Transgender Issues

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Disclosures

- None

- 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:
  - Identify the benefits and limitations of gender-affirming hormone therapy
  - Discuss the potential adverse effects/risks of gender-affirming hormone therapy
  - Be aware of the various hormone therapies available and the off-label nature of all hormone therapies for transgender/gender-diverse patients
  - Develop a monitoring plan for transgender/gender-diverse patients on gender-affirming hormone therapy

Stats Canada 2021 Census data

Asked those aged 15 or older if they identified as transgender or non-binary

Only national reporting on this worldwide thus far

Overall, 0.33% (or just under 101,000 people) identified as trans or non-binary

- 0.79% Gen Z (born 1997-2006)
- 0.51% Millennials (born 1981-2006)
- 0.19% Gen X (born 1966-1980)
- 0.15% baby boomers (born 1946 to 1965)
- 0.12% born in 1945 or earlier

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

Patient Expectations

- Has the patient already researched options for therapy/know other transgender individuals?
- 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?

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

Baseline Examination

- Be respectful
- Do you really need the patient to undress? If so, how much?
- Breast, genital, rectal exams not required for hormone therapy so only recommend considering these with patient discussion if there is a specific indication
- Typically, get height, weight, blood pressure, pulse and cardiovascular examination as a baseline unless there is another concern

Masculinizing therapy

EFFECTS AND TIME COURSE OF TESTOSTERONE

Physical Effects	Reversibility	Onset[a]	Expected maximal effect[a]
Skin oiliness/acne	Reversible	1-6 months	1-2 years
Body fat redistribution	Reversible/ Variable	1-6 months	2-5 years
Increased muscle mass/strength[b]	Reversible	6-12 months	2-5 years
Facial/body hair growth	Irreversible	3-6 months	4-5 years
Scalp hair loss	Irreversible	6-12 months[c]	Variable
Cessation of menses	Reversible	1-6 months	n/a
Clitoral enlargement	Irreversible	3-6 months	1-2 years
Vaginal Atrophy	Reversible	1-6 months	1-2 years
Deepened voice	Irreversible	6-12 months	1-2 years
Infertility	Variable	Variable	Variable

from:
https://www.rainbowhealthontario.ca/TransHealthGuide/pdf/QRG_full_rev2021.pdf

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/24h Usual maintenance dose: 5-10 mg/24h
Androgel® 1% (gel) 12.5 mg/pump or 25mg/2.5g or 50 mg/5g packet	Starting dose: 2 pumps or 1 x 2.5 g packet (25 mg daily) Usual maintenance dose: 4-8 pumps or 1-2 x 5 g packet (50-100 mg daily)
Natesto® (nasal gel) 4.5 w/w	Starting dose: 1 pump daily (1 nostril only) Usual maintenance dose: 2-4 pumps daily (1-2/nostril)
Progestins: May be used for contraception or to assist with suppression of 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. Accessed online Aug 23 2021

Table 2. Risks associated with gender affirming hormone therapy (bolded items are clinically significant) (Updated from SOC-7)

RISK LEVEL	Estrogen-based regimens	Testosterone-based regimens
Likely increased risk	**Venous Thromboembolism** **Infertility** Hyperkalemia[s] Hypertrigyceridemia Weight Gain	**Polycythemia** **Infertility** Acne Androgenic Alopecia Hypertension Sleep Apnea Weight Gain Decreased HDL Cholesterol and increased LDL Cholesterol
Likely increased risk with presence of additional risk factors	Cardiovascular Disease Cerebrovascular Disease Meningioma[c] Polyuria/Dehydration[s] Cholelithiasis	Cardiovascular Disease Hypertriglyceridemia
Possible increased risk	Hypertension Erectile Dysfunction	
Possible increased risk with presence of additional risk factors	Type 2 Diabetes Low Bone Mass/ Osteoporosis Hyperprolactinemia	Type 2 Diabetes Cardiovascular Disease
No increased risk or inconclusive	Breast and Prostate Cancer	Low Bone Mass/ Osteoporosis Breast, Cervical, Ovarian, Uterine Cancer

[c]cyproterone-based regimen
[s]spironolactone-based regimen

From: Coleman E et al. Standards of care for the health of transgender and gender diverse people version 8. (2022). International Journal of Transgender Health. 23(S1)

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).

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

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

FEMINIZING THERAPIES

Effects and expected time course of feminizing hormone therapy

Physical Effects	Reversibility	Onset[a]	Expected maximal effect[a]
Softening of skin/ decreased oiliness	Reversible	3-6 months	Unknown
Body fat redistribution	Reversible/ Variable	3-6 months	2-3 years
Decreased muscle mass/strength[b]	Reversible	3-6 months	1-2 years
Thinned/slowed growth of body/facial hair[c]	Reversible	6-12 months	>3 years
Scalp hair loss (loss stops, no regrowth)	Reversible	1-3 months	Variable
Breast growth	Irreversible	3-6 months	1-2 years
Decreased testicular volume	Variable	3-6 months	2-3 years
Decreased libido	Variable	1-3 months	3-6 months
Decreased spontaneous erections	Variable	1-3 months	3-6 months
Decreased sperm production	Variable	Variable	Variable
Reduced erectile function	Variable	Variable	Variable

From:
https://www.rainbowhealthontario.ca/TransHealthGuide/pdf/QRG_full_rev2021.pdf

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

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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.

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

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 the same as for hypogonadal cis-gender males
- Transgender females with testes intact need higher doses of estrogen in addition to an anti-androgen

Monitoring Plan Key Points

- Typically assessments every 3 months for the first year, then once or twice yearly thereafter once on stable therapy
- Assess for impact of masculinizing or feminizing effects of therapy
- Particular focus on risk factors for severe adverse effects
  - Especially venous thromboembolism and cardiovascular disease
  - Address any other risk factors to reduce these risks
- Other general health screenings should be based on the patient's age, risk factors and body parts

Resources/References

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. Coleman, E., Radix, A. E., Bouman, W.P., Brown, G.R., de Vries, A. L. C., Deutsch, M. B., Ettner, R., Fraser, L., Goodman, M., Green, J., Hancock, A. B., Johnson, T. W., Karasic, D. H., Knudson, G. A., Leibowitz, S. F., Meyer-Bahlburg, H. F.L., Monstrey, S. J., Motmans, J., Nahata, L., … Arcelus, J. (2022). Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *International Journal of Transgender Health*, *23*(S1), S1-S260.https://doi.org/10.1080/26895269.2022.2100644
5. Trans Care BC: www.phsa.ca/transcarebc
6. RainbowHealth Ontario: www.rainbowhealthontario.ca
7. Rainbow Health Ontario: guidelines for gender affirming primary care for trans and non-binary patients: a quick reference guide: www.rainbowhealthontario.ca/transhealthguide/pdf/QRG_full_rev2021.pdf
8. Trans Care Moncton: http://transcaremoncton.craigchisholm.me/