Hormonal and Surgical Treatment Options for Transgender Men (Female-to-Male)

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KEYWORDS

• Transgender • Hormone replacement • Sex reassignment surgery
• Gender affirmation

KEY POINTS

- Hormone therapy provides significant benefits, allowing many patients to live as male in society by 2 years of treatment.
- No increased risks of malignancy or cardiovascular end points with hormonal therapy are demonstrated in the literature, though minor increases might not be detectable at the current level of evidence.
- Mastectomy is the most common surgery necessary for transgender men as it significantly diminishes gender dysphoria, improves quality of life, and carries less risk than genital surgery.
- Individualized shared clinical decision-making is necessary, and clinicians should be able to provide the information needed for this process as provided by this review.

INTRODUCTION

Hormone replacement therapy (HRT) and surgery for transgender people have existed for almost a century. However, of the more than 5200 citations in Medline referencing transgender care, fewer than 1000 were published before 1990. Transgender health remains a relatively young field, and the quality and quantity of evidence is limited. Guidelines such as those published by the World Professional Association for Transgender Health[1] (known as the WPATH Standards of Care) and the Endocrine Society[2]

Financial Disclosures: Neither author has a conflict of interest nor are they receiving any funding for this work.
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Psychiatr Clin N Am ■ (2016) ■–■
http://dx.doi.org/10.1016/j.psc.2016.10.005 psych.theclinics.com

provide recommendations for care, though both recognize that the data are suboptimal and, thus, state that these are flexible recommendations especially when used by experienced clinicians. Care must be individualized, and not all patients need all treatments. For example, in a Dutch sample, only 58% of transgender men (transmen) who had decided on what treatment they would undertake requested full treatment (HRT, mastectomy, hysterectomy, and genital sex reassignment surgery [SRS]). Interestingly, the only universal request among patients was mastectomy, though only 2% declined testosterone (T). Reasons cited for not being interested in certain interventions were mostly related to surgical risks/outcomes but also included lack of genital dysphoria or a nonbinary gender identity.[3] Provider advocacy is also crucial for many patients to change identity documents and access sex-segregated facilities safely. Guidance for critically important letters can be found through the National Center for Transgender Equality (http://www.transequality.org/documents) and the Transgender Law Center (http://transgenderlawcenter.org/issues/id/id-please).

Hormone Regimens

In the United States, HRT in transmen is typically T by intramuscular injection (IM) or transdermally. Subcutaneous (SQ) pellets are also an option, and in other countries oral formulations are available. Most commonly, T cypionate (Tc) (depot T) or enanthate (Te) are used parenterally. Recommended dosages are 200 to 400 mg per month, divided weekly to every other week.[2,4] Earlier onset (by 3 months of treatment) of desired effects may be greater in patients receiving higher doses, but these differences disappear at 12 months.[5]

IM Tc and Te can produce supraphysiologic levels of T 2 to 3 days after injection and subtherapeutic levels at trough (especially if given every other week rather than weekly). Transdermal T patches or gel, with dosages from 2.5 to 10 mg daily, may better mimic physiologic levels of T.[2,4] T can be transmitted to others by skin-to-skin contact; however, the amount transferred is modest.[6] The authors recommend patients not shower for at least 4 hours after application because it can significantly decrease serum T levels.[7] The authors also strongly caution patients around those most sensitive to transferred T (pregnant women and small children) to choose another method or be assiduous about keeping sites clothed for 4 hours after application.

Some transmen and providers use Tc or Te SQ, dosed weekly. There is scant research about this practice, with only 3 published articles[8–10] and 2 conference abstracts.[11,12] Although only 2 of these studies were in transmen, one was in youths aged 12 to 24 years, and all were limited by small sample size (137 patients total across all 5 studies), findings suggest that there is no difference in bioavailability between SQ and IM T. One study of SQ T noted that in obese patients serum T levels were more than 40% lower after 30 days than in nonobese patients, but this difference diminished at 4 months.[12] In patients for whom IM administration would carry other risks (for example, patients on warfarin) benefits of SQ dosing may outweigh the risks.

In addition to injected or transdermal T, adjuvant HRT treatments can be used. These treatments include progestagens, 5-α-reductase inhibitors (5-ARIs), aromatase inhibitors (AIs), gonadotropin-releasing hormone antagonists (GnRHas), and clitoral application of T. As shown in **Fig. 1**, administered T can be converted to dihydrotestosterone (DHT) by 5-α-reductase and to estrogens by aromatase. Higher DHT levels contribute to androgenic alopecia (AA) (ie, male pattern baldness) and increased estrogen to fat redistribution and other effects. The 5-ARIs are sometimes used by transmen to prevent further AA while on T. The authors do not usually recommend AIs despite the fact that T use only decreases serum E levels modestly. In most patients, there is no significant benefit to justify their risks, although they may be helpful in rare