Masculinizing and Feminizing Medications for Trans* Identified Persons

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Transgender and gender non-conforming persons experience multiple health disparities including refusal of care and lack of provider knowledge regarding proper treatment. The 2011 National Transgender Discrimination Survey found that 50% of respondents reported having to teach their medical providers about transgender care. During this workshop, I will provide basic information regarding the medications often used for transgender persons experiencing gender dysphoria. I will review the risks and potential side effects of the medications as well as a timeline of expected changes. Finally, I will review the recommended lab tests needed to monitor therapy.

MASCULINIZING AND FEMINIZING MEDICATIONS FOR TRANS* IDENTIFIED PERSONS

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Disclosures

- No financial disclosures
- Non-FDA Approved Medications
- **Cisgender**
- **Lesbian**

Objectives

- Discuss healthcare discrimination in the trans* community
- Review side effects and risks of medications used to masculinize and feminize
- Understand the time course for expected changes caused by masculinizing and feminizing medications
- Analyze the lab tests recommended to monitor therapy

Transgender/Trans* Terms

- **Female To Male → Transman**
- **Male To Female → Transwoman**

- **Transition**
  - Process of moving from one gender to another
  - May no longer identify as trans* after transitioning to affirmed gender
  - "Pre-op" and "post-op" are outdated and should be avoided

Transgender Demographics

- Using broader definition of self-identifying as transgender
  - Massachusetts 2007-2009 phone interviews
  - 0.5% prevalence
    - 1/200 people
    - Average patient panel of 2500 = 12 transgender patients

UI LGBTQ Clinic Demographics

- October 2012-March 2014
- Evening clinic once/week ~ 75 weeks
- ~ 100 unique patients
- 70 trans* identified patients

Transgender Patients: Barriers to Healthcare

- Legalized discrimination
  - 34 states without employment non-discrimination policies
- Discrimination in Healthcare
  - Refusal of care: 19%
  - Violence in physician's offices: 2%
  - Lack of Provider knowledge: 50%
  - Postponing medical care: 28%

Transgender Healthcare: Medically Necessary?

- American Medical Association
- American Psychiatric Association
- American Psychological Association
- American Academy of Family Physicians
- National Association of Social Workers
- National Commission on Correctional Health Care
- World Professional Association for Transgender Health
- American Public Health Association
- American College of Obstetricians and Gynecologists

Outcomes of Gender Affirming Treatment

- Hormonal Therapy and Sex Reassignment: A Systematic Review and Meta-analysis of Quality of Life and Psychosocial Outcomes[12]
  - 28 studies
  - Improved gender dysphoria
  - Improvements in psychological functioning and comorbidities
  - Lower suicide rates
  - Higher sexual satisfaction
  - Overall improvement in the quality of life

American Medical Association

- 2008 Resolution
  - "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…Therefore, be it RESOLVED, that the AMA supports public and private health insurance coverage for treatment of gender identity disorder."

Transgender Care Guidelines

- World Professional Association for Transgender Health (WPATH)
  - Standards of Care for the Health of Transsexual, Transgender, and Gender Non-Conforming People, 7th version, released 2011.

- Criteria for Feminizing/Masculinizing Hormone Therapy
  - One referral or chart documentation of psychosocial assessment
    - Persistent, well-documented gender dysphoria
    - Capacity to make an informed decision and give consent
    - 18 years of age
      - if younger, follow the SOC for children and adolescents
    - Controlled medical or mental co-morbidities

WPATH Recommendations for Hormones and Surgery

- Mental Health Evaluation is required
- Psychotherapy is encouraged, but not required
- Hormones and surgery may be used in any combination to suit the needs of the individual patient

This sounds familiar…..

- Hormone replacement therapy
  - Estrogen and progesterone
- Male hypogonadism
  - Testosterone

Feminizing Hormones

- Estrogen
  - Route
    - Oral
    - IM
    - Transdermal
  - Contraindications
    - an estrogen-dependent cancer
    - Personal history of stroke, severe PE
- Progesterone
  - Route
    - Oral
    - IM
- Androgen Blocker: Spironolactone
  - Route
    - Oral
  - Contraindications
    - Acute kidney failure or significant kidney impairment
    - Chronic hyperkalemia

Feminizing Treatment Options

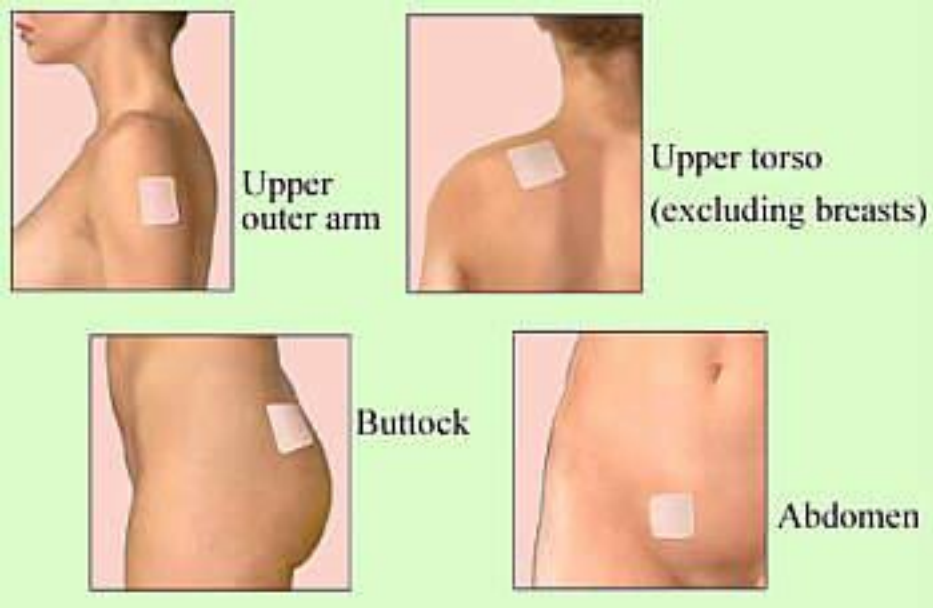
		Estrogen		
Agent		17β- estradiol[1]		
Administration		Transdermal[2]	Oral (sublingual)	Intramuscular[3]
Brand Name		Vivelle Dot/ Climara	Estrace	Depo-Estradiol (cypionate)/ Delestrogen (valerate)
Pre-orchiectomy	Starting Dose	0.1 mg/24 hrs	1-2 mg daily	10 mg q 1-2 weeks
	Max Dose	0.2 mg/24 hrs	6 mg daily (single or divided)	20-40 mg q 1-2 weeks
Post-orchiectomy[9]		0.05-0.1 mg/24 hrs weekly	1-2 mg daily	-------

Estrogen- oral

- Increased risk of blood clots with ethinyl estradiol (OCPs) and conjugated estrogens (Premarin)
  - Preferred is 17-βestradiol
- Use oral estrogen sublingually to decrease risk of VTE

Estrogen- Transdermal

- Lowest risk of VTE is transdermal
  - Use if tobacco abuse, family history of thrombosis or if >40 years



Estrogen- Intramuscular

- IM estradiol may be used to maximize breast growth
  - Use short term and switch to PO or transdermal option

Estrogen- post orchiectomy

- Need to continue estrogen post-orchiectomy
  - Maintain desired effects
  - Bone density

Feminizing Hormones: Anti-Androgens

	Androgen antagonist		Progesterone[7]		
Agent	Spironolactone	Finasteride[4]	Micronized progesterone	Medroxyprogesterone acetate	
Route	Oral	Oral	Oral	Oral	IM
Brand Name	Aldactone	Proscar (5mg)[5]	Prometrium[8]	Provera	Depo-Provera
Starting Dose	100 mg daily (single or divided)	1-5 mg daily	100 mg qhs	5 mg daily	150 mg IM q 3 months
Max Dose	200 mg BID	1-5 mg daily	200 mg daily (divided BID)	30 mg daily (divided BID)	x 2-3 years max
Post-orchiectomy	-------	1-2.5 mg daily[6]	---	---	---

Finasteride and Spironolactone

- May add finasteride to spironolactone
  - Higher doses if for systemic anti-androgen effect
  - Lower doses for male pattern baldness
  - Decreased libido, ED
  - PSA values decreased with possible increase in incidence of high-grade prostate cancer lesions
- Anti-androgens may be discontinued Post-orchiectomy
  - May continue finasteride for male pattern baldness

Progesterone

- Progesterone use controversial
  - thought to contribute to full nipple development
  - Consider 6 month trial
- Prometrium may have more favorable side effect profile
  - More expensive

Estrogen Side Effects

Risks associated with hormone therapy. Bolded items are clinically significant	
Likely increased risk	**VTE** Gallstones Elevated LFTs Weight gain **Hypertriglyceridemia**
Likely increased risk with presence of additional risk factors	Cardiovascular disease
Possible increased risk	**Hypertension** Hyperprolactinemia or prolactinoma
Possible increased risk with presence of additional risk factors	**Type 2 diabetes mellitus**
No increased risk or inconclusive	**Breast cancer**

WPATH Standards of Care, version 7.

MTF: Treatment Side Effects – Androgen Suppression

- Spironolactone
  - Hyperkalemia
  - Hypotension
- Finasteride
  - ↓libido
  - Sexual dysfunction
  - Breast tenderness
- Progestin
  - Depression
  - Weight gain
  - Lipid changes
  - ↑risk CAD, stroke, VTE

J Clin Endocrinol Metab. 2009;94(9):3132-54.
Journal of Transgenderism. 2006;9:111-34.

Feminizing Therapy Lab Tests

- Baseline
  - Lipids, fasting glucose, AST/ALT, potassium, creatinine
- 3 and 6 months after starting/changing dose
  - Testosterone, potassium, creatinine, ALT
- 12 months and annually
  - Testosterone, potassium, creatinine, ALT, lipids, fasting glucose, prolactin

Feminizing Therapy Lab Tests

- Estrogen may improve lipids, though increase triglycerides
- If elevation of ALT with oral estradiol, switch to transdermal
- Goal testosterone is low end of normal female
- Check prolactin annually for 1-3 years on stable dose
  - >40 → decrease estrogen dose by 50% and recheck in 6-8 weeks.
  - >100→ stop estrogen and recheck in 6-8 weeks. If continued to be elevated, consider MRI.

Feminizing Therapy

- Most effects reversible
- Breast development is permanent
- Impaired fertility may be permanent
- Treatment limitations
  - Voice unaffected
  - Breast growth and development is variable
  - Hormone tx may not alter body hair growth enough

Feminizing Treatment Effects

Effect	Expected Onset	Expected Maximum Effect
Body fat redistribution	3-6 months	2-5 years
Decreased muscle mass/strength	3-6 months	1-2 years
Softening of skin/decreased oiliness	3-6 months	Unknown
Decreased libido	1-3 months	1-2 years
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	Variable	Variable
Thinning and slowed growth of body/facial hair	6-12 months	>3 years
Male pattern baldness	No regrowth, loss stops 1-3 months	1-2 years

WPATH Standards of Care, Version 7.

Feminizing Treatment Cost

Medication	Average Cost (per month)
Vivelle-Dot (patch)	$85
Climara (patch)	$41
Estradiol (oral)	$8
Estrogen valerate (IM)	$150
Spironolactone (oral)	$35
Finasteride (oral)	$75
Progesterone (oral)	$63
Medroxyprogesterone	$10
Depo-Provera	$85

Masculinizing Hormones

- Testosterone
  - Route of Administration
    - IM
    - SQ
    - Transdermal
  - Contraindications
    - Pregnancy
    - Uncontrolled coronary artery disease

Masculinizing Treatment Options

		Intramuscular/Subcutaneous Injection[1]	
Agent		Tesosterone Cypionate	Testosterone Enanthate
Brand Name		Depo-Tesosterone	Delatestryl
Pre-oophorectomy	Starting Dose	50-100 mg weekly (or 100-200 mg q 2 weeks)[2]	
	Max Dose	125 mg weekly (or 250 mg q 2 weeks)[3]	
Post-oophorectomy	Decrease dose by 3/4		

Testosterone - Injections

- May be administered SQ or IM
  - Levels and effects appear to be the same
- 3 ml syringes (with 21 g. needles) - for drawing up
- 25 g 5/8" needles - for subcutaneous
- 23 g 1" – 1 1/2" needles for IM

Testosterone IM or SQ

- Start every two weeks
- Increase to weekly if history of mood disorders, PCOS, obesity, lack of menstrual cycle suppression
- Caution increasing too high
  - Excessive testosterone is converted to estrogen

Masculinizing Therapy- Transdermal

Agent	Transdermal Gel[5]	Transdermal Topical Solution	Transdermal Patch
	Testosterone crystals dissolved in gel[4]		
Brand Name	AndroGel[6]/Testim[7]	Axiron[8]	Androderm (2 or 4 mg/patch)
Starting Dose	50mg daily	30 mg (1 pump) to each underarm (60 mg/day)	2-4 mg daily
Max Dose	100 mg daily	120 mg/day	10 mg daily
Post-oophorectomy	Decrease dose by ¾		

Transdermal Testosterone

- Slower masculinization
- Possibility of virilizing others if skin-skin contact
- Transdermal may be a nice option for post-oophorectomy

Testosterone Post-oophorectomy

- Decrease dose by ¾
  - Must continue to maintain desired effects
  - Preserve bone health

Testosterone Side Effects

Risks associated with hormone therapy. Bolded items are clinically significant	
Likely increased risk	**Polycythemia** Weight gain Acne Androgenic alopecia Sleep apnea
Likely increased risk with presence of additional risk factors	
Possible increased risk	Elevated LFTs **Hyperlipidemia (↑TG, ↓HDL)**
Possible increased risk with presence of additional risk factors	**Destabilization of certain psychiatric disorders** **Cardiovascular disease** **Hypertension** **Type 2 diabetes mellitus**
No increased risk or inconclusive	Loss of bone density **Breast cancer** **Cervical cancer** **Ovarian cancer** **Uterine cancer**

WPATH Standards of Care, version 7.

Masculinizing Therapy Lab Tests

- Baseline
  - Lipids, CBC, fasting glucose, ALT
- 3 and 6 months after starting/changing dose
  - Testosterone, ALT, CBC
- 12 months and annually
  - Testosterone, ALT, CBC, lipids, fasting glucose

Masculinizing Lab Tests

- Testosterone may decrease HDL and increase risk of cardiovascular disease
- Compare H/H to normal male levels
- No strong evidence for checking liver enzymes
- Measure testosterone mid trough if IM
- Goal is normal male range for age

Testosterone Treatment Effects

- Most effect reversible
- Deepening of voice and changes to facial/scalp hair are permanent
- Fertility effects may be permanent

Journal of Transgenderism. 2006;9:111-34.

Testosterone Effects

Effect	Expected Onset	Expected Maximum Effect
Skin oiliness/acne	1-6 months	1-2 years
Facial/body hair growth	3-6 months	3-5 years
Scalp hair loss	>12 months	Variable
Increased muscle mass/strength	6-12 months	2-5 years
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

WPATH Standards of Care, Version 7

Testosterone Treatment Cost

Medication	Average Cost (per month)
Testosterone cypionate (IM)	$105
Testosterone enanthate (IM)	$87
AndroGel (packets)	$340
AndroGel (Pump)	$358
Testim (tubes)	$378
Axiron (pump)	$331
Androderm (patch)	$378

Take Home Points

- Trans* patients report a lack of provider knowledge and refusal of care
- Hormone therapy for trans* folks is similar to hormone therapy for cisgender people
- Side effects and co-morbidities can be managed

Questions???

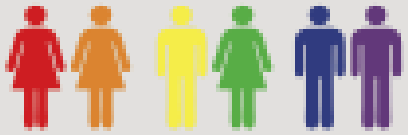
University of Iowa Hospitals and Clinics

Lesbian, Gay, Bisexual, Transgender, Queer, and Questioning Clinic

Nicole Nisly, MD (Internal Medicine) and
Katie Imborek, MD (Family Medicine).

Providing comprehensive primary care for adult and child (over 10 years) LGBTQ patients including:

- Routine physical exams and wellness
- Chronic disease management
- Urgent care visits
- Gynecologic and obstetric care
- Contraceptive management
- STI testing and treatment
- Hormone therapy
- Post-surgical care



HOURS
Tuesday evenings 5-8 p.m.

LOCATION AND CONTACT
UI Hospitals and Clinics
Iowa River Landing, 105
East 9th Street, Level 4
Coralville, IA
319-384-7444 (option 1)

www.uihealthcare.org/lgbt/

Resources

- Center of Excellence for Transgender Health
  - http://transhealth.ucsf.edu
- WPATH Standards of Care
  - http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351
- Endocrine Society Guidelines
  - http://www.endocrine.org/~/media/endosociety/Files/Publications/Clinical%20Practice%20Guidelines/Endocrine-Treatment-of-Transsexual-Persons.pdf