Primary Care and Hormonal Treatments for Transgender Patients

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- Residents
- Medical, NP, PA students
Overview

- Definitions (brief)
- Treatment overview
- Is this safe and what bad things can happen?
- The hard parts
Definitions

- **Sex** — male, female, intersex, transsexual

- **Gender** — masculine, feminine, androgynous

* Non Binary
Definitions

- Gender Identity
- Gender Expression
Definitions

- Transgender
- Transsexual
- Cisgender/Cisssexual
The Two Commandments
The Two Commandments
Primary Care and Hormone Therapy

- You already know 90% of what you need to know (or will by the end of training!)
- 100% of the medical treatments and most of the surgeries are used in cisgender patients
- Like any patient with rare disease
  - 1:30,000 FTM, 1:10,000 MTF
But now I have a patient in my office!

- Ask for help
  - Experienced clinicians
  - TransMedicine yahoo group
  - Your patient
- Buy a book
- Go to a conference
  - WPATH
  - GLMA, TransHealth
  - Others
- Consult Dr Google
- SFDPH's Tom Waddell Clinic Protocols
The Transgender Health Program was launched by Vancouver Coastal Health in June 2003 to bring together transgender people and loved ones, health care providers, health planners, and researchers to work on improving transgender health services in BC. We welcome anyone who has a transgender health question or concern. Our services are free, anonymous, and confidential.
Clinical Protocol Guidelines

- Care of the patient undergoing sex reassignment surgery (SRS) - 686K
  Cameron Bowman & Joshua Goldberg
- Caring for transgender adolescents in BC: Suggested guidelines - 877K
  ○ Clinical management of gender dysphoria in adolescents
    Annelou L.C. de Vries, Peggy T. Cohen-Kettenis, & Henriette Delemarre-Van de Waal
  ○ Ethical, legal, and psychosocial issues in care of transgender adolescents
    Catherine White Holman & Joshua Goldberg
- Counselling and mental health care of transgender adults and loved ones - 1030K
  Walter Bockting, Gail Knudson, & Joshua Goldberg
- Endocrine therapy for transgender adults in BC: Suggested guidelines - 1030K
  ○ Physical aspects of transgender endocrine therapy
    Marshall Dahl, Jamie L. Feldman, Joshua Goldberg, & Afshin Jaberi
  ○ Assessment of hormone eligibility and readiness
    Walter Bockting, Gail Knudson, & Joshua Goldberg
- Social and medical advocacy with transgender people and loved ones: Recommendations for BC clinicians - 975K
  Catherine White Holman & Joshua Goldberg
- Transgender primary medical care: Suggested guidelines for clinicians in BC - 1470K
  Jamie L. Feldman & Joshua Goldberg
- Transgender Speech Feminization/Masculinization: Suggested Guidelines for BC Clinicians - 844K
  Shelagh Davies, M.Sc., S-L.P.(C) & Joshua Goldberg
How does this all work?

- Not one size fits all!
- But we can talk about a typical narrative in enfranchised patients with access to care who 'follow the WPATH Standards of Care.'

www.wpath.org
Typical Narrative ('following SOC')

- Accept your own trans identity and seek help
  - Internet, local groups, organizations
- Find a therapist and receive a dx (and letter)
  - 3 month 'Real Life Experience' OR
  - Psychotherapy (duration TBD, usually 3+months)
- Find a physician/NP/PA
  - Start hormone therapy
  - Non-genital surgery (same time as HRT)
- 1 year successful – genital surgery
Typical Narrative (following SOC)

- Does everyone do it this way?
- If they don't should you still treat them?
Harm Reduction

- WPATH-SOC explicitly endorses harm reduction
Medical Treatments: Fundamentals

- Set realistic goals
  - What will, might, and won't happen
- Emphasize primary and preventative care
- Use the simplest hormonal program that will achieve goals
  - Every option doesn't work for every patient
  - Cost, ease of use, safety
Medical Treatments: Fundamentals

- Patience is a virtue
  - Puberty comparison
  - Take a long term outlook – safety and efficacy
- Side effects are in the eye of the beholder
  - Baldness
Medical Treatments: Fundamentals

- Hormone treatments are one of the easiest parts
- FTM – Testosterone up to normal male dose
  - Dose that masculinizes and stops menses is enough
- MTF – More difficult because must suppress testosterone production to get best results
  - Anti-androgen(s) – Spironolactone most common in US
  - Estrogens
Medical Treatments: MTF

- **Estrogens at high dose**
  - 3-5x normal female replacement doses
  - Partially to feminize
  - Partially to better suppress testosterone

- **Anti-Androgen**
  - Spironolactone and others
  - Orchiectomy

- **Results variable**
  - Age at starting is important
  - Genetics plays a big part
The Special Case of Transgender Girls
Hormones: MTF - Estrogens

- **Oral - $**
  - $$$ Premarin 1.25 – 10mg/d (usual 5mg)
  - $ Estradiol 1-5mg/d (usual 2-4mg)
  - $$ Ethinyl Estradiol (OCPs) – drug interactions (PIs, P-450, etc)

- **IM – Delestrogen $$**
  - 10-40mg q2weeks (usual 20)
  - Can't easily 'stop' in an emergency when patient immobilized
  - Strohecker's Compounding Pharmacy - www.stroheckersrx.com

- **Transdermal – Estradiol patch $$$**
  - 0.1-0.3mg/day (1-3 patches/week – overlapped)
  - Probably the safest for transwomen predisposed to thrombo-embolic and CV dz (age>40, smoking, FH, etc.)
Hormones: MTF - Estrogens

- **Estrogens - “Mixing E formulations”**
  - Some patients love this - ?psychological effect?
  - Need to keep track of total dose
  - $2 + 2 \neq 8$

- **Tendency for some to increase dose**
Hormones: MTF - Estrogens

- **Beneficial effects**
  - Breast growth
  - Suppress androgen production
  - Change of body habitus (muscle and fat)
  - Softening of skin

- **Contraindications/Precautions**
  - Same as in cisgender women
  - Individual risk/benefits (MTF get greater benefits r/t mental health than menopausal cisgender women.)
  - In transwomen with absolute CI – at least suppress testosterone fully
Hormones: Estrogens Adverse Effects

- **THROMBOEMBOLIC DISEASE**
- Hepatotoxicity (especially ORAL) – incr TA, adenomas
- Prolactinoma (if dose is too high)
- Decreased glucose tolerance
- Lipid profile
- Gallbladder Disease
- Worsening migraine/seizure control
- Breast Cancer
- Mood
- Decreased libido
Hormones: MTF - Anti-Androgens

- **Antiandrogens - All**
  - Decrease T production or activity
  - Slow/stop MPB, and decrease unwanted hair growth
  - Decrease erections/libido
  - Improve BPH

- **Spironolactone 50-300 mg/d divided bid**
  - Cheap, reasonably safe
  - Hyper-K+, diuresis, changes in BP, 'just don't like it'
  - Decreased H/H (T → erythropoietin)

- **Cyproterone**
Hormones: MTF - Anti-Androgens

- 5-α-reductase inhibitors
  - Finasteride, dutasteride, saw palmetto
- Finasteride (Proscar/Propecia)
  - Stops conversion of T → DHT
  - 5mg tabs = $35 for 30 at Costco
  - 1mg tabs = $65 for 30 at Costco
Androgenic Alopecia

Androgenic Alopecia

T

5-α-reductase

DHT

aromatase

E

not very active stuff

Finasteride
Hormones: MTF - Progestins

- Usually requested for breast growth based on anecdotal evidence of efficacy
- Decrease total estrogen dose if using progestins
- No medical need to cycle – emotional needs?
Hormones: MTF - Surgery?

- Stop E two weeks before any immobilizing event (incl SRS) resume a week after ambulating regularly
- Can increase anti-androgen (or add another) during this time
Hormones: MTF - Monitoring

- **Every Visit**
  - BP, Weight, BMI
  - Safety
  - Mental health
  - General screening based on age, organ, gender, and sex appropriate norms

- **Patient education**
  - S/Sx of TEDz
  - Healthy Habits
  - Vision changes or lactation
Hormones: MTF - Monitoring

- Clinical monitoring most important
- Same adverse events in cisgender pts w/ same meds (use what you know!)
- Labs
  - 0, 2, & 6 mo initially then (semi)annual or p changes
  - CBC, CMP, Lipids
  - PL and T
Hormones: MTF - Monitoring

- Pituitary Adenoma
- 1st Pass Metabolism

PL
AST/AST
Hormones: MTF – Adverse effects

- Elevated PL: Stop Estrogens (not anti-androgen)
  - If levels normalize, resume E at lower dose
  - If levels remain high MRI to r/o PL-oma
- Elevated LFTs
  - Look for other cause!
  - If due to E, lower dose or stop until LFT normal
Hormones: MTF - Efficacy

- What is adequate treatment?
  - **Pt outcomes** – breast growth (peak 2-3 yrs), changes in skin, hair, fat/muscle, libido
  - The floor – testosterone levels (female range)
  - The roof – prolactin level
    - >20 possibly too much (ask @ 'extra' E use or other meds)
      - >25 probably too much
      - >30 definitely too much
Medical Treatments: FTM

After years of intensive research, we finally have a clear picture of testosterone action.

ANDROGEN
↓
RECEPTOR
↓
THEN SOMETHING HAPPENS
↓
EFFECTS
Hormones: FTM

- **Testosterone Injected Esters (cheapest)**
  - **Cypionate**
    - 200mg/ml: 1-10ml vials
    - Cheapest - $60-100 for 10ml (~4mos supply)
  - **Enanthate**
    - Biggest vial is 5ml
    - Slightly more expensive
- **Other forms (not easily obtained in US)**
  - Intramuscular testosterone undecanoate (Nebido)
  - Higher levels from injected maybe better for earlier transition
Hormones: FTM

Therapeutic Range

200 mg
2 weeks

100 mg
week
Hormones: FTM

- Transdermal
  - Expensive: $7 day retail, $1/day compounded
  - Less variable levels
  - Daily administration
  - Risk of inadvertent transfer to others

5%, 1g QD

1%, 5g QD
Hormones: FTM - Monitoring

- Every Visit
  - BP, Weight, BMI
  - Safety
  - Mental health
  - General screening based on age, organ, gender, and sex appropriate norms

- Patient education
  - Vaginal bleeding
  - Healthy habits
  - Tx available for acne, MPB
Medical Treatments: Fundamentals

- Clinical monitoring most important
- Same adverse events in cisgender pts w/ same meds (use what you know!)
- Labs
  - 0, 2, & 6 mo initially then (semi)annual or p changes
  - CBC, CMP, Lipids
  - T (trough) in FTM
Treatment Effects (any delivery...)

- Nearly immediate
  - Increased sebum and resultant acne
  - Increased sex drive
  - Sometimes – amenorrhea
  - Metabolic changes start
  - Emotional effects of 'finally starting T'
Treatment Effects

- **1-6 months**
  - Voice change starts – parallels adolescence
  - Hair growth (and loss) begins: parallels adolescence*
  - Clitoromegaly starts
  - Most amenorrhea (but E only decreases modestly)*
  - Fat and muscle distribution changes
  - Metabolic changes


Treatment Effects

- 1-5 Years
  - Voice settles
  - Final fat and muscle redistribution
  - Clitoromegaly maxes
    - Length average 4-5cm (3-7 cm range)\(^1\)
    - Volume increases 4-8x\(^2\)
    - Greater change in younger patients\(^2\)

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Treatment Effects

- 5-10 years
  - Final hair growth
  - Androgenic alopecia can happen at any age – and does in 50% of FTMs by 13 years*

Hormones: FTM – Adverse effects

- Acne – MC side effect (chest/back)
- CV - worsening of surrogate endpoints - lipids, glucose metabolism, BP
- Polycythemia (normals for males)
- Unmask or worsen OSA
- Enhanced Libido
- Androgenic alopecia
- 'Other' hair growth
Hormonal Treatments: Is this safe?

  - DESIGN: Retrospective, descriptive study at university teaching hospital that is the national referral center for the Netherlands (serving 16 million people)
  - SUBJECTS: 816 MTF & 293 FTM on HRT for total of 10,152 pt-years
  - OUTCOMES: Mortality and morbidity incidence ratios calculated from the general Dutch population (age and gender-adjusted)
Hormonal Treatments: Is this safe?


293 FTMs c/w ♀ 10,152 pt years c/w ♂

816 MTFs c/w ♂

???
Hormonal Treatments: Is this safe?

  - MTF/FTM total mortality no higher than general popl'n
  - Largely, observed mortality not r/t hormone treatment
  - VTE was the major complication in MTFs. Fewer cases after the introduction of transdermal E in MTFs over 40
  - In MTFs increased morbidity from VTE and HIV and increased proportion of mortality due to HIV
Hormonal Treatments: Is this safe?


- 293 FTMs c/w ♀ no increase morbidity or mortality
- 816 MTFs c/w ♂ no increase mortality
- 10,152 pt years

Increase morbidity r/t HIV/VTE
Hormonal Treatments: Is this safe?


The absence of evidence is not evidence of absence.
Hormonal Treatments: Is this safe?

- Same clinic group as 1997 paper – now 2236 MTF, 876 FTM (1975-2006)
- Outcome M&M Data, data assessing risks of osteoporosis and cardiovascular disease, cases of hormone sensitive tumors and potential risks
Hormonal Treatments: Is this safe?

- Gooren L, et al. Cardiovascular Risks
  - Analyzed studies of surrogate markers for CVDz in MTF/FTM: Body composition, lipids, insulin sensitivity, vasc function, hemostasis/fibrinolysis, others (HC CRP)
  - Some worsen, some improve, some are unchanged – much of the worsening seems likely d/t weight
  - MTF do worse than FTM
  - Hard clinical endpoints show no difference*
  - Counsel patients about modifying CV risk
Hormonal Treatments: Is this safe?

- Gooren L, et al. Hormone Dependent Tumors
  - Lactotroph Adenoma
    - Rare
    - Check PL!
  - Prostate Cancer
    - Prostatectomy is not a part of SRS
    - Screen based on the organs present
    - Withdrawal of testosterone may decrease but doesn't eliminate the risk of BPH and malignancy
    - May falsely lower PSA
Hormonal Treatments: Is this safe?

- DRE is a little different
Hormonal Treatments: Is this safe?

- Gooren L, et al. Hormone Dependent Tumors
  - Breast cancer
    - MTF - Estrogen exposure: dose and duration
      - Screen c/w cisgender women of same age/risk
      - Take exposure levels/other risks into consideration
      - Progesterone use increases risk
  - FTM
    - Reported in 1 case 10 years after mastectomy
    - Mastectomy reduces but doesn't eliminate risk
    - Some testosterone is aromatized to estrogen
    - Family history
Hormonal Treatments: Is this safe?

- Gooren L, et al. Gynecologic Tumors
  - Gynecologic Tumors
    - Cervical
    - Ovarian
    - Endometrial
Gynecologic Cancer risks in FTMs

5 + ???

???
Gynecologic Cancer risks in FTM

If infrequent periods

ENDOMETRIAL CANCER
Gynecologic Cancer risks in FTMs
Gynecologic Cancer risks in FTM

Cervical Cancer Risk Reduction from Pap Smears

Gynecologic Cancer risks in FTMs
Gynecologic Cancer risks in FTM
Cervical Cancer FTM

- Same screening guidelines as cisgender women
- Consider HPV testing if very difficult paps
- Testosterone induces atrophy: tell the pathologist!
- Consider hysterectomy as alternative if greater surveillance needed in pts with extreme difficulty with paps (ex high grade SIL)
Hormonal Treatments: Is this safe?


- Conclusion: “It is clear now that sex reassignment of TSs benefits their well-being, although suicide rates remain high. Cross-sex hormone administration to TSs is acceptably safe in the short and medium term. However, potentially adverse effects in the longer term are presently unknown. The data, although limited, of surrogate markers of CVDz and the reports of cancer in transsexuals leave room for cautious optimism. But true insights can only come from close monitoring and thorough reporting of adverse effects in the literature.
What about regret ???

  - 74 f/u studies and 8 reviews published b/w 1961-1991
  - Less than 1% long term regret in over 400 FTMs
  - 1.5% regret in over 1000 MTFs
- Compare with regret rates for gastric bypass, breast recon after mastectomy, surgical sterilization
- Studies after 1991 show lower rates of regret (and found risk of regret correlates well with surgical success.)
Is it effective?

- Suicidality decreased from 20-30% pre-treatment to ~3% post treatment
- Decreased depressive symptoms, improved social functioning, regrets rare
The Hard Stuff: Advocacy

- Insurance
- Identity documents
- Lots of other issues...
Insurance: Denial of Care

- Exclusions
  - Individual and small group
  - Larger groups

- De facto exclusions - Medicaid
  - Title XIX: Medicaid agencies “may not arbitrarily deny or reduce the amount, duration, or scope of a required service under §§440.210 and 440.220 to an otherwise eligible recipient solely because of the diagnosis, type of illness, or condition” (§440.230(c))
Insurance: Denial of Care

- Medicaid Denials
  - Not medically necessary
  - Experimental
- AMA Policy Statement
Whereas, Gender Identity Disorder (GID) is a serious medical condition recognized as such in both the DSM-IV-TR and ICD-10.

Whereas, GID, if left untreated, can result in clinically significant psychological distress, dysfunction, debilitating depression and, for some people without access to appropriate medical care and treatment, suicidality and death.

Whereas, An established body of medical research demonstrates the effectiveness and medical necessity of mental health care, hormone therapy and sex reassignment surgery as forms of therapeutic treatment for many people diagnosed with GID.

RESOLVED, That the AMA support public and private health insurance coverage for treatment of gender identity disorder; and be it further

RESOLVED, That the AMA oppose categorical exclusions of coverage for treatment of gender identity disorder when prescribed by a physician.
Insurance: Health Care Reform???

- Medicaid???
- Exclusions like the Stupid Stupak Amendment?
Identity Documents

- Identity documentation change is one part of the medical treatment for GID
- Lack of appropriate ID
  - Vulnerability to interpersonal violence
  - Inability to
    - Get a job
    - Make a purchase with a credit card
    - Board a plane
    - Enter a federal building
  - Voluntary withdrawal from activities
Supportive Letters

- There are no gender cops
- It's not your job to enforce bad policy
- Your job
  - Advocate for your patients needs
  - Don't lie
  - Give your true medical opinion
  - Don't write something if you don't have experience
Supportive Letters: a thought experiment

- You are a doctor in NC in 1950. An 18 year old young man who is your patient asks you for help. He is white, but his great grandfather was African American. He was accepted to attend UNC-CH, but an anonymous letter to the school revealed his heritage. He was told he must provide a letter from a teacher, doctor, or minister verifying he is white to be allowed to enter UNC.
Supportive Letters: a thought experiment

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- You're pretty advanced for the 50's and understand race as a social construct and believe he really is white.... but know that UNC's policies and understanding of race would exclude him.
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Do you write the letter?
Supportive Letters

- There are no gender cops
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- Your job
  - Advocate for your patients' needs
  - Don't lie
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  - Don't write something if you don't have experience
Supportive Letters

- I am a physician licensed to practice medicine and surgery in the state of California.
- John Smith is a patient in my care at LMHS
- In my medical opinion Mr Smith is a transsexual man.
- I have determined that his male gender predominates and have provided him with appropriate and irreversible sex reassignment treatments.
- (In addition, he has undergone irreversible sex reassignment surgery that I have verified by my own examination.)
Supportive Letters

- As a result Mr Smith has completed all necessary medical (and surgical) procedures to fully transition from female to male.
- He should be considered male for all legal and documentation purposes – including drivers license, birth certificate, passport, and social security records.
- Indicating his gender as male is accurate and will eliminate the considerable confusion and bias Mr Smith encounters when using identification that does not reflect his current true gender.
and that concludes my presentation

any questions?

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