

Gender-Affirming Hormone Therapy in Times of Housing Instability

National Healthcare for the Homeless Conference
May 10, 2022

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Disclosures

- No financial relationships
- I will discuss some off-label medications
- I will discuss recommendations from transgender health standards of care, as well as those from expert opinion and my own clinical experience

Learning Objectives

- Prescribe gender-affirming hormone therapy (GAHT) using a patient-centered, informed-consent process
- Tailor GAHT according to a person's co-morbidities related to their lived experience of homelessness
- Tailor GAHT according to a person's social determinants of health
- Practice patient-centered GAHT titration and lab monitoring

LN

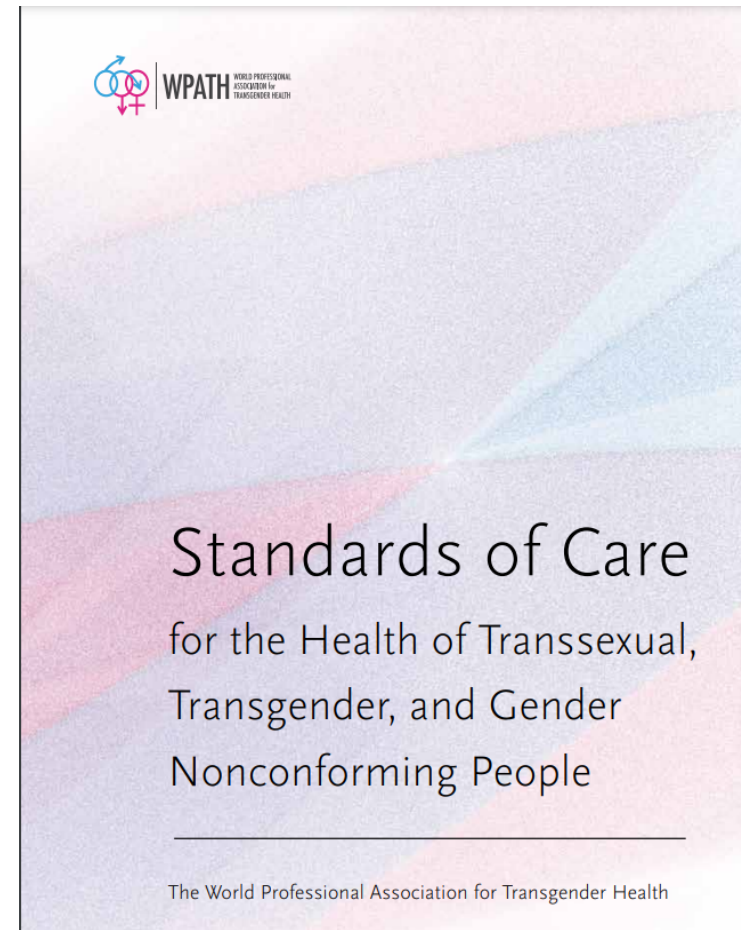
- 44 y/o transgender woman brought in by the street outreach team for GAHT
- She was born during the Vietnam War to a Vietnamese mother and African-American father
- She immigrated to the U.S. when she was 18 y/o and started living outside at 21 y/o
- She has been in the same homeless encampment by the creek and train tracks for many years
- She does not have many friends in the Vietnamese community, she thinks it's because her skin color is too dark, but she has developed a close group of friends around her encampment
- The outreach team has been visiting her encampment for a year
- She was referred to endocrinology for GAHT but never made it
- She is ready to start hormones if we are ready to prescribe them

Overarching Guiding Principles for GAHT

- Homeless healthcare providers can prescribe GAHT
- For patients who want GAHT, GAHT is medically necessary
- Informed Consent
 - Discussion and mutual agreement, not a physical contract requiring signature
 - Patients are most often knowledgeable and experienced
 - Patient-centered discussion of goals, expectations, reversible and irreversible changes
 - Shared decision-making
 - Harm-reduction

WPATH Standard of Care Guidelines

- Informed Consent, Criteria:
 - 1. Persistent, well-documented gender dysphoria
 - 2. Capacity to make a fully informed decision and to consent for treatment
 - 3. Age of majority in a given country
 - 4. If significant medical or mental health concerns are present, they must be reasonably well controlled



Patient-Centered Informed Consent

- Informed Consent, Criteria:
 - 1. Persistent, well-documented gender dysphoria
 - We are not searching for a specific gender narrative to “diagnose” their gender
 - Some people are not in “clinical distress” related to their gender
 - Me: “Tell me about your gender.”
 - LN: “This is me. I can’t hide my feelings. I am a woman.”
 - 2. Capacity to make a fully informed decision and to consent for treatment
 - Create a trauma-informed, safe space to have a discussion
 - Me: “We are going to talk about what hormones can and can’t do, and their side effects, so you can decide if they’re the right choice for you. Each person has their own hopes and desires for hormones. It’s important to please talk with me about the changes you hope for. Please let me know about any experiences you might have had with hormones. If you have questions, please ask. Asking questions will NOT affect your chance at getting hormones.”

LN

- She remembers identifying as a woman when she was 9 y/o, but gender-affirming therapy was not legally available
- When she moved to the U.S. she did not know where to get GAHT
- Three years ago at 41 y/o, she began hormones while in custody
- After she was released, she went back to the train tracks
- She didn't know where to get hormones and became depressed
- She found street hormones from Mexico and was on them for 2 years
- She was on a pill and doesn't remember the dose

Me: “What have hormones done for you in the past? What are you hoping hormones can do for you?”

LN: “I felt good. More calm. I want softer skin, breasts, less hair.”

Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
*Breast growth	3–6 mo	2–3 y
*Decreased testicular volume	3–6 mo	2–3 y
*Decreased sperm production	Unknown	>3 y
Decreased terminal hair growth	6–12 mo	>3 y ^a
Scalp hair	Variable	— ^b
Voice changes	None	— ^c

*permanent

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
*Facial/body hair growth	6–12 mo	4–5 y
*Scalp hair loss	6–12 mo	— ^a
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	— ^b
*Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
*Deepening of voice	6–12 mo	1–2 y

44 y/o with chronic homelessness, tobacco use disorder, hypertension, methamphetamine use disorder (smoking), PTSD, depression

Which estrogen therapy would you prescribe?

- A. Transdermal estrogen
- B. Estrogen injection
- C. Estrogen tablet
- D. Potentially A, B, or C

Overarching Guiding Principles for GAHT, cont'd

- There is no singular right way
 - WPATH Standards of Care Guidelines v7 (2011)
 - UCSF Primary Care Guidelines (2016)
 - Endocrine Society Guidelines (2017)
 - Expert Opinion
 - Patients as experts-- “Microdosing” (low-dose GAHT) approach

UC San Francisco Primary Care Guidelines

Welcome
Place a Referral
e-Consults (Internal to UCSF Medical Center only)
UCSF Transgender Care & Treatment Guidelines ▾
Introduction
Contributors
Grading of evidence
Terminology

Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People

Publication Date: June 17, 2016

Second Edition

[Download Guidelines \(PDF\)](#)

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TAILORING GAHT TO CO-MORBIDITIES OF HOMELESSNESS

- Tobacco use disorder
 - Increased VTE risk, esp if ethinyl estradiol, > 40 y/o, HIV, HTN, clotting d/o, CA
 - No head-to-head studies of transgender women comparing different formulations, doses, or estradiol levels
 - Due to VTE risk, expert recommendation is transdermal estrogen
 - 1st choice: Estradiol patch up to 0.1mg/day (dose?)
 - 2nd choice: Estradiol injection
 - ASA (no evidence)
 - Stop smoking—counsel that tobacco lowers estrogen levels (maybe not estrogen patch)
- Patches should be applied to a clean, dry skin area that does not tend to sweat or be hairy...

TAILORING GAHT TO SOCIAL DETERMINANTS OF HEALTH

- Challenges with personal hygiene
 - Hot/damp/sweaty climate—patches biweekly with tegaderm/tape or tincture of benzoin, pills, injections
 - Hygiene insecurity—patch hacks as listed above, pills, injections (give alcohol pads and needle supplies); in-clinic dispensing or in-clinic administration
- Sense of safety
 - Swept, lost or stolen meds—injections, patches; in-clinic dispensing or administration, limited quantities
 - Transphobic, dangerous living environment—pills, patches; in-clinic administration
 - Fear/dislike of going to pharmacy—injections; in-clinic dispensing or administration
- Barriers to accessing medical care
 - Competing priorities for survival
 - Difficulty with taking meds as a life priority—injections, patches; in-clinic administration
 - Not knowing the date/time—patches, injections, in-clinic dispensing or administration
 - Lack of transportation—pills, injections, patches; in-clinic administration or med delivery
- \$\$\$
 - Medi-Cal Formulary

Medi-Cal Formulary Coverage

- [Medi-Cal Formulary](#)

Class	Covered	Needs Prior Auth
Feminizing Hormone	Estradiol tabs Weekly estradiol patch (all strengths) Biweekly estradiol patch 0.1mg	Biweekly estradiol patch (all other strengths except 0.1mg) Estradiol valerate Estradiol cypionate
Anti-androgen	Spironolactone Finasteride Dutasteride Flutamide	Leuprolide (2-17 y/o with central precocious puberty) Leuprolide (18+) Bicalutamide (cancer treatment only)
Progestins	Medroxyprogesterone Depo medroxyprogesterone IM	Micronized progesterone

Medi-Cal Formulary Coverage

- [Medi-Cal Formulary](#)

Class	Covered	Needs Prior Auth
Masculinizing Hormone	None as of June 2022!!!	Testosterone restricted to primary hypogonadism, hypogonadotropic hypogonadism, delayed puberty, or metastatic mammary cancer in females

LN

- Lives in a tent → hot/sweaty/damp environment
- Tent is deep in the woods → no water/shower access, dislike of going to pharmacy, no nearby transportation
- Has 4 dogs → no one can watch dogs → can't go to pharmacy
- No phone → not sure of the date/time
- Relies on outreach team for transportation
- What does SHE want?
 - She does not want a patch. She heard injections work the best.
- Started on estradiol valerate 10mg IM every 2 weeks with nurse teaching, plan for self-administration, outreach team brings her to pharmacy to get meds

Notes on Hormone Injectables and Storage

- Self-administration
 - Ok for estrogen and testosterone to be at room temperature (59-86°)
 - Not recommended above 86°, but quality not affected after 1800 days
 - In colder temps, not ideal if crystallized/cloudy
 - Probably ok if not crystallized and viscosity has not changed
 - Single-dose vials often available in outpatient pharmacy
- In-clinic administration
 - Have estrogen and testosterone available for in-clinic administration
 - Multi-dose vials can be available in clinic
 - Testosterone pellet (implant lasts 3-4 months), testosterone undecanoate (injectable lasts 10 weeks)

Two weeks later...

- Outreach team brings LN back in for follow-up
- She found it hard to use the needle and couldn't even look at it
- She doesn't want to come into the clinic to get injections because she is too busy – needs to go to immigration office, food stamps, go to court, get a new phone

TAILORING GAHT TO CO-MORBIDITIES OF HOMELESSNESS

- Substance Use Disorder
 - Needlephobia/Needles as a trigger—pills, patches, clinic-administered injections
 - Chaotic lives/competing priorities—patches, injections with extended frequency; clinic-administered
- Mental health
 - Chaotic lives—patches, injections with extended frequency; clinic-administered
 - Capacity to self-administer meds — Injections with extended frequency
- Cognitive impairment—pills, patches, injections; clinic-dispensed or administered; blister packing, pillboxes

What next?

- Shared-decision making discussion
- Changed to estradiol tablets 2mg PO daily

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

Hormone	Initial-low ^b	Initial	Maximum ^c	Comments
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

44 y/o with chronic homelessness, tobacco use disorder, hypertension, methamphetamine use disorder (smoking), PTSD, depression.

Which estrogen therapy would you prescribe?

- A. Transdermal estrogen
- B. Estrogen injection
- C. Estrogen tablet
- D. Potentially A, B, or C

What is the best up-titration and lab monitoring plan for her?

- A. Increase estradiol by 2-4mg every 1-3 months, only if estradiol levels show that an increase in dose is needed
- B. Increase estradiol by 2-4mg every 1-3 months to the max recommended dose, without checking labs
- C. Increase estradiol by 2-4mg every 1-3 months, only if the patient feels like they haven't met their goals
- D. A, B, or C

PATIENT-CENTERED GAHT MONITORING

- Lab monitoring is not evidence-based
- Different expert opinion
- Higher estrogen and testosterone levels are not necessarily associated with specific secondary sex characteristics

Table 4. Laboratory monitoring for feminizing hormone therapy

Test	Comments	Baseline	3	6	12	Yearly	PRN
Estradiol			X	X			X
Total Testosterone			X	X	X		X

Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
 - a. Serum testosterone levels should be <50 ng/dL.
 - b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

PATIENT-CENTERED GAHT MONITORING

- Challenges with obtaining lab work
 - Transportation
 - Needlephobia/needles as a trigger
 - Competing priorities
 - Distrust of the medical system
 - “Why are you always drawing my blood?”
 - Can do in-clinic lab draws, but there may be limited time
 - Timing of lab draw relative to medication affects interpretation of result

PATIENT-CENTERED GAHT MONITORING

- Uptitration should be based on:
 - Patient goals, but sometimes people cannot fully articulate
 - Me: “How are the hormones feeling?”
 - LN: “Not quite right.”
 - Clinical effects
 - Safety
 - +/- Hormone levels
 - Shared-decision making
 - Harm-reduction

My Hormone Initiation and Uptitration

- Estrogen

- Estradiol 10mg IM q2 weeks (20mg q4 weeks) and go up in 5-10mg increments in 1-3 months
- Estradiol tablets 2mg PO qdaily and go up in 2-4mg increments in 1-3 months
- Estradiol patch 100mcg q weekly and go up in 50-100 mcg increments in 1-3 months

- Testosterone

- Testosterone 20mg SQ/IM weekly (40 q2weeks) and then go up in 1-3 month increments by 20mg q week at a time (0.1 ml of 200mg/ml concentration)
- Patches, gels, pumps (none of my patients on these)

- Microdosing (low-dose GAHT):

- Low- and slow-dosing with duration individualized from person to person

My Feminizing Hormone Lab Monitoring

- Estradiol:
 - Consider in patients with side effects or inadequate feminization, patients on injections or estradiol tablet dose >6mg/daily, or patients with h/o severe conditions that ?exacerbated with estrogen (e.g. pulmonary embolism, VTE, CAD s/p CABG)
 - Check q3-6 mo after dose change
 - Goal 100-200 pg/ml. Avoid < 400 pg/ml.
 - Check trough (mid injection) level or whenever if patch or PO. For SL because there is a faster on/off, have patient check ~3 hours after dose if possible, which will be a mid-level
 - Once target achieved, check yearly or prn
- Testosterone:
 - 7-9AM total testosterone if possible: baseline, q3-6mo after dose change; goal < 55 ng/dl. Once target achieved, check yearly or prn
- Prolactin: only if symptoms of prolactinoma (e.g vision changes, HA, galactorrhea)

My Masculinizing Hormone Lab Monitoring

- Total testosterone:
 - Considering using to titrate dosing and in patients with side effects, inadequate masculinization, or doses > 40-80mg per week (or 80 q2 weeks) unless their hemoglobin runs on the higher end
 - Check q3-6 mo after dose change. If level is at lower end of normal range and patient concerned about slow progress, ok to increase dose. Once levels greater than midpoint, unclear if dose increase will have any additional effects.
 - Ref range 260-1000 ng/dl. May be ok for higher levels if no breakthrough bleeding which would suggest aromatization of T to estrogen and therefore overdosing.
 - For trough (goal 200s): check 13-14d post 2wk injection or AM the day qweek shot is due
 - For peak levels (goal <1000): check day 3-4d post qweek injection or 7d post 2week injection
 - Check whenever if patch/gel (goal < 1000)
 - Once target achieved, check yearly or prn
- Estradiol:
 - Consider if pelvic pain or symptoms, persistent menses, or mood symptoms, otherwise no need to check if T level is appropriate. Goal < 50
- Hgb/Hct:
 - Baseline, q3-6 mo after dose change then q1yr. If menstruating regularly, use female lower limit of normal (12 g/dL) and male upper limit of normal (17.5 g/dL). If not menstruating, use male lower and upper limits of normal (13.5-17.5 g/dL).

Four weeks later...

- Needs early refill because meds lost in the creek
- Hormones were making her feel calmer and more stable. She noticed breast tenderness and is tolerating meds well.
- Me: “Are there times when you might’ve taken more than one tablet per day?”
LN: “I want the hormones to work faster. I’ve been taking 2 a day.”
- We agreed on 4mg estradiol per day
- Started spironolactone 50mg twice daily with plan for in-clinic lab draw of chemistry panel in 1-2 weeks

My Anti-androgen Therapy Practice

- Spironolactone—if patient wants
 - Controversial
 - Doesn't help lower testosterone?
 - Interferes with estrogen?
 - Reduced breast development due to premature bud fusion?
 - Cons:
 - Diuretic → polyuria, polydipsia → hard with bathroom and water insecurity
 - Hyperkalemia → needs lab monitoring
 - Hypotension → dizziness, problems if people living outside
 - Brain fog—fatigue, haziness, confusion → affects sense of safety living outside
 - Start 1-3 months after estrogen therapy. 50mg bid with chemistry in 1-2 weeks and increase 50-100mg q2-3 months if T not at goal and chemistry ok

MEDICAL EXAMINER
Spironolactone, a Standard Drug in Hormone Treatment for Trans Women, Has Controversial Side Effects

Deutsch, MB., UCSF Transgender Care, 2016. <https://transcare.ucsf.edu/guidelines>

Wierchx, K et al. J Sex Med, 2014

Leinung MC et al, Transgend Health, 2018

Green AV, Slate Magazine. 2018. <https://slate.com/technology/2019/06/spironolactone-hormone-trans-women-side-effects.html>

Two weeks later...

- Chemistry panel normal
- No side effects
- We agreed on continuing spironolactone and increasing estradiol 6mg daily with plan to f/u in 4 weeks

What is the best up-titration and lab monitoring plan for her?

- A. Increase estradiol by 2-4mg every 1-3 months, only if estradiol levels show that an increase in dose is needed
- B. Increase estradiol by 2-4mg every 1-3 months to the max recommended dose, without checking labs
- C. Increase estradiol by 2-4mg every 1-3 months, only if the patient feels like they haven't met their goals
- D. A, B, or C

Few months later...

- Encampment was swept
- Outreach team can't find her
- No one knows where she is

1 year later...

- Received phone call from OSH pharmacist asking for her previous hormone dose so she could be restarted in the hospital
- 3 months ago, she was run over by a train on the train tracks, maybe potential suicide attempt vs. attempted murder
- Had been admitted to the trauma unit and has been intubated
- After finally being extubated, she asked to restart hormones
- New diagnoses of paraplegia, HIV, and multiple decubitus ulcers
- Plan for discharge to skilled nursing facility for physical therapy
- Restart spironolactone 50mg twice daily and estradiol 6mg daily

Over the next year...

- Never went to skilled nursing facility because
 - They wanted to send her to a facility in Los Angeles but this was too far away
 - She felt mistreated in the hospital, judged for her HIV
- She chose to return to her encampment because
 - She missed her “children” (her dogs) and her boyfriend
 - “I feels like the creek is my home, where my friends are. My friends are my family. My blood family doesn’t accept me being gay...My family are the people who live outside with me. I am happy living outside because I feel free. I like getting food from the dumpster, I don’t know why. It’s just what I know. I want to live the life that I know, outside.”
 - "God wants me to sit right now, and so I don't care if I ever walk again. I am already almost 50 years old and if I live to be 50 or 60 years old and die from the wound because I’m living outside, then I will die smiling. I want to go back to the creek because it’s what I know, what I feel comfortable with, and what makes me happy.”

Over the next year...

- Recurrent hospitalization, due to
 - Leaving hospital early to go back to the creek
 - Domestic violence with boyfriend who abruptly abandons her → failure to thrive on her own
 - Sepsis from worsening decubitus ulcers and eventual osteomyelitis
- On estradiol 6mg daily only, no longer on spironolactone due to hypotension from intermittent sepsis
- Not happy with hormones
- Asked hospitalist team to draw labs
 - Estradiol of 84.6 (close to goal 100-200)
 - Testosterone of 291 (not at goal < 55)

Over the next year...

- Taking medicines consistently in the hospital, but then lost to follow-up when goes back to the creek
- Wants T to be lower. Wishing for more breast growth, still bothered by body hair on legs, chest, face, and arms. Doesn't feel right.
- Discussed orchiectomy, she doesn't want
- Discussed with her that for breast growth, max likely cup A or B and ideal treatment is breast augmentation, but cannot achieve this with ongoing sepsis and osteomyelitis
- Discussed with her that for unwanted hair growth, ideal treatment is electrolysis, but cannot achieve this while hospitalized and no income

What would you advise the hospitalist team to do next to augment her GAHT?

- A. Change to injectable estrogen
- B. Start leuprolide
- C. Start bicalutamide
- D. Start dutasteride
- E. Start progestin
- F. Any of the above are good options

My Anti-androgen Therapy Practice

- GnRH agonists—leuprolide
 - 11.25mg q3 months (or 7.5mg monthly)
 - Check T every 3 months during 1st year then yearly. Check serum LH, FSH, and prolactin at baseline and annually
- Androgen receptor blockers—bicalutamide, flutamide
 - Bicalutamide 25mg PO daily then 50mg daily if tolerated
 - MUST watch LFTs! Check at baseline then q3mo, then q6-12 mo or earlier if sx
- 5-alpha-reductase inhibitors
 - Finasteride 1-5mg PO daily
 - Dutasteride 0.5mg PO daily
 - Benefit?, sometimes not covered, no labs needed

My Progestogen Practice

- Progestins –if patient wants
 - Controversial
 - May lower T, more breast/areolar development, improved mood
 - Cons:
 - Weight gain likely leads to breast development
 - Depression
 - In WHI, cardiovascular events and breast cancer
 - Medroxyprogesterone 2.5-10mg PO qdaily, maybe for 10 days each month
 - Depo-medroxyprogesterone IM 150mg every 3 months
 - Micronized progesterone 100mg-200mg daily, maybe for 10 days each month
 - If no benefit after 2-3 years, consider discontinuation

TAILORING GAHT TO SOCIAL DETERMINANTS OF HEALTH

- Difficulty with lab monitoring—IM estrogen, leuprolide, finasteride/dutasteride? Progestin?
- Difficulty with taking daily medication—IM estrogen, leuprolide, finasteride/dutasteride? Progestin?

What would you advise the hospitalist team to do next to augment her GAHT?

- A. Change to injectable estrogen
- B. Start leuprolide
- C. Start bicalutamide
- D. Start dutasteride
- E. Start progestin
- F. Any of the above are good options (bicalutamide and dutasteride maybe not the best)

LN

- Only consistent follow-up is when she's hospitalized
- Will go back to the creek → Need a medicine that's long-acting and requires minimal lab monitoring
- Started on leuprolide 11.25mg every 3 months
- Leuprolide can be given in hospital or on street outreach
- Five months later, testosterone level 27
- Still in/out of the hospital

Food for thought: Tailoring GAHT to these co-morbidities?

- Informed consent?
 - Methamphetamine use disorder with psychosis
 - Schizophrenia
 - Cognitive impairment
 - Traumatic brain injury
- Clinical safety?
 - Hepatitis C
 - Alcohol use disorder
 - Cirrhosis
 - CAD
 - Stroke
- Drug interactions?
 - HCV treatment
 - HIV treatment
 - Taking emtricitabine/tenofovir for HIV prevention

Takeaways

- Many transgender/nonbinary individuals experiencing homelessness have very complicated lives
- Homeless healthcare providers should prescribe GAHT
- Know the guideline recommendations and expert opinion for GAHT, and then modify them according to a person's living situation, their co-morbidities, and what the person wants
- Have injectables and long-acting medications available in clinic
- Feel empowered! You can probably justify prescribing any hormone formulation, as well as any uptitration and lab monitoring schedule.

Questions?

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