CARING FOR TRANSGENDER AND NON-BINARY PATIENTS

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McGill Annual Refresher Course for Family Physicians

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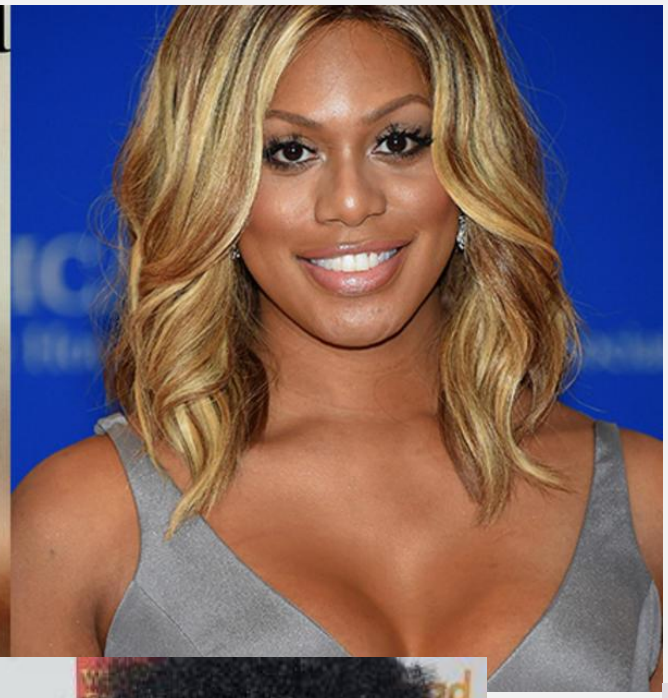
DISCLOSURES

I have no disclosures


"Call me Caitlyn"
By BUZZ BISSINGER Photos by ANNIE LEIBOVITZ




Ketel One
VODKA


STOP
ALTON
GAS

OUTLINE

- Introduction and terminology
- Responsibilities of hormone prescribing physicians
- Feminizing hormone therapy
  - Indications, contraindications and monitoring
- Masculinizing hormone therapy
  - Indications, contraindications and monitoring
- Case discussions

GUIDELINES

- Endocrine Society – 2017
- WPATH – World professional association for transgender health
  - SOC8 released Sept 2022
- Sherbourne Health – Rainbow Health Ontario - 2019

INDIVIDUALIZED APPROACH

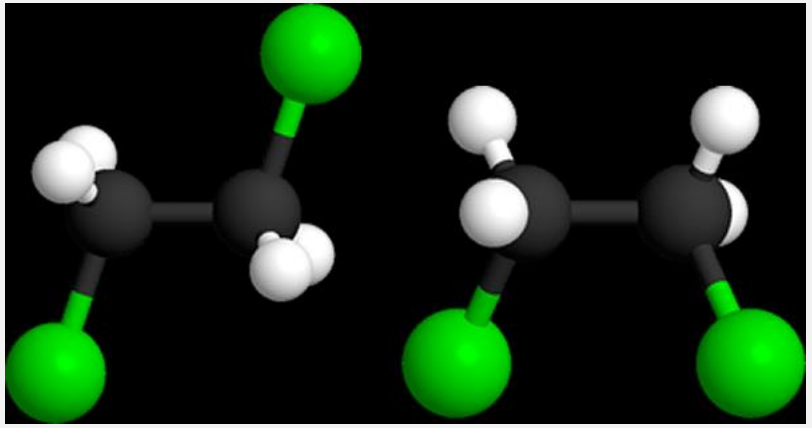
- Guidelines provide standards of care that are flexible.
- Aid physicians in providing optimal health care to transgender and non-binary patients.
- Take into account each patient's unique anatomic, social and psychological situation.
- What helps one person affirm their gender might be very different from what helps another person.
  - Some patients need hormonal therapy and surgery, some need one or the other, others need neither.

TERMINOLOGY

- Gender identity: ones internal, deeply held sense of gender
  - This is not visible to others
- Gender expression: ones external manifestation of gender
  - Eg. Clothing, haircut, pronouns
- Gender non-conformity: extent to which a person's gender identity, role, or expression differs from the cultural norms for people of a particular sex.
- Gender dysphoria: discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth.

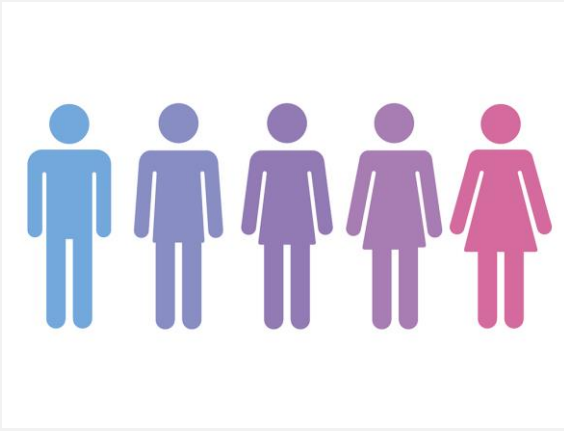
TERMINOLOGY

- Cis: gender identity is aligned with gender assigned at birth.
- Trans: gender identity is not aligned with gender assigned at birth.
- Male-to-Female (MTF) = Transwomen
- Female-to-Male (FTM) = Transman
- Non-binary: an umbrella term for anyone who does not identify with static, binary gender identities.



TERMINOLOGY

- Transgender and gender diverse (TGD)
- Gender-affirming hormone treatment (GAHT) = Not HRT
- Gender-affirming medical and/or surgical treatments (GAMSTs)
- Transition = the process during which a transgender person changes their physical, social and/or legal characteristics



SOC8 UPDATE

- Move away from a narrow focus on:
  - Psychological requirements for "diagnosing transgenderism"
  - Medical treatments for alleviation of "gender dysphoria"
- Goal is to provide gender-affirming care for the whole person.

DECISION TO INITIATE HORMONE THERAPY

- No longer require a "diagnosis of gender dysphoria"
- The experience of gender incongruence should marked and sustained.
- Physician deciding to initiate GAMST should be able to:
  - Identify and exclude other possible causes of apparent gender incongruence prior to the initiation of gender-affirming treatments.
  - Ensure that any mental health conditions that could negatively impact the outcome of gender-affirming medical treatments are assessed and cared for.
  - Assess the capacity to consent.
  - Consider the role of social transition together with the individual.

RESPONSIBILITIES OF HORMONE PRESCRIBING PHYSICIANS

1. Initial evaluation: discussion of a patient's physical transition goals, health history, physical examination, risk assessment, and relevant laboratory tests.
2. Discuss expected effects and the possible adverse health effects of feminizing/masculinizing medications.
3. Discuss reproductive options.
4. Confirm that patients have the capacity to understand the risks and benefits of treatment and are capable of making an informed decision about medical care.

RESPONSIBILITIES OF HORMONE PRESCRIBING PHYSICIANS

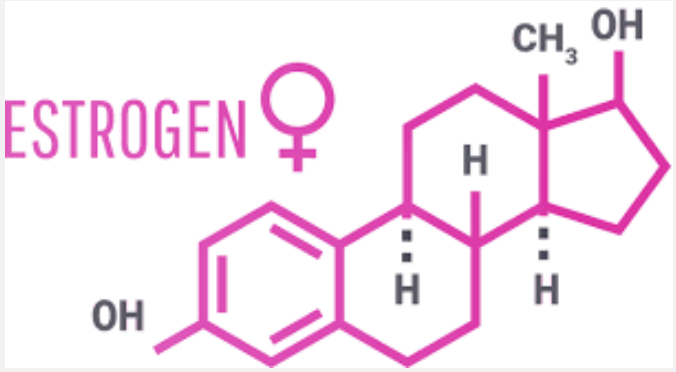
6. Provide ongoing medical monitoring, including regular physical and laboratory examination to monitor hormone effectiveness and side effects.

7. Communicate as needed with a patient's primary care provider, mental health professional, and surgeon.

8. If needed, provide patients with a brief written statement indicating that they are under medical supervision and care that includes feminizing/masculinizing hormone therapy.

FEMINIZING HORMONE THERAPY

- Goal of therapy -> Patient dependent
- Reduce the endogenous effects of Testosterone
- Induce feminine secondary sex characteristics
  - Addition of Estrogen
- Results in reversible and irreversible feminization



ANTI-ANDROGENS

- **Spironolactone:** mineralocorticoid and androgen receptor antagonist
  - Competes with DHT for binding to androgen receptor
  - Inhibits enzymes involved in androgen synthesis
- **Cyproterone:** anti-androgenic, anti-gonadotropic, and progestin-like activity
  - Decreases LH secretion -> decreased Testosterone production
- Finasteride: 5-alpha reductase 2 inhibitor -> **not recommended**
  - Prevents Testosterone conversion to DHT
  - Possible beneficial effects on scalp hair loss, body hair growth, sebaceous glands, and skin consistency.
- Flutamide: nonsteroidal androgen receptor antagonist -> not recommended

ESTROGENS

- Several routes of administration are available
- Most commonly used is oral 17-β estradiol (®Estrace)
- Lack of consensus on preferred timing of estrogen with respect to anti-androgen
  - E.g. anti-androgen 1-3 months prior to estrogen or simultaneous
- In patients > 50 years old on estrogen for several years, dose reduce to similar doses to those used by post-menopausal ciswomen

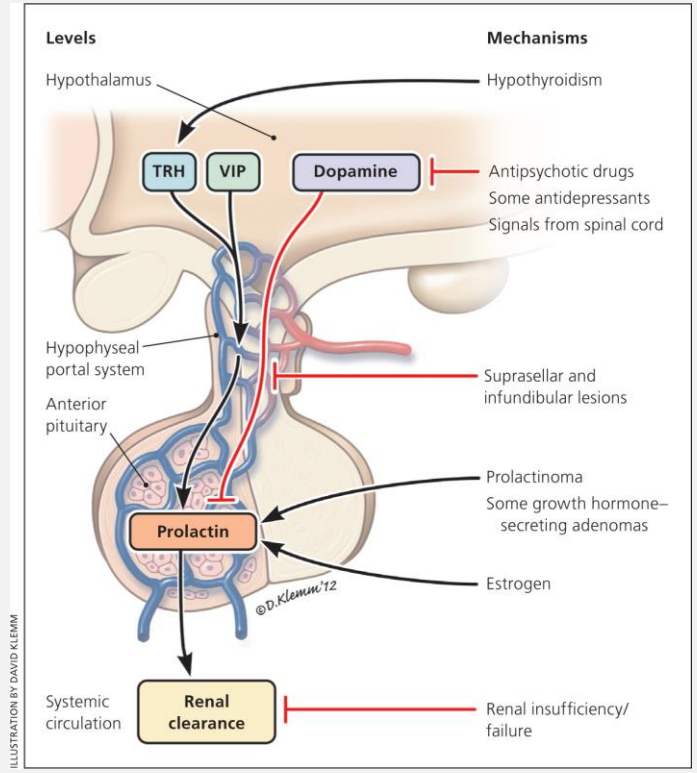
CONTRAINDICATIONS – FEMINIZING HORMONES

- Unstable ischemic cardiovascular disease
- Estrogen-dependent malignancy
- End stage chronic liver disease
- Psychiatric illness that limits informed consent
- Hypersensitivity to one of the components of the formulation

- Safety = transdermal estrogen is less thrombogenic and hepatotoxic
  - Preferred choice for patients over age 40 years with risk factors for CV, thromboembolic or liver disease

PROLACTIN

- Estrogen therapy can increase the growth of lactotroph cells.
- Several case reports of prolactinomas occurring after long-term, high dose Estrogen therapy.
- Cyproterone acetate has also been shown to increase prolactin levels.

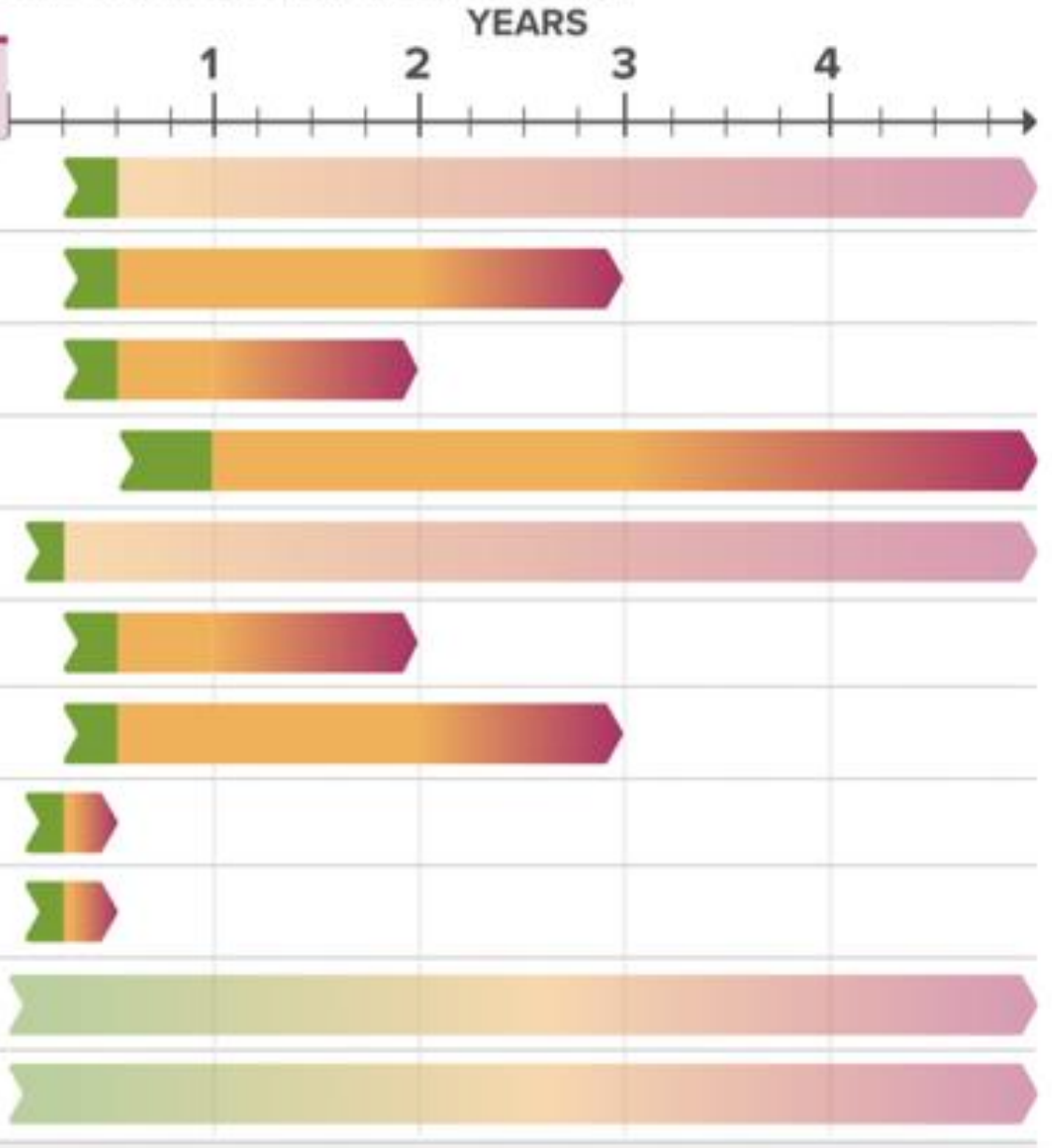


Formulations	Starting Dose	Usual Dose	Maximum Dose	Cost* (4 weeks)
Spironolactone (oral)	50 mg daily - BID	100 mg BID	150 mg bid[a]	$15–$41
Cyproterone (oral)	12.5 mg (1/4 50 mg tab) q2d - daily	12.5 mg (1/4 50 mg tab) – 25 mg (1/2 50 mg tab) daily	50 mg daily[a]	$16–$56
Estradiol (oral)*	1–2mg daily	4mg daily or 2mg bid	6 mg daily or 3 mg BID	$18–$54
Estradiol (transdermal, patch)*[b]	50 mcg daily/apply patch 2x/ week	Variable[c]	200 mcg daily/ apply patch 2x/ week	$39–$76[d]
Estradiol (transdermal, gel)*[e]	2.5 g daily (2 pumps, contains 150 mcg estradiol)	Variable[c]	6.25 g OD (5 pumps, contains 375 mcg estradiol), may be limited by surface area requirements for gel application	$58–$154
Estradiol valerate** Injectable (IM)[f]	3–4 mg q weekly or 6–8 mg q 2 weeks	Variable[c]	10mg q weekly	$36–$46

EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES

The degree and rate of physical effects are largely dependent on patient-specific factors such as age, genetics, body habitus and lifestyle, and to some extent the dose and route used (selected in accordance with a patient's specific goals and risk profile).[8]

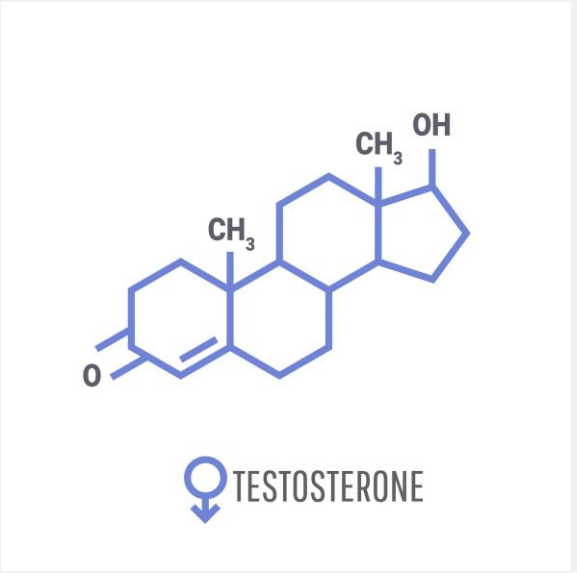
Physical Effects	Reversibility	Onset[a]	Expected maximal effect[a]
Softening of skin/ decreased oiliness	Reversible	3-6 months	Unknown
Body fat redistribution	Reversible/ Variable	3-6 months	2-3 years
Decreased muscle mass/strength[b]	Reversible	3-6 months	1-2 years
Thinned/slowed growth of body/facial 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



	Baseline	Month 3	Month 6	Month 12[e]	Yearly	According to guidelines for cis patients, or provider discretion
Exam/ Investigations	Focused Physical Exam. Include: height, weight, BP, +/- breast inspection/ measurement(s)*	BP, weight, +/- breast inspection/ measurement(s) at 12 months*			See Preventive care checklist for transfeminine patients and Accompanying Explanations in the full Guidelines.	
BLOODWORK						
CBC[a]	✓	✓	✓	✓	✓	
ALT[b]	✓	✓	✓	✓	✓	✓
Creatinine/Lytes[c]	✓	✓	✓	✓	✓	
HbA1c or Fasting Glucose	✓			✓		✓
Lipid profile	✓			✓		✓
Total Testosterone	✓	✓	✓	✓	✓	
Estradiol	✓	✓	✓	✓	✓	
Prolactin[d]	✓			✓	✓	✓
Other	Hep B and C					
	Consider: HIV, syphilis, and other STI screening as indicated, frequency depending on risk					

MASCULINIZING HORMONE THERAPY

- Cornerstone of therapy = Testosterone
  - Transdermal or injectable
- Goal of therapy = masculine secondary sex characteristics
- Reversible and irreversible masculinization



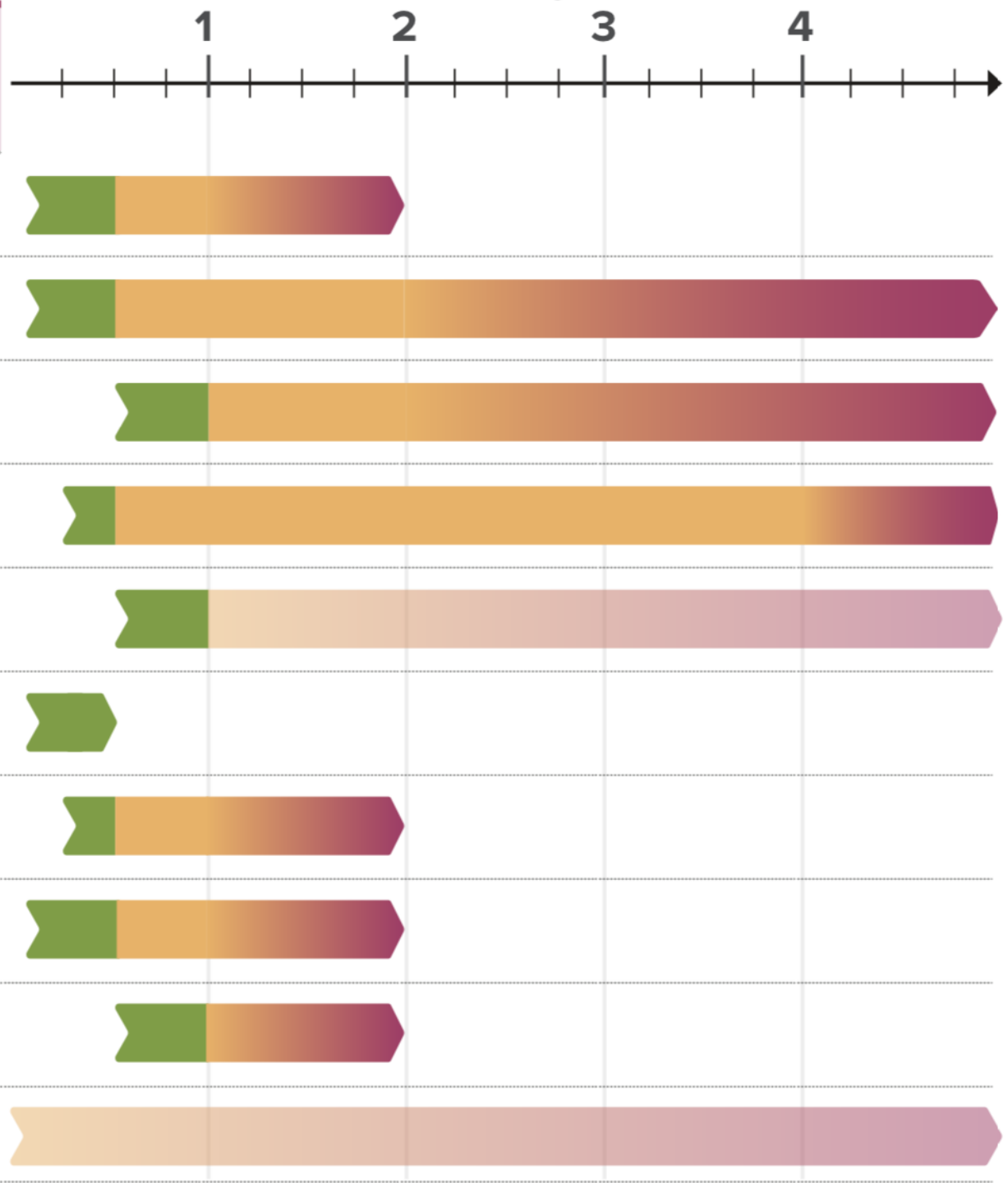
CESSATION OF MENSES

- Very distressing event for many transgender males
- Menses usually cease within a few months of starting Testosterone
- If uterine bleeding continues can consider progestational agent or endometrial ablation
- Can consider Progesterone or GnRH agonist prior to Testosterone therapy

CONTRAINDICATIONS – MASCULINIZING HORMONES

- Pregnancy or breast feeding
- Active known sex-hormone-sensitive cancer (e.g., breast, endometrial)
- Unstable ischemic cardiovascular disease
- Poorly controlled psychosis or acute homicidality
- Psychiatric conditions which limit the ability to provide informed consent
- Hypersensitivity to one of the components of the formulation

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



	Baseline	Month 3	Month 6	Month 12[b,c]	Yearly	According to guidelines for cis patients, or provider discretion
Exam/ Investigations	Focused Physical Exam with PAP if indicated. Include: height, weight, BP.	BP, weight			See ***Preventive Care Checklist for Transmasculine Patients*** and accompanying explanations in the ***Guidelines for Gender-Affirming Primary Care with Trans and Non-Binary Patients***.	
BLOODWORK						
CBC	✓	✓	✓	✓	✓	
ALT	✓		✓[c]			✓
HbA1c or Fasting Glucose	✓		✓[c]			✓
Lipid profile	✓		✓[c]			✓
Total Testosterone	✓	✓	✓	✓	✓	
LH[a]	✓			✓	✓	

Formulations	Starting Dose	Maximum Dose	Cost per unit*	Approx. Cost* (4 weeks)
Testosterone enanthate (IM/SC)[a]	20–50 mg q weekly or 40–100 mg q 2 weeks	100 mg q weekly or 200 mg q 2 weeks	$73.50 per 5mL vial (each vial contains 200 mg/mL x 5 mL = 1000 mg)	$14–$29 (covered by ODB with EAP request)
Testosterone cypionate (IM/SC)[a]			$64 per 10 mL vial (each vial contains 100 mg/mL x 10 mL = 1000 mg)	$13–$26 (covered by ODB with EAP request)
Testosterone path (transdermal)[b]	2.5–5 mg daily	5–10 mg daily	$164 / 60 x 2.5 mg patches $169 / 30 x 5 mg patches	$76.50–$315
Testosterone Gel 1% (transdermal)	2.5–5 g daily (2–4 pumps, equivalent to 25–50 mg testosterone)	5–10 g daily (4–8 pumps, equivalent to 50–100 mg testosterone)	$67 / 30 x 2.5 g sachets $110 / 30 x 5g sachets $175 / 2 pump bottles[c]	Sachets: $62–$205 Bottles: $81–$327

ENDOMETRIAL HEALTH

- Aromatization of Testosterone to Estrogen has been suggested as a risk factor for endometrial hyperplasia and carcinoma
  - No cases have been reported
- When transgender males undergo hysterectomy, the uterus is small and atrophied

TABLE 2: RISKS ASSOCIATED WITH HORMONE THERAPY. BOLDED ITEMS ARE CLINICALLY SIGNIFICANT

Risk Level	Feminizing hormones	Masculinizing hormones
Likely increased risk	Venous thromboembolic disease[A] Gallstones Elevated liver enzymes Weight gain **Hypertriglyceridemia**	Polycythemia Weight gain Acne Androgenic alopecia (balding) Sleep apnea
Likely increased risk with presence of additional risk factors[B]	Cardiovascular disease	
Possible increased risk	**Hypertension** Hyperprolactinemia or prolactinom[A]	Elevated liver enzymes **Hyperlipidemia**
Possible increased risk with presence of additional risk factors[B]	**Type 2 diabetes**[A]	**Destabilization of certain psychiatric disorders**[C] **Cardiovascular disease** **Hypertension** **Type 2 diabetes**
No increased risk or inconclusive	**Breast cancer**	Loss of bone density **Breast cancer** **Cervical cancer** **Ovarian cancer** **Uterine cancer**

DL - TRANSFEMALE

ID: 22 y/o transfemale

Preferred name: Annie

Preferred pronouns: She/her

PMHx:

- Asthma
- Depression, followed at student health

FMHx: Father - DLP

- No thrombosis, breast malignancy, DM2

Rx: None

All: None

Habits: negative x 3

Social: University undergraduate student living with both parents and one sibling.

DL - HISTORY

Gender story:

- Gender dysphoria since childhood, more prominent since age 16 years.
- Decided to start GAHT 1 year prior to consultation.

Social Support:

- Mother and friends informed of intent to start GAHT. Father and siblings are not.
- Anticipates resistance from father.
- Additional support from online trans support groups.

DL - HISTORY

Mental health:

- Ongoing mental health support.
- Previous thoughts of self-harm, never of suicide.

Reproductive goals:

- Possibly interested in genetic child in the future.

Transition goal:

- Desires legal name and gender change as well as GAHT.
- Uncertain if desires gender affirming surgery.

DL

P/E:

Dressed as male

Wt. 255.2 lbs, Ht. 6ft 1, BMI 33.6

BP: 124/85, P85

Thyroid: normal

CVS: normal HS, no mm

Baseline labs: Electrolytes/Creatinine N, Total Testosterone 13.1 nmol/L, Estradiol 289 pmol/L, Prolactin 13.1mcg/L, LH 5.9 IU/L, ALT 19 U/L, TG 0.92 mmol/L, LDL 1.8 mmol/L

DL

Impression: 22 Transfemale experiencing gender dysphoria and interested in starting GAHT without contraindication and with capacity to consent for treatment.

Plan:

- Letter from mental health professional
- Consult reproductive center
- Discussed reversible and irreversible effects of GAHT
- Discussed possible risks of GAHT
- Patient to follow-up when ready to start GAHT

DL – FOLLOW UP – 1 MONTH

- Letter from psychologist received that stable to start GAHT.
- Still confident that she wants to start GAHT.
- Still has not disclosure gender identity to father with whom she lives.
- Uncertain about fertility preservation. Cost is a barrier.

Plan:

- Reviewed temporary and permanent effects of GAHT
- Reviewed potential risk of treatment
- Estrace® 1mg DIE, Androcur® 25mg DIE
- Follow-up 3 months

DL – FOLLOW UP – 3 MONTHS

- Feels great
- Softer skin and hair
- More emotional (saw this as positive)
- Less energetic
- Early breast development and tenderness

Labs:

TestT 13.1 -> 2.42 nmol/L

Estradiol 289 -> 298 pmol/L

Metabolic profile unchanged

Plan:

- Increase Estrace® 2mg DIE
- Continue Androcur® 25mg DIE

DL – FOLLOW UP

- 6 month visit: no Estradiol level measured, patient not satisfied with breast development.
  - Estrace® increased to 3mg DIE
- 9 month visit: Estradiol level 751 pmol/L, TestT 1.89 nmol/L
  - Estrace® 3mg DIE continued
- Three years after initial consultation, patient not satisfied with breast development despite Estradiol levels ~ 1000 pmol/L
  - Estrace® increased to 4mg DIE

DL – FOLLOW UP

3 months after Estrace® increased:

- Patient noticed very minimally increase in breast growth
- Increased breast sensitivity
- New galactorrhea

Labs: FSH < 0.1 IU/L, LH < 0.1 IU/L, Estradiol – cancelled, Prolactin 13.1 -> 298 mcg/L

Plan: D/C Androcur® and transition to Spironolactone 50mg BID

Continue Estrace®

- Repeat pituitary profile 3 months

TRANSFEMALE TAKE HOME MESSAGE

- Try to avoid supraphysiological hormone doses.
  - Even if patient unsatisfied with breast development.
- Androcur® dose should ideally be limited to 10mg DIE to avoid risk of meningiomas.
- Monitor Prolactin during transfeminine GAHT.

AH - TRANSMALE

ID: 18 y.o. transmale

RC: GAHT

Preferred name: David

Preferred pronouns: he/him

PMHx: none

FMHx: adopted/unknown

Rx: none

All: NKDA

Habits: negative x 3

Social: Cegep student, lives with two parents and two siblings

AH - HISTORY

- Gender story:
  - Gender dysphoria onset at puberty, persistent and progressive since that time.
  - Presenting in male role and using chosen male name for two years.
- Social support:
  - Parents, siblings and friends all aware and supportive of transition.
- Mental Health:
  - Consulted a psychologist prior to presenting for GAHT who agreed with starting GAHT without mental health concerns.

AH – HISTORY

- Reproductive goals:
  - No desire for fertility preservation.
  - Very grateful to his adopted family and may desire adoption in the future.
- Transition goals:
  - Very excited about this visit.
  - Has read a lot about Testosterone therapy and is well versed in reversible and irreversible clinical effects as well as side effects.
  - Desires facial hair growth as well as increased muscle bulk.
  - Eventually desires gender affirming surgery (top + bottom).

AH

P/E: dressed as male

Wt: 61Kg, Ht: 151cm

BP 117/83

CVS: normal HS, no murmurs

Labs:

Bhcg negative

Total Testosterone 0.9 nmol/L, LH 1.7 IU/L

CBC normal, TSH 1.42

AH – IMPRESSION + PLAN

Impression: 18 Transmale presented for GAHT without medical or psychological contraindication. No desire for fertility preservation.

Plan:

- Complete baseline evaluation including LFTs, Lipids and A1C
- Delatestryl® 25mg sc q 2 weeks Rx to start after baseline labs complete
- Follow-up in 3 months

FOLLOW UP – 3 MONTHS

- Overall doing very well
- Legally changed name
- Clitoromegaly
- Acne
- Mild increased muscle bulk and weight gain 5Kg
- No facial hair growth
- Continued regular menses, very bothersome
- Energy unchanged
- Mild mood lability, attributed to pandemic

FOLLOW UP – 3 MONTHS

Labs:

Total Testosterone: 0.9 nmol/L -> 3.2 nmol/L

Hgb 143 -> 153

LFTS/Lipids/lytes/Creat normal

Plan:

- Increased Delatestryl® to weekly
- Provera® 5mg PO DIE for menses cessation

FOLLOW UP - 6 MONTHS

- Doing very well
- Increased libido
- Facial hair growth
- Mild voice deepening
- Mild fatigue day before injection
- Complete menstrual suppression
- Planned for mastectomy

P/E:

- Weight 61 -> 60.2Kg
- BP 100/70
- Mild facial hair growth

Labs:

Total Testosterone: 0.9 -> 3.2 -> 9.2 nmol/L

Hgb 157, hct 0.47

FOLLOW-UP 6 MONTH

- 19 Transmale on GAHT x 9 months, very satisfied with hormonal transition, mild hematocrit elevation.
- Continue Delatestryl® idem.
- D/C Provera®. Patient to inform me if menses resume.
- Follow-up 6 months.

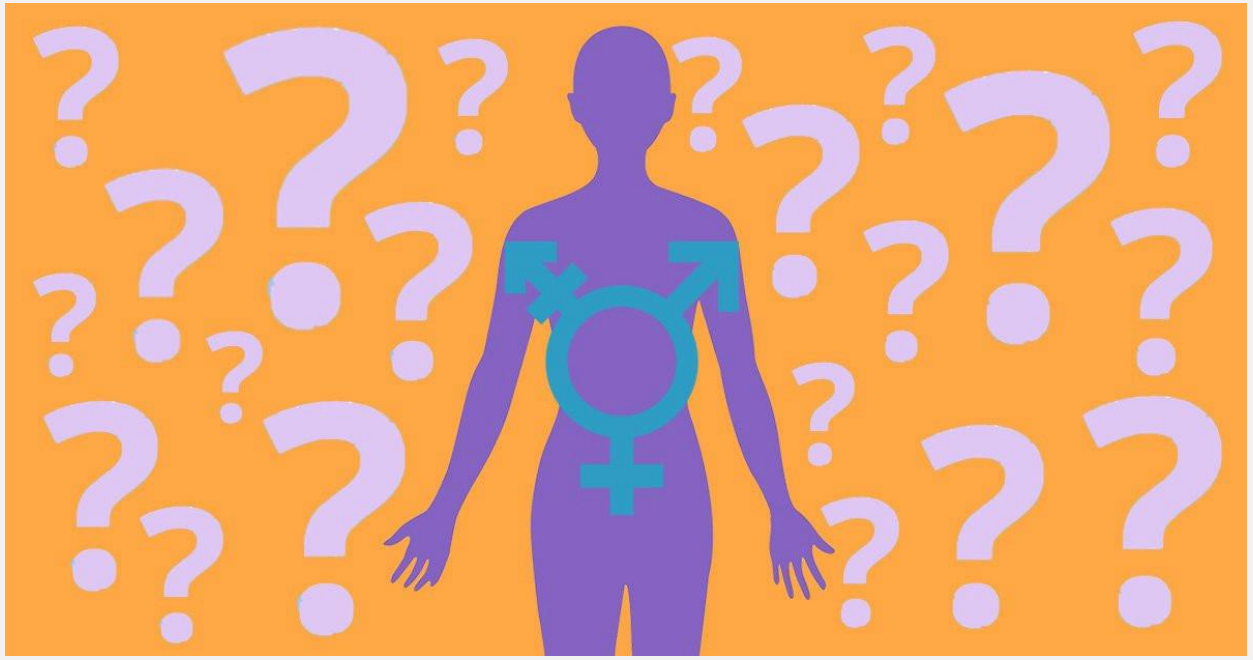
TRANSMALE TAKE HOME MESSAGE

- Try to avoid supraphysiological hormone doses
- Injection Testosterone can be given IM or SC
  - Shorter intervals between injections -> increased stability of levels
- Discuss menses cessation

SUMMARY

- Gender dysphoria is NOT required in order to start GAHT.
- Patients should be counselled on treatment options available as well as reversible and irreversible effects and possible side effects of GAHT.
- Reproductive plans should be discussed PRIOR to initiating GAHT.
- GAHT is a relatively simple and low risk treatment that can significantly improve the quality of life of TGD people.

QUESTIONS



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