Medical Needs of Trans Youth: Cross Hormones

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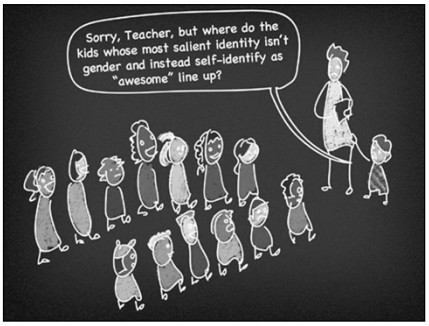
Disclaimers

- Neither estrogen nor testosterone products have US FDA or Health Canada indications for use in trans individuals
- Hormones, phenotypic sex and puberty are generally binary—please excuse the use of binary language



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The overarching treatment goal

- *… to assist transsexual, transgender, and gender-nonconforming people with safe and effective pathways to achieving lasting personal comfort with their gendered selves, in order to maximize their overall health, psychological well-being, and self-fulfillment*

WPATH *Standards of Care*, 7th version, 2011

Why treat kids under age 18?

- studies show better post-operative function is related to the "ability to pass"
- physical outcomes much better if patient treated before breast development, beard growth, deepening of the voice, etc.
- prevent developmental problems related to increasing discrepancy between body and mind
- patients are suffering!

Withholding treatment

- Refusing timely medical interventions for adolescents might prolong gender dysphoria and contribute to an appearance that could provoke abuse and stigmatization.
- As the level of gender-related abuse is strongly associated with the degree of psychiatric distress during adolescence, withholding puberty suppression and subsequent feminizing or masculinizing hormone therapy is not a neutral option for adolescents.

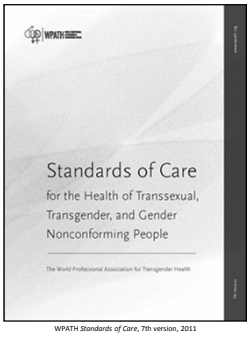
WPATH *Standards of Care*, 7th version, 2011

How are kids different than adults?

- still growing
- still accruing bone-mineral content
- still going through the physical changes of puberty
- still going through the psychological and developmental changes/tasks of adolescence
- their gender identity may not be as consolidated
- they have to deal with the school system

Our approach to treating youth

- different from treating adults
- more of an attempt to mirror natural puberty
- therefore, end results appear more gradually
- use available guidelines and published experience
  - WPATH, Netherlands, Endocrine Society
- still lots to learn about timing, dosing, long-term effects—good and bad



WPATH *Standards of Care*, 7th version, 2011

Endocrine Society CPG: *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons*, 2017

Therapy for transgender youth

- fully reversible interventions:
  - social transition
  - puberty blockers
  - androgen blockers
  - menstrual suppression
- partially reversible interventions:
  - masculinizing or feminizing hormones
- irreversible interventions:
  - gender-affirming surgery
- done in coordination w/ mental health providers

WPATH *Standards of Care*, 7th version, 2011

Informed consent

- Hormone treatment should be provided only to those who are legally able to provide informed consent.
- This includes persons who have been declared by a court to be emancipated minors and incarcerated persons who are considered competent to participate in their medical decisions.
- Informed consent implies that the patient understands that hormone administration limits fertility.

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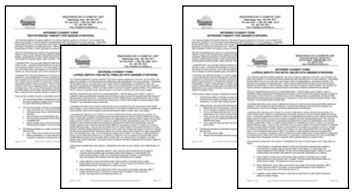
Informed consent

- know your local laws (BC Infants Act)



- harm-reduction model

based on: Vancouver Coastal Health, Transgender Health Program, 2006

Who should provide hormones?

- transgender hormone therapy is best undertaken in the context of a complete approach to health care that includes comprehensive primary care and a coordinated approach to psychosocial issues.
- endocrinologists, adolescent medicine, primary care providers, nurse practitioners
- cooperation with mental health professionals
- good communication among all

WPATH *Standards of Care*, 7th version, 2011

Responsibilities of hormone provider

- initial history, goals, physical, risk assessment, labs
- discuss expected effects of feminizing/masculinizing medications and the possible side-effects and health risks, as well as reproductive options
- confirm that patient has the capacity to understand the risks and benefits of treatment and is capable of giving informed consent
- provide ongoing medical monitoring
- communicate as needed with the patient's primary care provider, mental health provider and surgeon
- provide patients with a "carry letter"

WPATH *Standards of Care*, 7th version, 2011

Fully reversible interventions

- social transition: clothing, names, pronouns, legal
- puberty blockers:
  - GnRH agonists
- androgen blockers:
  - spironolactone
- menstrual suppression:
  - continuous or extended-cycle OCP
  - progesterone-only OCP
  - depot medroxyprogesterone
  - IUD

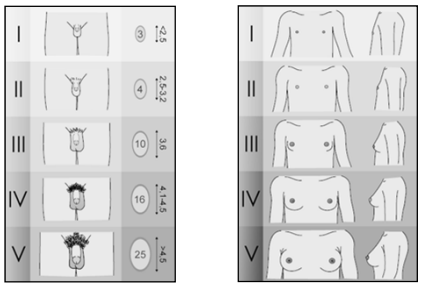
Partially reversible interventions

- masculinizing hormones for trans boys:
  - testosterone
- feminizing hormones for trans girls:
  - estrogen
  - progestins?
- long-term effects not completely known
- ideally, both done with patient/parental informed consent

Normal puberty

- girls:
  - breast development starts at 10 (8–12)
  - growth spurt peak at 11½ (9½–12½)
  - first period at 12½ (10½–14½)
- boys:
  - testicular enlargement starts at 11 (9–13)
  - growth spurt peak at 13½ (11½–15½)
- considerable variability

Tanner staging



Sex-hormone therapy: eligibility 1

- Adolescents are eligible for sex hormone treatment if:
- A qualified MHP has confirmed:
  - the persistence of gender dysphoria,
  - any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
  - the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of, weigh the benefits and risks of, and give informed consent to this (partly) irreversible treatment,

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Sex-hormone therapy: eligibility 2

- And the adolescent:
  - has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
  - has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

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Sex-hormone therapy: eligibility 3

- And a pediatric endocrinologist or other clinician experienced in pubertal induction:
  - agrees with the indication for sex hormone treatment,
  - has confirmed that there are no medical contraindications to sex hormone treatment.

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Sex-hormone therapy: age

- *"We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment."*

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Sex-hormone therapy: my general approach

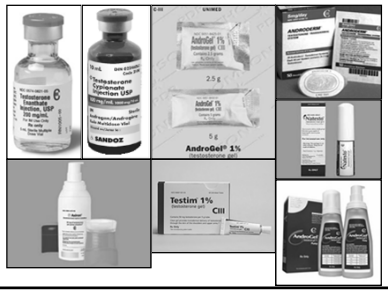
- generally start with ~25% of adult dose, increasing by 25% every 6 months
- make sure patient is tolerating dosage before increase
- check blood levels when nearing adult dosages

Endocrine Society CPG: *Endocrine Treatment of Transsexual Persons*, 2009

Virilizing therapy: testosterone route and cost

- route:
  - shot: testosterone enanthate (Delatestryl®) or cypionate (Depo-Testosterone®) q1–2 weeks
  - shot: testosterone undecanoate (Aveed®) q12 weeks (not in Canada)
  - patch: Androderm® daily
  - gel: Androgel®, Testim®, Axiron® (axillary), Natesto® (nasal)
  - oral: Andriol® BID–TID
- cost:
  - shots: $32/month (Aveed® ~$400/month)
  - patch: $125/month
  - gel: $125/month

Virilizing therapy: formulations



Virilizing therapy: puberty induction

- testosterone enanthate or cypionate IM/SQ:
  - 25 mg/m^2 q2 or 12.5 mg/m^2 q1 week × 6 months
  - 50 mg/m^2 q2 or 25 mg/m^2 q1 week × 6 months
  - 75 mg/m^2 q2 or 37.5 mg/m^2 q1 week × 6 months
  - 100 mg/m^2 q2 or 50 mg/m^2 q1 week × 6 months
  - titrate to adult dose with labs
- can go faster in older youth

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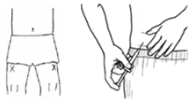
Virilizing therapy: adult doses

- shot (enanthate or cypionate): 50–100 mg q1 week or 100–200 mg q2 weeks: intramuscular or subcutaneous



- patch: 2.5–7.5 mg daily
- gel: 5–10 g daily
- oral (undecanoate): 160–240 mg daily divided BID–TID
- Aveed®: 1000 mg q12 weeks IM

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Virilizing therapy: what I do

- I get informed consent from patient.
- I discuss reproductive options.
- I use Delatestryl® (testosterone enanthate).
- I increase dosage q6 months over 2 years:
  - start: 20 mg IM/SQ q1 week (or 40 mg q2 weeks IM) × 6 months
  - then: 40 mg IM/SQ q1 week (or 80 mg q2 weeks IM) × 6 months
  - then: 60 mg IM/SQ q1 week (or 120 mg q2 weeks IM) × 6 months
  - then: 80 mg IM/SQ q1 week (or 160 mg q2 weeks IM) × 6 months
  - then: titrate to adult dose with labs
- can go faster in older youth

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Virilizing therapy: benefits

- permanent:
  - growth of pubic, axillary, body hair and beard
  - increased height (if epiphyses are not fused)
  - accretion of bone-mineral content
  - deepening of voice, Adam's apple
  - enlargement of the clitoris
- not permanent:
  - increased muscle mass, male fat distribution
  - increased libido
  - cessation of periods

Virilizing therapy: what it doesn't do

- shrink breast tissue completely
- make the clitoris grow to the size of a penis ("rule of thumb")
- make the uterus or ovaries regress
- change bony structures

Virilizing therapy: side-effects

- permanent:
  - male-pattern balding
- not permanent:
  - acne
  - vaginal dryness
  - behavior changes

Virilizing therapy: monitoring youth

- every 3–6 months:
  - anthropometry: height, weight, sitting height, blood pressure, Tanner stages
- every 6–12 months:
  - testosterone level
  - midway between injections or >2 h after patch/gel
  - hemoglobin/hematocrit, lipids, testosterone, 25-OH-vitamin D
- every 1–2 years:
  - BMD using DXA until 25–30 or peak mass attained
  - bone age on X-ray of the left hand (if clinically indicated)

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Virilizing therapy: what I do

- I get informed consent from patient.
- I discuss reproductive options.
- I use Delatestryl® (testosterone enanthate).
- I increase dosage q6 months over 2 years:
  - start: 20 mg IM/SQ q1 week (or 40 mg q2 weeks IM) × 6 months
  - then: 40 mg IM/SQ q1 week (or 80 mg q2 weeks IM) × 6 months
  - then: 60 mg IM/SQ q1 week (or 120 mg q2 weeks IM) × 6 months
  - then: 80 mg IM/SQ q1 week (or 160 mg q2 weeks IM) × 6 months
  - then: titrate to adult dose with labs
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Virilizing therapy: monitoring adults

- every 3 months:
  - testosterone, until physiologic
  - midway between injections or >2 h after patch/gel
  - maintain physiologic level
- every 3 months × 1 year, then every 6–12 months:
  - hemoglobin/hematocrit
- "regular intervals": weight, blood pressure, lipids
- cervix, breast: as per usual
- BMD if high-risk or if not taking or compliant with hormones

Endocrine Society CPG: *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons*, 2017

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Feminizing therapy: estrogen route and cost

- route:
  - pill: (Estrace®, Premarin®, others) daily
  - patch: (Estraderm®, Estradot®, Oesclim®) 2×/week
  - gel: (Estrogel®, Divigel®) daily
  - US: shot: (Delestrogen®) q2 weeks
- cost:
  - pills: $20–40/month
  - patch: $25–50/month
  - gel: $40–80/month
  - shot: can be compounded, expensive!

Feminizing therapy: formulations

Feminizing therapy: puberty induction

- oral micronized 17β-estradiol PO/SL daily:
  - 5 µg/kg/d × 6 months
  - 10 µg/kg/d × 6 months
  - 15 µg/kg/d × 6 months
  - 20 µg/kg/d × 6 months
  - then: titrate to adult dose with labs
- transdermal 17β-estradiol patch q3.5 days:
  - 6.25–12.5 µg/d × 6 months (¼–½ of a 25-µg patch)
  - 25 µg/d × 6 months
  - 37.5 µg/d × 6 months
  - then: titrate to adult dose with labs
- can go faster in older youth

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Feminizing therapy: adult doses

- supraphysiologic doses often required to suppress testosterone
- oral micronized 17β-estradiol:
  - 2–6 mg PO/SL daily
- 17β-estradiol transdermal patch:
  - 25–200 µg/day, replaced 2×/week
- estradiol cypionate or valerate injectable:
  - 2–10 mg IM q1 week or 5–30 mg q2 weeks

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Feminizing therapy: what I do

- I get informed consent from patient.
- I discuss reproductive options.
- I use Estrace® or generic (micronized 17β-estradiol).
- I increase dosage q6 months over 2 years:
  - start: 0.5 mg PO/SL daily × 6 months
  - then: 1 mg PO/SL daily × 6 months
  - then: 1.5 mg PO/SL daily × 6 months
  - then: 2 mg PO/SL daily × 6 months
  - then: titrate to adult dose with labs
- can go faster in older youth

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Feminizing therapy: benefits

- permanent:
  - breast development (may take a few years)
  - accretion of bone-mineral content
- not permanent:
  - softer skin
  - decreased muscle mass
  - female fat distribution
  - less body hair (not complete)
  - slower balding

Feminizing therapy: what it doesn't do

- raise the voice pitch
- shrink the Adam's apple
- shrink the penis
- cause regression of the beard
- change bony structures

Feminizing therapy: side-effects

- permanent:
  - decreased adult height
- not permanent:
  - nausea
  - decreased libido
  - decreased erections
  - impaired fertility
  - testicular shrinkage
  - behavior, emotional changes

Anti-androgens

- block T synthesis, action, conversion to DHT
  - spironolactone (Aldactone®, generic)
  - cyproterone (Androcur®)
  - flutamide (Euflex®)
  - finasteride (Propecia®, Proscar®)
  - dutasteride (Avodart®)
- used to block the effect of androgens on the hair follicles
- used if not taking GnRH analog
- each has its own benefits and side-effects

Progestins

- possibly beneficial for breast/nipple growth, mood, libido
- very little published, Endocrine Society does not commit to recommending
- weak androgen-receptor stimulation, depression, weight gain, and lipid changes
- can give PMS, feeling of "cycling"
- formulations (oral):
  - Prometrium® (micronized progesterone, ? safer)
  - Provera® (medroxyprogesterone)

Spironolactone

- fully reversible
- dose: 100 mg PO BID
- cost: $15/month
- "side-effect": gynecomastia!
- can cause hyperkalemia:
  - check electrolytes and creatinine
- patients must be counselled about discontinuing with fasting or vomiting


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Reproductive health 1

- We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults.

Endocrine Society CPG: *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons*, 2017

Reproductive health 2

- many trans people want to have children
- many trans (and cis) teens have no clear plan
- hormones and surgery obviously interrupt fertility, often permanently
- need to have discussion about semen preservation in trans girls before starting spironolactone and/or estrogen
- need to think about ovarian/oocyte/embryo cryopreservation in trans boys before starting testosterone

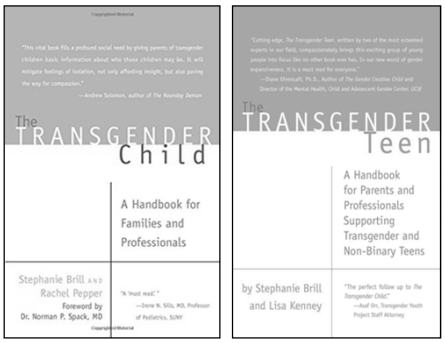
WPATH *Standards of Care*, 7th version, 2011

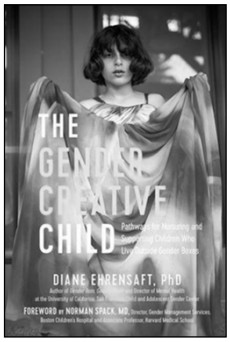
Resources

- Trans Care BC: transcarebc.ca
- BC Children's Hospital Gender Clinic: endodiab.bcchildrens.ca
- Canadian Professional Association for Transgender Health: cpath.ca
- US Professional Association for Transgender Health: uspath.org
- Endocrine Society: endocrine.org
- World Professional Association for Transgender Health: wpath.org

EDU Website

http://endodiab.bcchildrens.ca





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