21st Century Strategies: Transgender Hormone Care

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DISCLOSURES

No conflicts of interest

Just about the entire talk is "off-label"

LEARNING OBJECTIVES

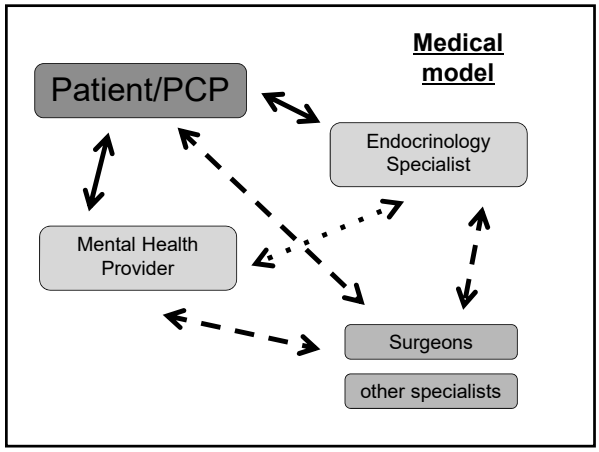
1. Articulate the change in landscape for transgender medical care
2. Outline transgender hormone strategies
3. Consider transgender hormone monitoring strategies

Endocrine Society Clinical Practice Guideline New Pediatric/Adolescent Recommendations:

- Recognition that there may be <u>compelling reasons</u> to start cross-sex hormones prior to age 16 years in some GD/Gender Incongruent adolescents
  - —Potential risks to bone health with prolonged hypogonadism
  - —Potential risks to mental health if pubertal development is markedly out of sync with peers
- Pubertal induction
- Lab surveillance

Endocrine Society Clinical Practice Guideline New Adult Recommendations:

- <u>Enhanced communication</u> by replacing older language.
- <u>Removal of the obligation</u> that the transgender diagnosis be made by a <u>mental health provider</u> in favor of:
  - The suggestion that the diagnosis be made by a knowledgeable clinician and
  - A statement of the expertise required among treating clinicians independent of specific specialty (i.e. knowledge of transgender-specific diagnostic criteria, mental health concerns, hormone prescribing, and primary care).
- <u>Recognition</u> that for non-binary persons tailoring of current protocols may be done within the context of accepted safety guidelines, using a multidisciplinary approach including mental health.
- <u>Explicit suggestion</u> that fertility preservation options need to be discussed in a timely fashion.
- <u>Updated gender affirming hormone regimens</u>, based upon recently published treatment protocols.



Presentation of Transgender Individuals

… **presentation in adulthood is common and late adolescence more the norm** than the exception.

Articulation? Awareness? Not known.

Fertility is addressed in an ad hoc fashion.

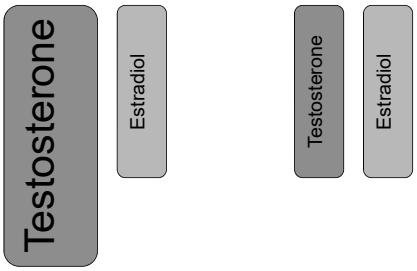
Strategy:

Strategy:

The Boston Globe

December 11, 2011

Male hormones **Female hormones**



Chan KJ, et al, 2018 Endocrine Practice

Current Approach to Therapy

Adolescents: GnRH agonists at Tanner 2

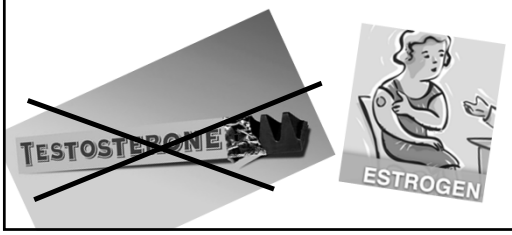
…… and discussion of transgender hormone Rx at earlier ages ….

Current Approach to Therapy

Adult Transmen: androgen supplementation – can be lifelong.

Current Approach to Therapy

Adult Transwomen: blockade to some degree of androgen production or action along with some degree of estrogen supplementation – thrombosis concerns.



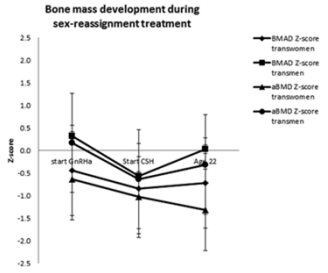
Case 1:

- 11 year old recorded male at birth
- "I *am* a girl" for many years
- Socially transitioned since kindergarten
- Supportive parents
- Female gender identity confirmed

Case 1:

- Exam
  - Testes: Tanner 2-3 → (Tanner 2)
  - What would you do?

Case 1: Conundrum: Bone Density and Early Pubertal Youth



Current Treatment Model Bone Mineral Density: 6 yr Follow-Up

- Potential study limitations:
  - Relatively small "N" (34: 15 MTF, 19 FTM)
  - ? Relatively low hormone dosage during Rx
  - No data on other factors influencing bone mass
    - —Dietary calcium intake
    - —Vitamin D levels
    - —Weight-bearing exercise

Klink D et al. JCEM, 2015

Case 2:

- 55 year old with male external anatomy
- Lived as a man until 1 year ago… But recent publicity has helped her recognize her life-long incongruence
- Denied hormone therapy: it is "too dangerous"
- Quadriplegic due to MVA
- DVT during hospitalization; Rx'd w/ warfarin

Case 2:

- Would you prescribe estrogen to this patient?
- What would be your reasoning?

Case 2:

- A mainstay of transgender hormone treatment is estrogen for which there is a clear thrombosis risk for ethinyl estradiol and a likely risk for less thrombogenic 17 beta estradiol
- There has been at least one proposal for treatment with parallel prophylaxis when needed.

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

Endocrine Treatment of Gender Dysphoric/Gender Incongruent Persons: Endocrine Society Practice Guidelines 2017.

Case 2:

- Asscheman et al. (2014) 1% incidence of VTE among 1076 transwomen (5.4 years)
- Gooren et al. (2008), no increase in VTE among 2236 transgender women on estradiol from 1975 to 2000 (Ethinyl estradiol = 6–8% incidence)
- Wierckx et al. (2013) 5% of 214 MTF individuals developed VTE within the first three years of estrogen therapy *BUT* 10 out of 11 of these women had at least one VTE risk factor (smoking, immobilization/ surgery, or thrombophilia)

Treatment safety

Low DVT incidence with oral estradiol

1 recorded event

among 676 trans women

averaging 2 years of Rx with oral estradiol

Arnold et al 2016 (JSM)

Case 3:

- 65 year old transgender man
- Has been living as a man for years on a stable testosterone therapy regimen (200 mg IM q 2 weeks).
- Recent pruritus and feeling flushed
- Hct 56%

Case 3:

- What treatment related condition has he experienced?
- What changes do you recommend?

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Case 3:

- Testosterone stimulates erythropoiesis.
- Androgen stimulated hct usually w/i normal range but polycythemia may be unmasked.
- Tobacco, sleep apnea should be addressed
- Hematological evaluation may be required

Case 3:

- It is acceptable to mitigate high hematocrit with lower dose testosterone as long as levels are sufficient to maintain good bone health and to prevent menses.

Case 4:

- 38 year old transgender man
- Has been living as a man for years on a stable testosterone therapy regimen for 18 years.
- He and his non-trans female partner of 1 year want to know their fertility options.

Fertility in Transgender Men

- 54% desired children
- 38.5% would have considered oocyte/embryo cryopreservation
- Costs
  - Donor sperm $500-1,000/vial
  - Sperm cryopreservation $1,000-1,500 (with FDA testing)
  - IVF $15,000/cycle
  - Gestational carrier $50,000+

Wierckx, K. Human Reproduction, 2012.

Discussion

What are this couple's options for fertility?

- **Donor sperm**
- **Controlled ovarian hyperstimulation (IVF) with gestational carrier**
- **Long term androgen does not appear to deplete primordial follicle pool**
- **Extremely limited data on fertility preservation**

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	total	male	female
Type of surgery			
Chest or top surgery (n = 25)	25% (25)	50% (14)	17% (12)
Breast augmentation	40% (10)	0% (0)	91% (10)
Breast reduction	8% (2)	7% (1)	9% (1)
Mastectomy	48% (12)	86% (12)	0% (0)
Unspecified type	8% (2)	7% (1)	9% (1)
Genital or bottom surgery (n = 13)	13% (13)	14% (4)	13% (9)
Orchiectomy	33% (5)	0% (0)	56% (5)
Vaginoplasty	13% (2)	0% (0)	22% (2)
Penectomy	7% (1)	0% (0)	11% (1)
Unspecified type	20% (3)	25% (1)	22% (2)
Penile implant	7% (1)	25% (1)	0% (0)
TAH SBO	13% (2)	50% (2)	0% (0)
Facial surgery	8% (8)	0% (0)	11% (8)
Age at first procedure, years			

Prevalence and types of gender affirming surgery Endocrine Practice 2017.

Case 4:

- **One case series of 41 trans men s/p hysterectomy reported that endometrial tissue to be atrophic.**
- **There are no other published data.**
- **There are no published data demonstrating increased female repro tract CA risk in transgender men (4.7).**

Case 5

- 48 year old transgender woman with intermittent hormone use for the past four years presents for refills of medication
- Prescribed estradiol valerate 20 mg IM qo week, estradiol 2 mg PO daily
- Would like to maintain erectile function
- How would you manage this patient?

Health concerns – long term?

The <u>only pitfalls known</u>…

are HYPOGONADISM (<u>osteoporosis</u> and perhaps metabolic concerns) and

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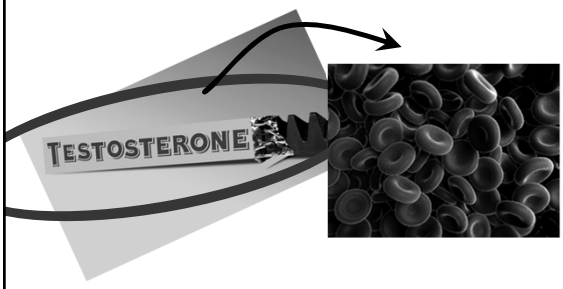

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