is present.

- Anyone with a cervix should be screened per current ASCCP guidelines
- Screening may still be required in individuals who have undergone hysterectomy and have a history of abnormal pap smears; follow current ASCCP guidelines.

- HPV testing/Pap smears offer an opportunity for STI screening; however, GC/CT screening can also be completed without exam using urine or self-collected vaginal swab.

Additional planning may be needed for conducting HPV testing/pap smears in TNB individuals. Patients may experience heightened emotional distress and anxiety in regard to pelvic exams, and building rapport is a critical step in ensuring patient well-being. Additionally, patients who are taking testosterone may experience physical pain with pelvic exam due to atrophic tissue and, in some cases, rare vaginal penetration. Sexual practices range widely among TNB individuals; some patients may engage in receptive vaginal intercourse routinely, while for others the HPV testing/pap smear may their first ever experience of vaginal penetration. Rates of abnormal and unsatisfactory pap results are also higher in people taking testosterone, possibly due to atrophic changes, patient discomfort with exam, and/or provider discomfort with performing the exam.

Strategies for improving HPV testing/pap smear outcomes and patient experience of pelvic exam include:

- Short course (one to three months) of vaginal estradiol prior to exam to repair atrophic tissue.
- Use of the smallest speculum possible.
- Use of an adequate amount of water-based lubricant.
- Application of a topical anesthetic such as lidocaine at time of exam to prevent pain. Lidocaine jelly can be applied alone or mixed with water-based lubricant to both the introitus and the bills of the speculum.
- Use of several different types of collection devices to increase likelihood of obtaining adequate endocervical sample (i.e. collect a total of three samples using a brush, a broom, and a spatula).
- Use of oral anxiolytics to decrease procedural anxiety.

Chest Care

- Mammograms will continue to be necessary per current guidelines in patients who have not undergone double mastectomy, including those who have had breast reduction surgery
- Chest cancer screening may be appropriate for patients with who have undergone double mastectomy and have a family or personal history of breast cancer. Shared decision making should be used to determine if screening will be performed. Chest ultrasound or MRI should be considered in the place of mammogram, as mammography may be technically difficult or impossible based on the specific patient's anatomy.

Bone Density

Risk factors for osteoporosis are dependent on length of testosterone therapy and the presence or absence of gonadal tissue. DEXA is recommended for patients:

- Aged 65 or older with no additional risk factors
- Aged 50 to 64 years with risk additional risk factors
- Any age, if the patient has undergone gonadectomy and has gone 5 or more years without hormone therapy

Colorectal Cancer

Use USPSTF screening guidelines.

Sexually Transmitted Infection Screening

Patients should be screened for STIs based on CDC guidelines, anatomy present, anatomy of sexual partners, sexual behavior, and overall context. The CDC offers screening for cisgender individuals only, so clinical discernment should be used when deciding on screening regimens in TNB individuals. The following are good rules of thumb, however appropriate screening varies by patient.

- All HIV negative patients between 13 and 64, as well as those who request STI screening regardless of age, should be screened annually for HIV
- For HIV negative patients who are sexually active with partners with vaginas only: use current CDC screening guidelines for “women”
- For HIV negative patients who are sexually active with partners with penises, and these partners do NOT also partner with people with penises: use current CDC screening guidelines for “women”
- For HIV negative patients whose sexual partners include people with penises, and these partners DO also partner with people with penises: use current CDC screening guidelines for “men who have sex with men”
- See full CDC guidelines for screening in HIV positive patients

Discontinuation of Hormone Therapy

Some patients may decide to discontinue hormone therapy or present with a clinical reason for discontinuation. These patients should be offered support and ongoing culturally responsive routine preventive care. Many patients who choose to discontinue hormone therapy feel that their providers and peers will judge them negatively for this decision. It is important that healthcare providers demonstrate their support, remembering that gender affirmation is a nuanced and very personal process that does not follow a linear path or have one set endpoint. There is not one “right” way to live in the world as a TNB person, and patients are the experts on their own gender identity and their desire for gender affirmation. Patients may prefer to titrate their dose down prior to cessation, but this is not required. It is safe to discontinue testosterone at any time.

Additional Resources

Guide To Masculinizing Hormone Therapy
Transfeminine Preventative Care Module
Surgical Care Guide

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