

Hormone Therapy for Transgender Men

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KEYWORDS

- Transgender medicine • Transmasculine hormone treatment
- Endocrine Society clinical practice guidelines

KEY POINTS

- Transgender men may seek hormone therapy to align their external physical appearance with their gender identity.
- Physicians should provide patients an overview of the adverse effects and benefits prior to initiating hormone therapy.
- Because of associated adverse effects with long-term use of hormone therapy, it is important that patients be monitored over time for adverse outcomes.

INTRODUCTION

Transgender individuals who seek medical intervention often begin with sex steroid hormones to modify their external physical appearance to align with gender identity.¹ A safe and effective regimen is required to maintain the hormone levels within the normal physiologic levels for the individual's affirmed gender.² This article provides an update on the current practices of hormone therapy for transgender men.

Transgender men are individuals with male gender identity despite typical female external anatomy. Masculinizing hormone therapy is used to induce virilization.² Most transgender men seeking gender-affirming surgeries will already have started transgender sex steroid hormone therapy under medical supervision prior to obtaining surgery.¹ The most common type of hormone treatment for transgender men is exogenous testosterone. Older concerns regarding liver toxicity due to testosterone treatment were limited to oral forms of testosterone that are no longer in

use, with the result that the concern is now considered obsolete.^{1,3}

The 2017 Endocrine Society Clinical Practice Guidelines provide detailed recommendations regarding hormone support to for adolescent and adult transgender individuals seeking medical intervention.⁴ The guidelines recommend against prescribing transgender hormone therapy to pre-pubertal children and that clinicians prescribe pubertal hormone suppression only after the first signs of puberty.

Although hormone therapy under physician supervision is safe and effective, there are some transgender men who self-prescribe hormones due to easy Internet access to these hormones, societal pressures, and/or lack of a thorough understanding of the adverse effects.^{5,6} Hence it is important that before commencing hormone treatment, these individuals undergo a thorough assessment including query regarding other hormone sources prior to seeking medical support.

Disclosure: The authors have nothing to disclose.

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Clin Plastic Surg ■ (2018) ■-■

<https://doi.org/10.1016/j.cps.2018.03.004>

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PRINCIPLES OF HORMONE THERAPY

The goals of gender-affirming hormone therapy are mostly drawn from the recommendations that exist for treatment of hypogonadal cis men, wherein circulating blood testosterone concentrations are raised to a cis men physiologic range (300 to 1000 ng/dL).^{2,7} Few studies have been performed to determine the relationship between testosterone dosage and time required for the onset of specific physical responses to the testosterone therapy. Nakamura and colleagues⁷ found that physical changes were observed earlier in a group who received the highest doses, but that after 6 months most patients achieved expected physical responses.

Prior to initiating hormone therapy, the physician should clearly explain the potential adverse effects and benefits (short- and long-term) to the patient and develop an ongoing maintenance plan for monitoring adverse events during hormone therapy (**Box 1**). Patients should initially be monitored approximately every 3 months, and doses should be adjusted as necessary to ensure that planned serum testosterone concentrations are being achieved. Upon stabilization of hormone dosing, routine annual or biannual evaluation should be sufficient.⁸ It is important to measure the baseline hematocrit and lipid profile levels. Baseline bone mineral density may be checked as well if there is concern prior to initiation of hormone therapy.^{2,9}

Typical early (within the first 3 months) physical changes from hormone therapy include cessation of menses, increase in body and facial hair, increase in muscle mass, change in the fat distribution to a more masculine pattern, and increased libido.^{10,11} These changes are followed in subsequent months and years by deepening of the voice and clitoral enlargement.¹²

Box 1

Suggested monitoring for long-term care

1. Regular clinical and laboratory monitoring with each dose change (typically every 3 months) during the first year followed by once or twice yearly when dose is stable
2. Periodic assessment of hematocrit (or hemoglobin) and lipid levels
3. If risk of osteoporosis exists (eg, after gonadectomy), then bone mineral density measurements should be obtained

Adapted from Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Guidelines on Gender-Dysphoric/Gender-incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* November 2017;102(11):3869–902.

For adolescents, treatment can be initiated using gradually increasing doses after clinicians (both medical and behavioral health) have confirmed the diagnosis of gender dysphoria/gender incongruence and that the patients have an ability to give informed consent to ongoing treatment.⁴ A study in 101 youth between the ages of 12 to 23 reported that use of hormones over a period of 2 years was safe and did not require frequent clinical and laboratory examinations.¹³

TREATMENT REGIMENS

There are many routes to administer exogenous testosterone including intramuscular or subcutaneous injections, transdermal applications (gels or patch), and subcutaneous implants. Parentally administered testosterone preparations include testosterone enanthate and testosterone cypionate. Both can be given weekly with typical doses of 50 to 100 mg.⁸ Larger doses administered every 2 weeks can minimize frequency of injections but are associated with greater periodicity in levels. Sometimes longer-acting testosterone undecanoate permits administration only every 8 to 12 weeks.² Often clinicians start with lower doses (to account for the size of transgender men compared with cis men) and then increase the dose as needed. The doses for testosterone gels or transdermal patches are typically 2.5–10 g/d and 2.5–7.5 mg/d, respectively.² In case of transdermal gels, patients should keep the injection site clothed for 1 to 4 hours after application to avoid transferring testosterone (by skin-to-skin contact) to others. For maximal absorption, showering should be deferred for 4 hours after application.¹⁴ **Table 1** identifies the current testosterone administration regimen for transgender men.

Slow-release testosterone pellets implanted subcutaneously to provide long-acting androgenic effect contain 75 mg of testosterone, and the number of pellets inserted at each pass depends on the individual's daily testosterone requirement to achieve normal physiologic levels. Most patients require repeat implantation after 3 to 4 months.²

LONG-TERM MONITORING AND POTENTIAL ADVERSE EVENTS

There are several undesired adverse effects associated with the use of testosterone therapy including acne, altered cholesterol and triglyceride levels, alopecia, and possible increase in systolic blood pressure.¹² A study by Elbers and colleagues¹⁵ found that after 12 months of hormone therapy, transgender men had increased thigh muscle mass, but suffered greater visceral fat

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