Transgender Issues

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Disclosures

- Ad boards: Abbott, Boehringer Ingelheim
- Honoraria: Eli-Lilly, Astra Zeneca

- Of note, all of the medical therapies that will be discussed today are off-label

Objectives

- By the end of this presentation, for adult patients, the participants should be able to:
  - Be aware of baseline characteristics that may impact gender-affirming hormone therapy
  - Identify the major benefits, risks and limitations of gender-affirming hormone therapy
  - Be more comfortable with the prescribing/monitoring of gender-affirming hormone therapy

Initial Approach

- I rely on other professionals to ascertain that an individual who desires gender-affirming hormone therapy meets criteria of gender dysphoria (DSM-5), is ready to proceed with hormone therapy and is competent to make such decisions
- As often the initial prescribing physician, I reconfirm that information

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen

Very high risk of adverse outcomes:

- Thromboembolic disease

Moderate risk of adverse outcomes:

- Macroprolactinoma
- Breast cancer
- Coronary artery disease
- Cerebrovascular disease
- Cholelithiasis
- Hypertriglyceridemia

Transgender male: testosterone

Very high risk of adverse outcomes:

- Erythrocytosis (hematocrit > 50%)

Moderate risk of adverse outcomes:

- Severe liver dysfunction (transaminases > threefold upper limit of normal)
- Coronary artery disease
- Cerebrovascular disease
- Hypertension
- Breast or uterine cancer

Hembree WC et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. JCEM Nov 2017, 102 (11): 3869-3903

General history

- Ask patient preferred pronoun and name
- Full history with emphasis on the potential relative or absolute contra-indications of therapy
- Social history:
  - smoking/drug/alcohol use
  - Relationships/supports
  - Drug plan
- What is patient doing thus far?
  - Physical appearance changes – eg hair removal, breast binding etc.
  - Current medications

Being Respectful

- Discuss with your patients when, where and how you might need to touch
- Do you really need the patient to undress? How much?
- Breast, genital, rectal exams: Do you really need to do these exams at this visit?

Patient Expectations

- Has the patient already researched options for therapy/know other transgender individiduals?
- Is the patient aware of the limitations of hormone therapy?
- Does the patient desire surgical interventions in future?
- Does the patient want to preserve fertility?

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
Facial/body hair growth	6–12 mo	4–5 y
Scalp hair loss	6–12 mo	—[a]
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	—[b]
Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
Deepening of voice	6–12 mo	1–2 y

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

[a] Prevention and treatment as recommended for biological men.

[b] Menorrhagia requires diagnosis and treatment by a gynecologist.

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Medication	Dose instructions
Testosterone	
Testosterone cypionate 100mg/mL (injectable, suspended in cottonseed oil) **Testosterone enanthate 200mg/mL** (injectable, suspended in sesame oil)	Starting dose: 25 mg IM or SC q weekly Usual maintenance dose: 50-100 mg weekly If local skin reaction occurs, switch oils Weekly dosing is preferred to minimize peak/trough variation Biweekly injection (of 2x the weekly dose) may be tolerated in some individuals
Androderm® (patch)	Starting dose: 2.5 mg patch/24 h Usual maintenance dose: 5-10 mg/ 24h apply
Androgel® 1% (gel) 12.5 mg/pump or 25mg/2.5 mL sachet	Starting dose: 2 pumps daily Usual maintenance dose: 4-8 pumps daily (50-100 mg testosterone)
Compounded testosterone (cream) 12.5 or 25 mg/0.2 mL Not covered but cheaper than other transdermal forms	Starting dose: 25 mg daily Usual maintenance dose: 50-100 mg daily
Progestins: May be used for contraception or to assist with monthly bleeding (menses)	
Medroxyprogesterone IM (Depo-Provera®)	150 mg IM q 12 weeks
Progesterone releasing IUD Higher dose progesterone preferred for suppression of monthly bleeding (menses)	Inserted by MD or NP. Devices effective for 3-5 years

From: Trans Care BC: Gender-affirming care for trans, two spirit and gender diverse patients in B.C.: a primary care toolkit. October 2018

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:[a]
   a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
   c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

[a] Adapted from Lapauw *et al.* (154) and Ott *et al.* (159).

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NOTE: Testosterone 400-700 ng/dL = 13.9 to 24.3 nmol/L

Medication	Dose
Androgen Blockers	
Spironolactone First line due to lower cost, effectiveness and tolerability May not significantly lower T levels alone	Starting dose: 50 mg po daily Usual maintenance dose: 200-300 mg daily Can be divided bid
Cyproterone Eligible for special authority if spironolactone is contraindicated, not tolerated or ineffective	Starting dose: 25 mg po daily Usual maintenance dose: 25 – 100 mg daily
Finasteride An anti-androgen with peripheral action only Eligible for Special Authority if needed to augment effect of primary anti-androgen	2.5 mg po every other day
Estrogen	
17-beta estradiol (Estrace®) Lowest risk of all estrogens and first choice	Starting dose 1-2 mg po daily Usual maintenance dose 4-8 mg daily Can be divided bid
Estradiol patch (Estradot®/Estraderm®) Eligible for Special Authority for clients >40 years old with additional risk factors	Starting dose 50 mcg patch twice per week. Usual maintenance dose 100-200 mcg twice weekly
Estradiol valerate (injectable) Only available compounded	Starting dose 10 mg IM/SC q 2 weeks Usual maintenance dose 10-20 mg IM/SC q 2 weeks

From: Trans Care BC: Gender-affirming care for trans, two spirit and gender diverse patients in B.C.: a primary care toolkit. October 2018

Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 mo	2–3 y
Decreased testicular volume	3–6 mo	2–3 y
Decreased sperm production	Unknown	≥3 y
Decreased terminal hair growth	6–12 mo	≥3 y[a]
Scalp hair	Variable	—[b]
Voice changes	None	—[c]

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157).

[a] Complete removal of male sexual hair requires electrolysis or laser treatment or both.

[b] Familial scalp hair loss may occur if estrogens are stopped.

[c] Treatment by speech pathologists for voice training is most effective.

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Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
   a. Serum testosterone levels should be <50 ng/dL.
   b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

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Note: Testosterone 50ng/dL = 1.74 nmol/L
Estradiol 100-200 pg/mL = 367-734 pmol/L;
Normal range for follicular phase estradiol (TMH lab): 77 to 922 pmol/L

Key Points

- Very few absolute contraindications to hormone therapy for transition
  - Eg: active thromboembolic disease or coronary artery disease
- Need to address both expectations AND limitations of therapy
- Therapies can result in permanent infertility so MUST discuss prior to initiation of therapy

Further Key Points

- Testosterone therapy for transgender males very similar to hypogonadal cis-gender males
- Transgender females with testes intact need higher doses of estrogen in addition to an anti-androgen
- Other preventative health screenings depend on risk factors and anatomy

References/Resources

1. Hembree WC et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. JCEM Nov 2017, 102 (11): 3869-3903

2. Canadian Professional Association for Transgender Health (CPATH): www.cpath.ca
3. World Professional Association for Transgender Health (WPATH): www.wpath.org
4. Trans Care BC: www.phsa.ca/transcarebc