TRANSGENDER MEDICINE: A CASE BASED APPROACH

Amanda Swenson, MD MSPH

ACP Conference 2021

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

I have no relevant financial relationships to disclose.

0.5% of the population in the United States identifies as a transgender person

TERMINOLOGY

- **Gender identity**
- **Transgender/Cisgender**
- **Transsexual (also Transexual)**
- **Gender diverse** (nonbinary, genderqueer, gender fluid, transgender or non-cisgender identities)
- **Gender expression/presentation**
- **Intersex**

TERMINOLOGY

- **Transition** includes some or all of the personal, legal and medical adjustments: telling others, changing one's name and/or sex on legal documents; hormone therapy

- **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.

- **Misgendering:** using the wrong gendered language, pronouns, or form of address(sir/ma'am) for someone

PRONOUNS

Normalize asking of pronouns and offering your pronouns.

Correct your mistakes when you misgender someone.

If you don't know how to use someone's pronouns, practice!

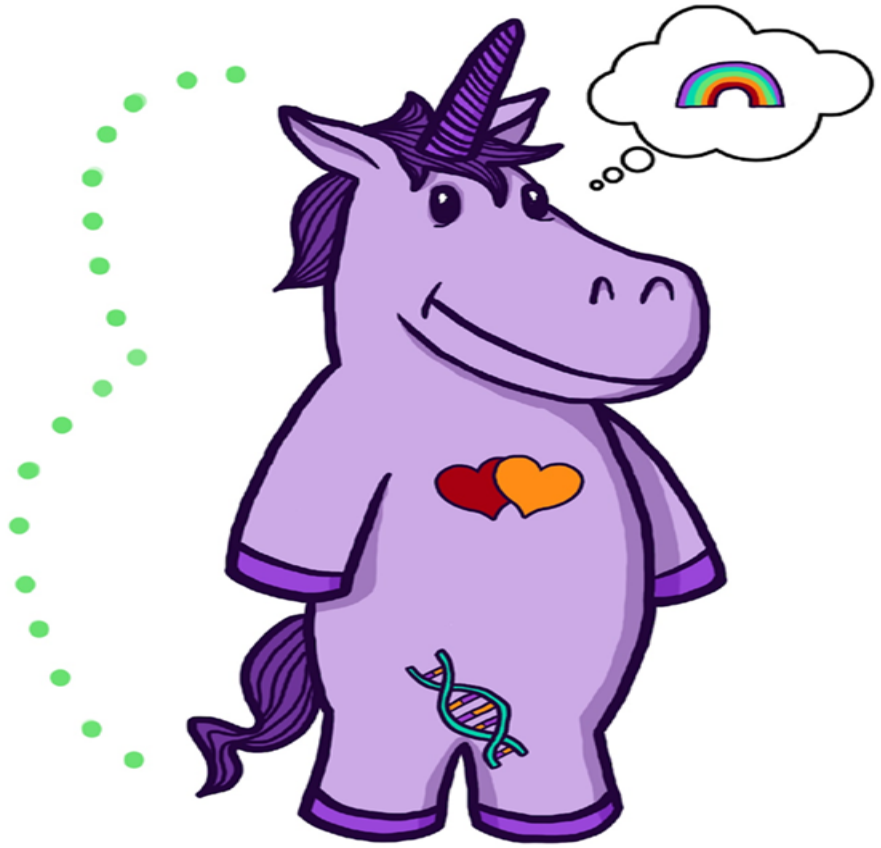
PRONOUNS

Using correct pronouns:

-Conveys respect
-It's affirming and feels good
-It conveys support for that person's identity

The Gender Unicorn

Graphic by:
TSER
Trans Student Educational Resources



Gender Identity
- Female/Woman/Girl
- Male/Man/Boy
- Other Gender(s)

Gender Expression
- Feminine
- Masculine
- Other

Sex Assigned at Birth
Female | Male | Other/Intersex

Physically Attracted to
- Women
- Men
- Other Gender(s)

Emotionally Attracted to
- Women
- Men
- Other Gender(s)

To learn more, go to:
www.transstudent.org/gender

Design by Landyn Pan and Anna Moore

GENDER EXPRESSION

Gender expression is…

How we communicate our gender to ourselves and others.

How we affirm our gender.

Clothes, hair style, gestures/movements, word choice, vocal

GENDER NEUTRAL LANGUAGE

CREATING WELCOMING CLINIC

- Having materials or signage that the transgender affirming
- Train support staff to use gender neutral greetings, and not assume gender by name or pitch of voice
- Correct name/pronouns should be obvious when glancing at chart
- Call back by last name for first appointment
- Use correct name and pronouns in notes
  - Have conversations with minors about if this is safe for them

CREATING WELCOMING CLINIC

- Avoid having people use their deadname to use
- Say “could your chart be under a different name?” or “what is the name on your insurance card?”
- Would NOT want to say “we don’t have you in our records.” “Oh, your name is actually___.” “what is your real name?”

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

Testa, RJ. Suicidal ideation in transgender people: gender minority stress and interpersonal theory factors. *J Abnormal Psych* 2017

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

TESTOSTERONE

Table 1. Hormone preparations and dosing (Grading: T O M)

Androgen	Initial - low dose[b]	Initial - typical	Maximum - typical[c]	Comment
Testosterone Cypionate[a]	20 mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	For q 2 wk dosing, double each dose
Testosterone Enthanate[a]	20mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	"
Testosterone topical gel 1%	12.5-25 mg Q AM	50mg Q AM	100mg Q AM	May come in pump or packet form
Testosterone topical gel 1.62%[d]	20.25mg Q AM	40.5 - 60.75mg Q AM	103.25mg Q AM	"
Testosterone patch	1-2mg Q PM	4mg Q PM	8mg Q PM	Patches come in 2mg and 4mg size. For lower doses, may cut patch
Testosterone cream[e]	10mg	50mg	100mg	
Testosterone axillary gel 2%	30mg Q AM	60mg Q AM	90-120mg Q AM	Comes in pump only, one pump = 30mg
Testosterone Undecanoate[f]	N/A	750mg IM, repeat in 4 weeks, then q 10 weeks ongoing	N/A	Requires participation in manufacturer monitored program[f]

EXPECTED EFFECTS

TABLE 1A: EFFECTS AND EXPECTED TIME COURSE OF MASCULINIZING HORMONES [A]

Effect	Expected Onset[B]	Expected Maximum Effect[B]
Skin oiliness/acne	1-6 months	1-2 years
Facial/body hair growth	3-6 months	3-5 years
Scalp hair loss	>12 months[C]	variable
Increased muscle mass/strength	6-12 months	2-5 years[D]
Body fat redistribution	3-6 months	2-5 years
Cessation of menses	2-6 months	n/a
Clitoral enlargement	3-6 months	1-2 years
Vaginal atrophy	3-6 months	1-2 years
Deepened voice	3-12 months	1-2 years

A Adapted with permission from Hembree et al. (2009). *Copyright 2009, The Endocrine Society.*
B Estimates represent published and unpublished clinical observations.
C Highly dependent on age and inheritance; may be minimal.
D 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 amenorrhea 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

ESTRADIOL 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 contraceptive options. What is available for him to use?

CONTRACEPTION

- Continue to remind patients of pregnancy possibility and discuss contraception if having intercourse with partners assigned male at birth
- 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, different route of testosterone, 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

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

ENDOMETRIAL 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

CASE 8

- 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 10mg orally daily
  - Prometrium 100-200mg daily
  - Depo-Provera 150mg IM every 3 months

Table 1. Hormone preparations and dosing (Grading: T O M)

Hormone	Initial-low[b]	Initial	Maximum[c]	Comments
Estrogen				
Estradiol oral/sublingual	1mg/day	2-4mg/day	8mg/day	if >2mg recommend divided bid dosing
Estradiol transdermal	50mcg	100mcg	100-400 mcg	Max single patch dose available is 100mcg. Frequency of change is brand/product dependent. More than 2 patches at a time may be cumbersome for patients
Estradiol valerate IM[a]	<20mg IM q 2 wk	20mg IM q 2 wk	40mg IM q 2wk	May divide dose into weekly injections for cyclical symptoms
Estradiol cypionate IM	<2mg q 2wk	2mg IM q 2 wk	5mg IM q 2 wk	May divide dose into weekly injections for cyclical symptoms
Progestagen				
Medroxyprogesterone acetate (Provera)	2.5mg qhs		5-10mg qhs	
Micronized progesterone			100-200mg qhs	
Androgen blocker				
Spironolactone	25mg qd	50mg bid	200mg bid	
Finasteride	1mg qd		5mg qd	
Dutasteride			0.5mg qd	

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 .

World Professional Association for Transgender Health (WPATH). Standards of care for the health of transsexual, transgender, and gender nonconforming people, 7th Version. WPATH; 2012 [cited 2016 Mar 10].

- **Caring for Transgender and Gender-Diverse Persons: What Clinicians Should Know**
  DAVID A. KLEIN, MD, MPH; SCOTT L. PARADISE, MD; and EMILY T. GOODWIN, MD,. *Am Fam Physician.* 2018 Dec 1;98(11):645-653.

Speck, N. Management of Transgenderism. JAMA 309(5) Feb 2013.

Hembree, W. Endocrine treatment of transsexual persons: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 94(9). Sept 2009.

http://www.glaad.org/reference/transgender

Protocols for Hormonal Reassignment of Gender

Tom Waddell Health Center (San Francisco, CA). December 12, 2006.

REFERENCES

Healthy People 2020: Lesbian, Gay, Bisexual, and Transgender Health. Overview, objectives and data, and evidence-based resources from this important U.S. public health initiative.

Perrone AM, Cerpolini S, Maria Salfi NC, Ceccarelli C, De Giorgi LB, Formelli G, et al. Effect of long-term testosterone administration on the endometrium of female-to-male (FtM) transsexuals. J Sex Med. 2009 Nov;6(11):3193-200.

Goldstein Z, Khan M, Reisman T, Safer JD. Managing the risk of venous thromboembolism in transgender adults undergoing hormone therapy. *J Blood Med*. 2019;10:209-216
https://doi.org/10.2147/JBM.S166780

Fenway Institute National LGBT health education center

Testa, RJ. Suicidal ideation in transgender people: gender minority stress and interpersonal theory factors. *J Abnormal Psych* 2017