Endocrinology and the Transgender Patient

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The following faculty and planning committee members have no financial relationships to disclose:

- Mathew C. Leinung, MD
- Cynthia H. Miller, MD, AAHIVS
- Sarah J. Walker, MS
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Learning Objectives:

- Discuss hormone therapy.
- List ways to provide cross-gender therapy to transgender patients by reviewing their effects, benefits and risks.
- Review key drug interactions with hormone therapy.
Definitions

• Gender Dysphoria (DSM-V)
  – “discomfort or distress that is caused by a discrepancy between a person’s gender identity and that person’s sex assigned at birth”
  – Previously “Gender Identity Disorder”
  – “transsexual” or “transgender” when one has crossed the assigned gender (transsexual when accompanied by permanent change in gender role)

How Common is Transsexualism?

Prevalence:

– MtF 1:11,000, FtM 1:30,000¹
– 0.3% of population (700,000 in U.S.)²

²Gates GJ. How many people are lesbian, gay, bisexual, or transgender? The Williams Institute 2011
Rates of Male/Female Transsexuals

AMC Transsexual Clinic, n = 370

% FtM

Age at Rx at AMC

Year (3 year rolling average)
Gender Dysphoria in Childhood and Adolescence

- Gender dysphoria not uncommon in childhood: persists into adulthood 5-15%
  - Generally resolves prior to puberty
- Gender dysphoria in adolescence persists into adulthood
- Treatment of adolescents: GnRH to (reversibly) suppress puberty with variable delay of hormone therapy

WPATH Standards of Care, version 7, for references

HIV and Transsexualism

- CDC\(^1\) data for 2013, rates of newly confirmed HIV testing events were 1.9% in Trans women, 0.9% in males
- Overall rate from multiple state or city level surveys: 1-2% of HIV population is transgender
  - In certain areas, this rate is as high as 50\(^2\) (with 90-100% of these trans women)


\(^2\)AIDS Behav DOI 10.1007/s10461-016-1656-7
AMC Experience with HIV and Transsexuals

- 371 patients
  - 274 MtF, 22 HIV positive (12%)
  - 97 FtM, 1 HIV positive (infection acquired after transition)

HIV Trans Women
CDC Division HIV/AIDS, 2009-2011 MMP data

- Trans women socioeconomically more marginalized
- Same rates of prescription or ART, But:
  - Lower rates of ART adherence
  - Lower rates of durable viral suppression
  - Increased need for supportive services

Mizuno et al. LGBT Health 2015 DOI: 10.1089/lgbt.2014.0099
Transsexual Roots in the U.S.

Harry Benjamin (1885-1986)

- Came to U.S. 1914
- Started treating transsexuals 1948
- *The Transsexual Phenomenon* 1966
- The Harry Benjamin International Gender Dysphoria Association* 1979

Results of Treatment?

- Johns Hopkins study 1979
- Meta analysis 2010* (30 studies) found significant improvement in:
  - Dysphoria (80%)
  - Psychological symptoms (78%)
  - Quality of life (80%)
  - Sexual function (72%)

Potential Harm With Therapy?

- Studies (Gooren et al) reported increased risk of VTE in the late 90’s. By the early 2000, ethinyl estradiol was becoming identified as the culprit and those groups moved to estradiol or transdermal estrogen, and rates have dropped significantly.


VTE Experience at AMC

- Through 2009, with 1300 patient years of follow up, we had 5 events (2 PE’s, 1 probable PE, and two with leg edema):
  - 2 events occurred prior to seeing us while taking non-prescribed hormones
  - 1 patient was subsequently diagnosed with a clotting disorder
  - 2 events in patients taking Premarin prior to our switching to estradiol around 2006
  - No known events since switching to estradiol*
Potential Harm with Therapy?

• MtF show some worsening in cardiac risk factors but no increase risk has been demonstrated
• Case reports of endocrine related cancers (e.g., breast, prostate)

Gooren JCEM 2008;93;19-25

Diagnosis of Gender Dysphoria

• Done by qualified mental health professionals with experience in gender issues
• At AMC, individuals must be referred by (or have been seen by) mental health professionals (or we will make the appropriate referral)
The Guidelines drafted by the Endocrine Society are not evidence-based recommendations, but rely on clinical experience and parallels in general expertise sex hormone treatment in hypogonadal (nontranssexual) subjects.

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**Treatment Approach**

- “We suggest that cross-sex hormone levels be maintained in the normal physiological range for the desired gender”
- Do not start at full dose therapy: puberty takes many years. I start at moderate dose and work up to full dose by around 1 year
  - Breast development in girls treated for absent puberty is not normal if the process is rushed (a more tubular as opposed to full shape)
**MtF**

- Estrogen *(not ethinyl estradiol)*
- Antiandrogen
  - GnRH
  - Spironolactone
  - Cyproterone (Europe, not US)
  - Finasteride
  - Progestins

**MtF: AMC**

- Oral estradiol 2, working up to 6 mg daily
  - Estrogen patch: generally not strong enough but can be used post-op, older patients, and DVT risk
- Goal is $17\beta$ estradiol level 100-200, testosterone level < 100
- Medroxyprogesterone as needed
  - Progesterone does not directly feminize
  - If estrogen levels are good but testosterone not suppressed, add Provera 2.5 to 10 mg
- Spironolactone or finasteride for hair
Results of Therapy in MtF

- Fat redistribution
- Skin softening
- Breast development
- Decreased libido (often)
- Testicular atrophy
- Decreased body hair
- No change in voice or skeletal size

Estrogen Contraindications

- VTE due to underlying hypercoagulable state
- Estrogen dependent cancer
- End stage liver disease
Estrogen Use: Potential Risks

Likely associations:
- VTE (don’t use EE, consider transdermal)
- Lipids: marked increase in triglycerides (uncommon, seems less likely with transdermal route)
- Liver: increase in transaminases has been described, also gall stones

Estrogen Use: Potential Risks

Possible association
- Diabetes (not according to Endo Society, and WHI)
- Prolactin elevation (but OCP’s are a recommended therapy in women with hypoestrogenic state from prolactinomas)
- Hypertension
- Migraines
Estrogen Use: Potential Risks

Inconclusive or No Increased Risk
- Breast Cancer: has been reported in trans males, but also in cis-males
- Duration of exposure, family history, obesity, progestin use may influence risk

FtM
- Testosterone
  - Parenteral or transdermal
    - Transdermal often not potent enough prior to oophorectomy
  - In general, follow approach for hypogonadal males
  - Goal is to achieve normal male levels
Results FtM

- Increased acne
- Increased muscle mass
- Increased facial and body hair
- Cessation of menses (generally within 6 months)
- Clitoromegaly
- Increased libido
- Vaginal atrophy

Testosterone Contraindications

- Active coronary artery disease
- Pregnancy
- Polycythemia (Hct > 55%)
Testosterone Risks

- Polycythemia
- Weight gain (visceral fat)
- Liver transaminase (uncommon)
- Sleep apnea?
- Hypertension?
- CAD?
- Ovarian/endometrial cancer?
- Breast Cancer?

General Observations

- Social transition easier at younger age (family, career, etc.)
- Improving social acceptance over the past decade
General Observations MTF

- Hormonal therapy yields better cosmetic results when started at a younger age
- Surgical outcomes are generally quite good

General Observations FTM

- Hormonal therapy not as age dependent and generally yields very good results
- Social transition seems to be easier than FTM
- Surgical outcomes are not as good
Need for Monitoring and Individualizing Therapy

Testosterone vs. Estradiol Dose

- Testosterone (ng/dl)
  - n=21
  - n=112
  - n=16

(Mean)

Estradiol (mg) 4 8 8 Post op
Estradiol Level and Testosterone Suppression

17-Beta Estradiol levels on Oral Estradiol
Drug Interactions

- Efavirenz
  - Has been associated with oral contraceptive failures
  - We have seen some instances of inability to get sufficient estradiol levels and suppression of testosterone in patients on this medication (even with medroxyprogesterone use)
  - Problem may be bypassed with transdermal route

NY State
Transgender Related Care and Services
Effective date: 3/11/15

Pursuant to authority vested in the Commissioner of Health by Sections 201 and 206 of the Public Health Law and Sections 363-a and 365-a(2) of the Social Services Law, Section 505.2 of Title 18 (Social Services) of the Official Compilation of Codes, Rules and Regulations of the State of New York is amended as follows, to be effective upon, publication of a Notice of Adoption in New York State Register.
NY State:

Subdivision (l) of section 505.2 is repealed and a new subdivision (l) is added to read as follows:

(l) Gender dysphoria treatment. As provided in this subdivision, payment is available for medically necessary hormone therapy and/or gender reassignment surgery for the treatment of gender dysphoria.

(2) Hormone therapy, whether or not in preparation for gender reassignment surgery, may be covered for individuals 18 years of age or older.

NY State:

(3) Gender reassignment surgery may be covered for an individual who is 18 years of age or older, or 21 years of age or older if the surgery will result in sterilization, and has letters from two qualified New York State licensed health professionals who have independently assessed the individual and are referring the individual for the surgery. One of these letters must be from a psychiatrist or psychologist with whom the individual has an established and ongoing relationship. The other letter may be from a licensed psychiatrist, psychologist, physician or licensed clinical social worker acting within the scope of his or her practice, who has only had an evaluative role with the individual.
NY State (cont)

(i) has a persistent and well-documented case of gender dysphoria;
(ii) has received hormone therapy appropriate to the individual's gender goals, which shall be for a minimum of 12 months in the case of an individual seeking genital surgery, unless such therapy is medically contraindicated or the individual is otherwise unable to take hormones;
(iii) has lived for 12 months in a gender role congruent with the individual's gender identity, and has received mental health counseling, as deemed medically necessary, during that time;

Summary

- Gender dysphoria is not a choice
- Therapy is effective and safe
- Hormonal therapy requires individualization and monitoring