LGBT Health 101
What ever PA needs to know about Masculinizing and Feminizing Hormone Therapy

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The Center for LGBT Health Equity

of Chase Brexton Health Care

Presenter: Debb Dunn

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Family Practice Physician Assistant

Physician Assistant (PA-C): Howard University
MBA: Johns Hopkins University
Gender Affirming Care: WPATH (World Professional Association for Transgender Health) certification courses completed

- Provides primary medical care, staff leadership, and coordination of care for about 5000 gender expansive patients at Chase Brexton
- Helped develop the Gender JOY (Journeys of Youth) program, a multidisciplinary care team model for gender diverse youth
- Served on a national team of experts to write medical transition best practice guidelines for gender expansive adults and adolescents
- Dynamic trainer, frequently requested speaker, organizational and government consultant, subject matter expert on Gender Affirming Care and HIV Care
- Named 2018 Physician Assistant of the year by MAPA (Maryland Academy of Physician Assistants)
- LGBTQ Commissioner for Maryland State Government

Gender Dysphoria

- *Clinically significant distress* associated with conflict between a person's sex assigned at birth and their authentic gender.
  - Simply being transgender or gender expansive is not a psychiatric concern

- People with gender dysphoria may be very uncomfortable with the sex they were assigned, expressed as:
  - Extreme discomfort with their body (particularly genitals, chest, and secondary sex characteristics)
  - Extreme discomfort with the expected roles of their assigned gender.

American Psychiatric Association, 2016

Informed Consent

- Informed Consent is when an adult gives permission (consent) to make an adult decision for themselves
- Letters from a therapist are not required for treatment, including hormone therapy. Nobody has to “approve” your medical transition.
- This model of care preserves patient autonomy and gives non-binary people more freedom to decide for themselves which parts of medical transition they undergo.

Obtaining consent for treatment

Additional challenges arise when parents have discordant opinions about their TGNC child, or if a youth is in the custody of the courts. If both parents maintain medical decision-making for the youth then it becomes the task of the medical and mental health providers to help both parents understand the necessity of medical interventions. This process is not always straightforward, can take a lot of time, and sometimes necessitates involvement of legal assistance. For youth in the child welfare system, judges can order that medical intervention, including the administration of gender-affirming hormones, be undertaken.

"Health considerations for gender non-conforming children and transgender adolescents"
UCSF

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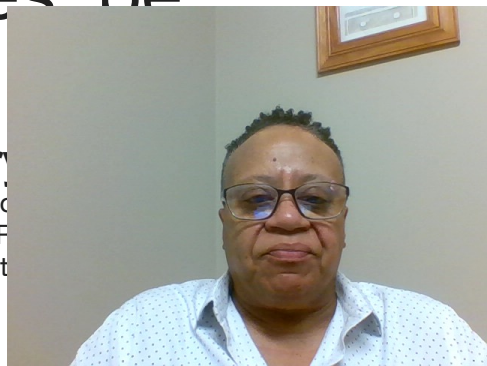

WPATH: Criteria for Hormone Therapy

- Persistent, well-documented gender dysphoria
- Capacity to make a fully informed decision and to consent for treatment
- Age of majority in a given country (18 years)
- If significant medical or mental health concerns are present, they must be reasonably well controlled

WPATH standards of care (2007)

Feminizing Hormonal Treatment Guidelines

Feminizing Therapy: Therapeutic Goals

- Testosterone level < 50 ng/dL (normal cis-female range)
- Estradiol level 100-200 (mean of premenopausal range)
- Potassium within normal range (K < 5.3 mg/dL)
- No established hormonal reference ranges in the MtoF population, some providers treat per clinical response
- Targeting at least Tanner 3 breast development

Endocrine Society guidelines (2017)

Table 2. Laboratory monitoring for feminizing hormone therapy

Test	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
* In first year of therapy only ** Used to calculate bioavailable testosterone; monitoring bioavailable testosterone is optional and may be helpful in complex cases (see text)							
BUN/Cr/K+ (CMP)	Only if spiro used	X	X	X	X	X	X
Lipids	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
A1c or glucose	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					
Estradiol	Test estradiol levels if suspect the dose is high	X					X
Total Testosterone		X	X	X	X		X
Sex Hormone Binding Globulin (SHBG)**	Only if not able to obtain optimal hormone level						
CBC		X	X	X	X		
Prolactin	Only if symptoms of prolactinoma	X					

Feminizing Hormones

Hormone	Initial-low[b]	Initial	Maximum[c]	Comments
Estradiol oral/sublingual	1 mg/day Adolescents	2-4mg/day	8mg/day	if >2mg recommend divided bid dosing
Estradiol transdermal Climera Patches Vivelle DOT	0.05mg - 0.2mg (Concentrations of 0.025, 0.0375, 0.05, 0.075, 0.1mg patch/day)	0.025, 0.0375, 0.05 mg	0.4mg (4x 0.1mg patches)	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	5 mg IM weekly or 10mg IM q 2 wk	20 mg weekly or 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 dos weekly injectio cyclical sympt

Feminizing Hormone Regimens

Table 1. Hormone preparations and dosing (Grading: T O M)				
	Doses	Initial	Maximum	Comments
Progesterone				
Medroxyprogesterone acetate (Provera)	2.5,5, 10mg	5 mg qhs	5-10mg qhs	The risks of using progestogens in transgender women are likely minimal or even absent
Micronized progesterone Prometrium	100 mg	100 mg	200mg qhs	Can cause weight gain and/or moodiness.
Premarin (Estrogen)	.0375, .05 mg	.06, .09 mg	1.25 mg	Increased risk of VTE

Anti-Androgens

Anti-Androgens	Start/Usual Dose	Absolute Max Dose	Frequency	Pros	Cons
Spironolactone (Oral) **(Aldactone)**	100mg - 300mg (Concentrations of 25mg, 50mg, 100mg tablets)	400mg (4x 100mg tablets)	Daily	• Inexpensive • Very effective to decrease endogenous testosterone levels	• • Hyperkalemia • Single or divided doses dependent on preference • Diuretic effect can result in fatigue, dehydration side effects • Erectile dysfunction •
Finasteride (Oral) **(Propecia or Proscar)** **As adjuvant anti-androgen**	5mg (1x 5mg tablet)	5mg (1x 5mg tablet)	Daily	• Slows and prevents balding due to androgenic alopecia and decreases other secondary sexual hair growth in youth • Used as adjuvant because decreases DHT but not Testosterone. Can use alone if goal is only for partial feminization	
Leuprolide Acetate (IM) **(Lupron, Eligard)**	11.25mg (1 IM shot of 1.25mg/1.5mL dilutant)	22.5mg (2 IM shots of 11.25mg/1.5mL dilutant)	Every 3 months	• GnRH receptor agonist, very effective • For Teens: Best option for puberty suppression; can use either alone or with exogenous hormones • • For Adults: Especially beneficial if can't use spiro and/or on a lower estrogen dose and/or having difficulty suppressing endogenous hormone production	• Expensive if not cov insurance • Not ideal for long-ter due to bone density

Less Frequently Used Anti-Androgens

Anti-Androgens	Start/ Usual Dose	Absolute Max Dose	Frequency	Pros	Cons
Bicalutamide (Oral) (Casodex)	50mg (1x 50mg tablet)	50mg (1x 50mg tablet)	Daily	• Non-steroidal androgen receptor antagonist	• Non-Preferred due to high risk of liver toxicity— Don't use if +G6PD, or increased risk of methemoglobinemia (e.g. smokers); caution if other hepatotoxic drugs or alcohol • If utilized must check LFT at baseline, 1 mo, 2 mo, then every 6 mo for lifetime
Aspirin (Oral)	81mg	N/A	Daily	• To decrease risk of CVD	• Consider use if other CVD risk factors present

Suggestions for Prescribing Feminizing Hormones

1. Start / Initial:
    a. Estrace 2 mg once per day, spiro 100 mg once per day.
2. Follow up in 4-6 weeks :
    a. Increase the dose: estrace 4 mg and spiro 200 mg
3. Follow up in 4-6 weeks :
    a. Increase the dose estrace 6 mg. Continue spiro 200 mg.
4. Follow-up in three months.
    a. If still experiencing dysphoria, increase estrace to 8 mg.

Feminizing HRT, continued

1. Delestrogen injectable:
    1. Start at delestrogen 5 mg weekly if just starting.
    2. Start at delestrogen 10 mg weekly if switching from tablets
2. Follow up in one month
    a. Increase the dose to 10-2 mg weekly.

Progesterone

1.) Prometrium 100 mg – once tab once per day

a. Follow up in 6 weeks to check mood.

b. Increase to Prometrium 200 mg if still needed for the treatment of dysphoria.

2.) Provera

a. Start Provera 2.5 mg once per day.

b. Follow up in 4- 6 weeks to check mood

c. Increase to Provera 5 mg if needed for the treatment of dysphoria.

Adjusting Feminizing HRT After Orchiectomy

- Discontinue spironolactone shortly before surgery. There is NO need for antiandrogen therapy s/p orchiectomy
- HOLD estrogen for 2-6 weeks perioperatively to minimize thromboembolic risk
- Most patients will typically need 25-50% less estrogen to achieve similar serum levels of estradiol post-operatively

Slide Credit: Ava Port, MD

Hormone Therapy Management in Older Adult Patients

- Older patient will have a slower, less pronounced response to feminizing and masculinizing HRT if transitioning later in life

- In older trans women, can consider inducing “menopause” by gradually lowering HRT any time after age 50 yrs. (Only if there is no worsening dysphoria)

- Consider baseline bone density scan prior to HRT or screening at age 60 years for older individuals who stop therapy or have a history of non-compliance

Slide Credit: Ava Port, MD

Rough Dose Equivalent Chart

Injectable	Transdermal Patch	Oral	Pellets (2 pellets per 25 mg injected weekly)
5mg weekly (0.25mL of 20mg/mL solution)	0.05mg	2mg	300mg (4x 75mg pellets)
7.5mg weekly (0.375mL of 20mg/mL solution)	0.1mg	4mg	450mg (6x 75mg pellets)
10mg weekly (0.5mL of 20mg/mL solution)	0.2mg	6mg	600mg (8x 75mg pellets)
20mg weekly (0.5mL of 40mg/mL solution)	0.4mg	8mg	900mg (12x 75mg pell

Obstet Gynecol. 1997 Mar;89(3):340-5.

Single-dose pharmacokinetics of sublingual versus oral administration of micronized 17 beta-estradiol.

Price TM[1], Blauer KL, Hansen M, Stanczyk F, Lobo R, Bates GW.

Author information

Abstract

OBJECTIVE: To investigate the pharmacokinetic profiles of different doses of micronized 17 beta-estradiol administered by oral or sublingual routes.

METHODS: Single doses of micronized 17 beta-estradiol were administered orally (1 mg, 0.5 mg) or sublingually (1 mg, 0.5 mg, 0.25 mg) to six postmenopausal women in a randomized clinical trial. We calculated pharmacokinetic parameters for estradiol (E2) and estrone (E1) of maximum serum concentration, time to maximum serum concentration, terminal half-life, area under the concentration curve, and oral clearance. Serum levels of E1 sulfate also were compared at 4, 12, and 24 hours after dosing.

RESULTS: Sublingual administration resulted in rapid absorption with significantly higher E2 levels than did comparable oral dosing. Estrone levels did not vary with route of administration but correlated with the dosage administered. Estrone sulfate levels correlated with the dosage administered and also tended to be higher with sublingual administration. Sublingual administration resulted in a significantly lower E1 to E2 ratio during the 24 hours than did oral administration.

CONCLUSION: Sublingual administration of micronized 17 beta-estradiol results in a rapid, burst-like absorption into the systemic circulation yielding high E2 levels that fall rapidly over the first 6 hours.

PMID: 9052581 DOI: 10.1016/S0029-7844(96)00513-3

[Indexed for MEDLINE]

J Thromb Haemost. 2010 Aug;8(8):1736-44. doi: 10.1111/j.1538-7836.2010.03953.x. Epub 2010 Jun 14.

The effect of estrone on thrombin generation may explain the different thrombotic risk between oral and transdermal hormone replacement therapy.

Bagot CN[1], Marsh MS, Whitehead M, Sherwood R, Roberts L, Patel RK, Arya R.

Author information

Abstract

BACKGROUND: The metabolism of estrogen contained within hormone replacement therapy (HRT) is influenced by the route of administration, and this may affect the risk of venous thromboembolism. Thrombin generation, a global coagulation assay, is a marker of hypercoagulability and is of potential use in determining the thrombotic risk associated with particular HRT administration routes.

OBJECTIVES: To determine whether any effect of oral and transdermal HRT on thrombin generation is related to the plasma estrogen profile.

METHODS: We investigated the effects of oral, transdermal and no HRT (controls) in 52, 39 and 52 postmenopausal women, respectively, on thrombin generation, standard markers of thrombophilia, estradiol level and estrone level.

RESULTS: All parameters of thrombin generation were altered in women using oral HRT as compared with controls ($P<0.001$ for all comparisons). No such differences were found in women using transdermal HRT. Estrone levels correlated with peak thrombin generation ($R=0.451$, $P<0.001$) in women using oral HRT, but there was no correlation in women using the transdermal route.

CONCLUSIONS: Thrombin generation is significantly increased in women who use HRT administered by the oral route. This is probably mediated by the hepatic first-pass metabolism of estrone, the main metabolite of oral estradiol, which is avoided by the transdermal route. The effect of estrone on thrombin generation may provide the explanation for the higher thrombotic risk seen in women using oral rather than transdermal HRT.

Feminizing Effects of Estrogen Therapy

EFFECT	ONSET[a]	MAXIMUM[a]
Redistribution of body fat	3 – 6 months	2 – 3 years
Decrease in muscle mass and strength	3 – 6 months	1 – 2 years
Softening of skin/decreased oiliness	3 – 6 months	Unknown
Decreased libido	1 – 3 months	3 – 6 months
Decreased spontaneous erections	1 – 3 months	3 – 6 months
Male sexual dysfunction	Variable	Variable
Breast growth	3 – 6 months	2 – 3 years
Decreased testicular volume	3 – 6 months	2 – 3 years
Decreased sperm production	Unknown	> 3 years
Decreased terminal hair growth	6 – 12 months	> 3 years[b]
Scalp hair	No regrowth	n/a
Voice changes	None	n/a

Medical Risks of Estrogen Therapy

- **Venous thromboembolism / clotting risk**
- Hypertension and/or edema
- Weight gain
- Migraine headaches
- Coronary artery disease
- Cerebrovascular disease
- Hypertriglyceridemia
- Elevated liver enzymes
- Cholelithiasis
- Macroprolactinoma or hyperprolactinemia
- Breast cancer risk

Masculinizing Hormonal Treatment Guidelines

Masculinizing Therapy: Therapeutic Goals

- Testosterone level 400-800 ng/dL (normal cis-male range)
- Estradiol level < 30 (postmenopausal range)
- No established reference range, some treat per clinical response
- Consider reducing testosterone dose if hematocrit > 50% and HOLD therapy with hematocrit > 53%

Medication	Start/Usual Dose	Absolute Max Dose	Frequency	Pros	Cons	Notes
Intramuscular or Subcutaneous (Testosterone Cypionate or Testosterone Enanthate) 200 mg/ml	25- 50 mg	80-100 mg	Weekly	Comparatively less frequent administration Peak of injectable may better suppress endogenous hormone production	Peak/trough fluctuation effect Self-injection/needle use or frequent in-office injections	Cypionate formulated in cottonseed oil (use if allergic to sesame) Enanthate formulated in sesame oil (use if allergic to cottonseed) Enanthate has slightly shorter half-life than cypionate
Patch (Androderm)	2mg – 4mg (2mg and 4mg patches)	6- 8mg (2x 4mg patches)	Daily	No needle use Less fluctuation in levels Good for more gradual effects	Slower to stop menses and may not fully stop at lower doses Adhesive irritation, falling off with sweat Daily application Expensive if not covered by insurance	Androderm no longer manufactures 2.5mg or 5mg patches
Topical Gel (Androgel, Axiron, Testim)	20mg – 60mg Androgel 1% is 12.5mg/actuation so need 2-5 pumps respectively Androgel 1.62% is 20.25mg/actuation so need 1-3 pumps respectively Axiron is 30mg/actuation so need 1-2 pumps respectively Testim is 50mg/5g so need 2.5g-5g respectively	100mg Androgel 1% is 12.5mg/actuation so need 8 pumps Androgel 1.62% is 20.25mg/actuation so need 2-5 pumps Axiron is 30mg/actuation so need 3-3.5 pumps Testim is 50mg/5g so need 10g	Daily	No needle use Less fluctuation in levels Good for more gradual effects More titratable dose	Slower to stop menses and may not fully stop at lower doses Risk of transferring to others/pets so must instruct how to apply per package insert Daily application Expensive if not covered by insurance	

Suggestions for Starting Masculinizing HRT

1. Start:
    a. Testosterone cypionate 25 mg weekly

2. Follow-up in 4-6 weeks :
    a. Increase the dose testosterone 50 mg weekly

3. Follow- up in 4-6 weeks
    a. Increase dose of testosterone to 80 mg weekly

4. Follow up in three months.
    a. Can increase to 100 mg weekly

Rough Dose Equivalent Chart

Injectable	Transdermal Patch	Transdermal Gel	Compounded Testosterone Cream	Pellets (2 pellets per 25 mg injected weekly)
50mg weekly (0.25mL of 200mg/mL solution)	2mg	25mg	12.5mg	300mg (4x 75mg pellets)
75mg weekly (0.375mL of 200mg/mL solution)	1mg + 2mg or 4mg	37.5mg	25mg	450mg (6x 75mg pellets)
100mg weekly (0.5mL of 200mg/mL solution)	6mg	50mg	50mg	600mg (8x 75mg pellets)
200mg weekly (1mL of 200mg/mL solution)	10mg	100mg	100mg	900mg (12x 75 pellets)

Masculinizing Effects of Testosterone Therapy

EFFECT	ONSET[a] (months)	MAXIMUM[a] (years)
Skin oiliness/acne	1 – 6	1 – 2
Facial/body hair growth	6 – 12	4 – 5
Scalp hair loss	6 – 12	variable[b]
Increased muscle mass/strength	6 – 12	2 – 5
Fat redistribution	1 – 6	2 – 5
Cessation of menses	2 – 6	n/a[c]
Clitoral enlargement	3 – 6	1 – 2
Vaginal atrophy	3 – 6	1 – 2
Deepening of voice	6 – 12	1 – 2

Medical Risks of Testosterone Therapy

- **Erythrocytosis (hematocrit > 50%)**
- **Severe liver dysfunction (transaminases > 3x upper limit)**
- Weight gain with bodyfat redistribution
- Hypertension and edema
- Coronary artery disease
- Cerebrovascular disease
- Possible risk of breast or uterine cancer
- Migraine headaches
- Metabolic problems → dyslipidemia, diabetes, sleep apnea
- Behavior changes → aggression, increased libido, mood swings

Finally

Be aware of the issues so that you can provide the best care possible to your patients regardless of gender or sexual orientation!

References

1.) **Madeline B. Deutsch, MD, MPH**
Editor; *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People*
2. Director of Clinical Services; UCSF Center of Excellence for Transgender Health

References

1.) **Madeline B. Deutsch, MD, MPH**
Editor; *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People,*
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2.) Grant JM, Mottet LA, Tanis J, Harrison J, Herman J, Keisling M. National Transgender Discrimination Survey; Report on Health and Healthcare (link is external)[Washington, DC: National Center for Transgender Equality and National Gay and Lesbian Task Force; 2010 Oct [cited 2016 Mar 10]

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1. Transline:
   - https://transline.zendesk.com/hc/en-us
2. Center Of Excellance Transgender Health
   - http://transhealth.ucsf.edu/
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