TRANSGENDER CARE: A CASE BASED APPROACH
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OBJECTIVES

• Review terminology

• Review hormone therapy for people over 18 using a case based approach

• Discuss common issues that arise from hormone therapy

• Discuss health maintenance
0.5% of the population in the United States identifies as a transgender person
TERMINOLOGY

- Gender identity
- Transgender
- Transsexual (also Transexual)
- Cisgender
- Gender expansive (gender nonconforming/genderqueer/gender non-binary)
- Gender expression/presentation
- Intersex

TERMINOLOGY

- **Transition** includes some or all of the personal, legal and medical adjustments: telling one's family, friends and/or co-workers; changing one's name and/or sex on legal documents; hormone therapy; and possibly one or more forms of surgery.

- **Gender affirming/confirming Surgery or Sex Reassignment Surgery (SRS)** Refers to surgical alteration, and is only one small part of transition. Not all transgender people choose to or can afford to have surgery.

- **Gender dysphoria** refers to people who experience significant discontent with the sex they were assigned at birth. DSM-V diagnosis, diagnosis used for coding and billing a medical visit.
HELPFUL CLINIC INTAKE

- Gender identity (two-step):
  - What is your gender identity?
    - ☐ Male
    - ☐ Female
    - ☐ Transgender man / Transman
    - ☐ Transgender woman / Transwoman
    - ☐ Genderqueer / Gender nonconforming
    - Additional identity (fill in) ________________
    - ☐ Decline to state

- What sex were you assigned at birth?
  - ☐ Male
  - ☐ Female
  - ☐ Decline to state

CASE 1:

- Hayden is a 21 year old trans male who is establishing care to begin gender affirming hormone therapy. He is healthy. He has a history of depression and anxiety, and these are well controlled. He wants to begin hormone therapy today.
• Important to assess mental health during office visits

• 40% of transgender individuals experience serious psychological distress due to systematic stressors

• 40% of transgender adults attempt suicide compared to 4.6% of the non-trans adults

• Using and respecting chosen name and pronouns are protective factors against suicide

FIRST STEPS

• Letter is not needed from a therapist to start hormonal therapy

• Discuss future fertility goals

• Discuss health history and perform health maintenance

• Discuss goals of transition, different for each person

• Review hormone therapy, pros/cons, risks/benefits, reversible/irreversible changes and document informed consent
### Table 1. Hormone preparations and dosing (Grading: T O M)

<table>
<thead>
<tr>
<th>Androgen</th>
<th>Initial - low dose*</th>
<th>Initial - typical</th>
<th>Maximum - typical*</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone Cypionate</td>
<td>20 mg/week IMSQ</td>
<td>50mg/week IMSQ</td>
<td>100mg/week IMSQ</td>
<td>For q 2 wk dosing, double each dose</td>
</tr>
<tr>
<td>Testosterone Enanthate</td>
<td>20mg/week IMSQ</td>
<td>50mg/week IMSQ</td>
<td>100mg/week IMSQ</td>
<td></td>
</tr>
<tr>
<td>Testosterone topical gel 1%</td>
<td>12.5-25 mg Q AM</td>
<td>50mg Q AM</td>
<td>100mg Q AM</td>
<td>May come in pump or packet form</td>
</tr>
<tr>
<td>Testosterone topical gel 1.62%</td>
<td>20.25mg Q AM</td>
<td>40.5 - 60.75mg Q AM</td>
<td>103.25mg Q AM</td>
<td></td>
</tr>
<tr>
<td>Testosterone patch</td>
<td>1-2mg Q PM</td>
<td>4mg Q PM</td>
<td>8mg Q PM</td>
<td>Patches come in 2mg and 4mg sizes. For lower doses, may cut patch</td>
</tr>
<tr>
<td>Testosterone cream</td>
<td>10mg</td>
<td>50mg</td>
<td>100mg</td>
<td></td>
</tr>
<tr>
<td>Testosterone axillary gel 2%</td>
<td>30mg Q AM</td>
<td>60mg Q AM</td>
<td>90-120mg Q AM</td>
<td>Comes in pump only, one pump = 30mg</td>
</tr>
<tr>
<td>Testosterone Undecanoate</td>
<td>N/A</td>
<td>750mg IM, repeat in 4 weeks, then q 10 weeks ongoing</td>
<td>N/A</td>
<td>Requires participation in manufacturer monitored program2</td>
</tr>
</tbody>
</table>

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### Table 1A: Effects and expected time course of masculinizing hormones

<table>
<thead>
<tr>
<th>Effect</th>
<th>Expected Onset*</th>
<th>Expected Maximum Effect*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin oiliness/acne</td>
<td>1-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Facial/body hair growth</td>
<td>3-6 months</td>
<td>3-5 years</td>
</tr>
<tr>
<td>Scalp hair loss</td>
<td>&gt;12 months*</td>
<td>variable</td>
</tr>
<tr>
<td>Increased muscle mass/strength</td>
<td>6-12 months</td>
<td>2.5 years*</td>
</tr>
<tr>
<td>Body fat redistribution</td>
<td>3-6 months</td>
<td>2.5 years</td>
</tr>
<tr>
<td>Cessation of menses</td>
<td>2-6 months</td>
<td>n/a</td>
</tr>
<tr>
<td>Clitoral enlargement</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Vaginal atrophy</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Deepened voice</td>
<td>3-12 months</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

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* Adapted with permission from Hembree et al (2009), Copyright 2009, The Endocrine Society.

* Estimates represent published and unpublished clinical observations.

* Highly dependent on age and inheritance, may be minimal.

* Significantly dependent on amount of exercise.
Testosterone, available in several forms: IM/SQ, transdermal patch or gel, or subcutaneous implant and other longer term options.

- IM/SQ usually start with testosterone 50-200mg IM every 2 weeks, can also change interval to every 7 or 10 days with dosing change as appropriate
- Depending on goals, patch or gel may be more appropriate for therapy
- Rarely, doses as high as 250mg every 2 weeks are needed, but usually only if trough levels remain in the low normal range on 200mg every 2 weeks.

MONITORING LABS

- Monitor labs at baseline, at 3, 6 and 12 months and then yearly if stable.
- CBC, CMP, lipids, total testosterone
LAB SURVEILLANCE

- Be sure to compare hemoglobin levels to age-appropriate male levels. Transgender men with testosterone levels in physiologic male ranges and amenorrheic would be expected to have H&H values in the male normal range.

- Also use male reference ranges for creatinine and alkaline phosphatase

HORMONE LEVELS

- When measuring hormone levels in patients using injected forms of testosterone, a mid-cycle level is often sufficient.

- If a patient is experiencing cyclic symptoms such as migraines, pelvic cramping, or mood swings. Peak (1-2 days post injection) and trough levels of testosterone may reveal wide fluctuations in hormone levels over the dosing cycle

- Can change route of testosterone or shorten injection interval
HORMONE LEVELS

• Clinical response can be measured objectively by the presence of amenorrhea by 6 months.

• A higher level will not result in a greater degree of virilization once in male reference range. Lab reference ranges for total testosterone levels are generally very wide (roughly 350-1100ng/dl).

• Assess physical changes and satisfaction

• A total testosterone of about 700 is ideal

ESTRAADIO L LEVEL

• Physiologic female estradiol ranges are wide and vary over the menstrual cycle-hard to interpret

• Levels not routinely done

• If done, estradiol levels should be less than 50.
POST-GONADECTOMY

• No reduction of testosterone required

• Ok to lower dose, as long as enough being used to maintain bone density

• May have reduced muscle mass, energy and libido if dose lowered

OTHER MEDS FOR TRANSMEN

• For male-pattern baldness (MPB): finasteride or minoxidil. Caution patients that finasteride will likely slow or decrease secondary hair growth, and may slow or decrease clitoromegaly.

• For patients with too significantly increased sexual interest: low dose SSRIs.
BACK TO CASE 1

- When reviewing Hayden’s goals of transition, he wanted deeper voice, more hair growth, body shape changes, more muscle tone and planned top surgery in the future.

- Ordered CBC and CMP

- Started testosterone 50 mg SQ weekly

- Follow up in 3 months

CASE 2

- Jeremy is a 29 year old trans male patient on testosterone therapy for the last 1.5 years. He has a new male partner and wants to discuss contraception options. What is available for him to use?
CONTRACEPTION

• Continue to remind patients of pregnancy possibility and discuss contraception if having intercourse with males

• Can use all forms of contraception, including OCPs, IUDs, etc

• Preferred would be depo-provera, IUDs, nexplanon

VAGINAL PAIN

• He also notes extreme discomfort with intercourse. What can be done to improve this?
CASE 2

- Likely causes: atrophic or infectious vaginitis, cervicitis, cystitis, STIs, musculoskeletal

- Treatment options: Topical estrogen, lubrication, more even testosterone transdermal regimen, pelvic floor therapy, and treatment of any identified underlying medical problems

CASE 3

Steven is a 45 year old transgender male, taking testosterone for transition for 3 years. He is planning on having a hysterectomy next year along with oophorectomy. What are some important considerations when counseling about surgery?
**BONE HEALTH**

- People taking gender affirming hormone therapy (regardless of birth-assigned sex) should begin bone density screening at age 65.

- Screening between ages 50 and 64 should be considered for those with established risk factors for osteoporosis.

- Patients (regardless of birth assigned sex) who have undergone gonadectomy and have a history of at least 5 years without hormone replacement should also be considered for bone density testing, regardless of age.

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**CASE 4**

- Erik is a 43 year old trans male, using testosterone 150 mg IM every 2 weeks for transition. He has been taking testosterone for 18 months. He was not having periods until recently. He is having vaginal spotting each month for the last 3 months. What are some things to consider?
• Menses should cease within 6 months of initiating hormone therapy

• Continued ovulatory bleeding may occur despite testosterone treatment

• Ensure that patient is taking medication correctly and consistently

• Consider changing route and dosing of testosterone, also consider adding progesterone, like depo-provera

• Check testosterone levels and FSH/LH levels

• Consider structural causes such as endometrial polyps, adenomyosis, leiomyomata, endometrial hyperplasia, or malignancy
• Pelvic exam was performed on our patient with some discomfort, but no obvious abnormalities.

• Pap smear was negative for malignancy and high-risk HPV

• Our patient’s uterine ultrasound was normal: no fibroids, no obvious endometrial polyps, thin endometrial stripe

• Testosterone level was 650.

• We changed his testosterone to 75 mg weekly and with increasing the frequency of injections, his bleeding resolved.
CASE 5

• Jason is a 21 year old gender nonconforming patient who prefers they/them pronouns. Wants to appear more masculine, mainly wants top surgery and voice deepening.

• Consider testosterone patch or gel

• Can stop testosterone once optimal irreversible changes are achieved
CASE 7

• Shawn is a trans male on testosterone 100 mg IM weekly who has yearly labs done that show a hgb of 17.5 and hct of 54. He is having increased headaches. Are you concerned about this?

POLYCYTHEMIA

• HCT of 54 is the threshold for immediate action

• Concern is increased blood viscosity and possible thrombosis

• In men with polycythemia vera, annual incidence of thrombotic events ranges from 1.8% in those under 40 to 5.1% in patients older than 70

• Symptoms may include chest pain, dyspnea, fatigue and lethargy, headaches and neurologic symptoms
POLYCYTHEMIA

- In patients on testosterone therapy, increased red blood cell volume apparent by 3 months of treatment and peaks at 9 to 12 months

- Older patients more likely to develop increased Hgb/Hct and develop symptoms/complications

- More likely to occur with injectable testosterone

POLYCYTHEMIA

- First check testosterone levels, including peak level and dose adjust accordingly

- Change to a more frequent dosing schedule or transdermal preparation

- Blood donation may be an appropriate short term solution

- Need to exclude other causes, like sleep apnea, tobacco use, neoplasms and cardiopulmonary disease
• Referred patient to hematology, had full work up that was negative.

• Changed testosterone to transdermal gel, 50 mg a day and treated new sleep apnea diagnosed on a home sleep study

• Repeat hematocrit 46%

CERVICAL CANCER SCREENING

• Screening for transgender men, including interval of screening and age to begin and end screening, follows recommendations for cisgender women
ENDO METRIAL CANCER

- Routine screening for endometrial cancer in transgender men using testosterone is NOT recommended.

- A case control study performed histopathology on samples comparing trans men on androgens for at least one year to pre and post-menopausal women undergoing hysterectomy or histopathology, and found trans men had endometrial atrophy similar to that found in post-menopausal women.

OVARIAN CANCER

- Transgender men should receive the same recommended counseling and screenings for anyone with ovaries based on history and presentation.
Jennifer is a 22 year old trans female who has been taking gender affirming hormone therapy for one year. She is taking estradiol 2 mg twice daily and spironolactone 100 mg twice a day. Lab work showed potassium of 5.1. She desires less body hair and more androgen blocking. Estradiol level is 65 and total testosterone is 255.
HORMONE THERAPY

- Anti-androgen therapy
- Estrogen therapy
- Progesterone

ANTI-ANDROGEN

- Anti-androgens: Spironolactone most common

- Initial dose of spironolactone is 100mg daily in a single or divided dose, with titration to a typical dose of 200mg daily (with occasional patients -- especially larger or younger -- requiring as much as 400mg daily).
5-ALPHA REDUCTASE INHIBITORS

- Another androgen blocker
- May be used alone or in combination with spironolactone.
- In larger doses, finasteride 5 mg, used as second line therapy for patients intolerant to spironolactone.
- Dutasteride 0.5 mg may have more dramatic feminizing effects, but is often more expensive.

BICALUTAMIDE

- Synthetic progestogen with anti-androgen activity
- Has a small but not fully quantified risk of liver function abnormalities and possible failure.
- Not currently first line treatment until more research done
ESTROGEN

Most commonly used forms:
- Estradiol tablets (Estradiol)
- Estrogen transdermal (Estroderm, Climara, Alora, Vivelle)
- Estradiol valerate injection (Delestrogen)

ESTROGEN

- All estrogens increase risk of thromboembolism and prolactinoma.
- Patches may be the preferred form for all especially patients who are older, have underlying liver disease or have elevated lipids. Also consider injectable.
- Oral preparations have the advantage of being easy to titrate or stop in case of adverse effects
- Ethinyl estradiol is not safe for transition.
ASPIRIN

• Consider adding aspirin 81 mg for all patients at risk of thromboembolism (cigarette smoker, age greater than 40, obese, highly sedentary, cardiac risk factors)

PROGESTERONE

• Progesterone
  • Risks and benefits of progesterone are not well-characterized. Some patients and providers have found it to have positive effects on the nipple, areola and libido.

• Different progesterone regimens
  • Medroxyprogesterone 5 to 10 mg orally daily
  • Prometrium 100-200 mg daily
  • Depo-Provera 150 mg IM every 3 months
LAB MONITORING

- Monitor labs at baseline, at 3, 6 and 12 months and then yearly if stable.

- CMP, total testosterone, estradiol level

- Lipids, A1c if indicated

- Prolactin if symptomatic
HORMONE LEVELS

• For transgender care, The Endocrine Society recommends monitoring of the total testosterone level, with a target range of <55ng/dl. Wanting testosterone as low as possible.

• Serum estradiol should not exceed peak physiologic range for young, healthy females with ideal levels 100-200 pg/mL. Levels up to 300 likely okay.

CASE 8

• Back to Jennifer, we increased her estradiol to 6mg daily (divided twice a day) and added finasteride to her regimen.
CASE 9

Linda is a 52 year old trans female wanting to start gender affirming hormone therapy. She has a history of uncontrolled diabetes, hypertension, COPD, and depression. She tells you that this is the time for her to live her true life. She wants to begin hormones now.

• Few contraindications for hormone therapy for gender transition. Some of these contraindications are suicidality, psychosis, pregnancy, estrogen positive cancer

• No set upper age limit for hormonal therapy. Patients beginning hormones after age 40 generally will progress more slowly.

• Upper age limits might limit some surgical options. Anticipated recovery times may be longer.
• She started on oral estradiol due to cost and was taking 2 mg twice a day, spironolactone 100 mg twice a day and provera 5 mg daily.

• She went to the ER with chest pain and was found to have a 95% blockage in her LAD. Had stent placement and was advised to stop all hormone therapy.

• Presented 3 months later in distress due to increasing coarse hair growth and body shape changes.

Goldstein ET AL (2019)
• 13 studies between 1989 and 2018 that investigated the effects of hormone therapy, including types of estrogens use
• Route of hormone administration, patient demographics, and patient comorbidities all affect estrogen’s link with VTE.
• Avoiding ethinyl estradiol might make the use of hormone therapy in trans feminine individuals safer than oral birth control.
• Transdermal estrogens dosed up to 0.1 mg/day or below appear lower risk for VTE than other forms of estrogen
• even if the risk from exogenous estrogen use remains significant statistically, the absolute clinical risk remains low.
BACK TO OUR CASE

Linda was given transdermal estrogen 0.1 mg twice a week and spironolactone 50 mg twice a day

Continued her daily aspirin

No further cardiac events a year later

Estradiol level 155 and total testosterone <20

BREAST CANCER SCREENING

- Screening mammography should be performed every 2 years, once the age of 50 and 5-10 years of feminizing hormone use criteria have been met. Providers and patients should engage in discussions to review risks and benefits
PROSTATE CANCER SCREENING

• No increased need to screen. PSA is not as useful if patient is on estrogen. Small increase in PSA will be more concerning.

I would be happy to answer any questions you may have. My email is:
Swensona@health.missouri.edu
REFERENCES

Center of Excellence for Transgender Health, Department of Family and Community Medicine, University of California San Francisco. Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People; 2nd edition. Deutsch MB, ed. June 2016. Available at www.transhealth.ucsf.edu guidelines.


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Fenway Institute National LGBT health education center

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