Masculinizing and Feminizing Medications for Trans* Identified Persons

Katie Imborek, MD
University of Iowa Carver College of Medicine, Clinical Assistant Professor, Co-Director
UI LGBTQ Clinic

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.
MASCU LINIZING AND FEMINIZING MEDICATIONS FOR TRANS* IDENTIFIED PERSONS
APRIL 12, 2014

Katie Imborek, MD
Assistant Professor
Family Medicine
Co-Director UI LGBTQ Clinic
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  - “Pre-op” and “post-op” are outdated and should be avoided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
  - 28 studies
  - Improved gender dysphoria
  - Improvements in psychological functioning and comorbidities
  - Lower suicide rates
  - Higher sexual satisfaction
  - Overall improvement in the quality of life
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

<table>
<thead>
<tr>
<th></th>
<th>Estrogen</th>
<th>17β-estradiol&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Administration</strong></td>
<td>Transdermal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Oral (sublingual)</td>
</tr>
<tr>
<td><strong>Brand Name</strong></td>
<td>Vivelle Dot/Climara</td>
<td>Estrace</td>
</tr>
<tr>
<td><strong>Pre-orchiectomy</strong></td>
<td>Starting Dose</td>
<td>0.1 mg/24 hrs</td>
</tr>
<tr>
<td></td>
<td>Max Dose</td>
<td>0.2 mg/24 hrs</td>
</tr>
<tr>
<td><strong>Post-orchiectomy&lt;sup&gt;9&lt;/sup&gt;</strong></td>
<td>0.05-0.1 mg/24 hrs weekly</td>
<td>1-2 mg daily</td>
</tr>
</tbody>
</table>
Estrogen- oral

- Increased risk of blood clots with ethinyl estradiol (OCPs) and conjugated estrogens (Premarin)
  - Preferred is 17-β estradiol
- 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

<table>
<thead>
<tr>
<th>Agent</th>
<th>Androgen antagonist</th>
<th>Progesterone&lt;sup&gt;7&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>Finasteride&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Micronized progesterone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medroxyprogesterone acetate</td>
</tr>
<tr>
<td>Route</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Brand Name</td>
<td>Aldactone</td>
<td>Proscar (5mg)&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Starting Dose</td>
<td>100 mg daily (single or divided)</td>
<td>1-5 mg daily</td>
</tr>
<tr>
<td>Max Dose</td>
<td>200 mg BID</td>
<td>1-5 mg daily</td>
</tr>
<tr>
<td>Post-orchiectomy</td>
<td>-------</td>
<td>1-2.5 mg daily&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Risks associated with hormone therapy. Bolded items are clinically significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely increased risk</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Likely increased risk with presence of additional risk factors</td>
</tr>
<tr>
<td>Possible increased risk</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Possible increased risk with presence of additional risk factors</td>
</tr>
<tr>
<td>No increased risk or inconclusive</td>
</tr>
</tbody>
</table>

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.
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

<table>
<thead>
<tr>
<th>Effect</th>
<th>Expected Onset</th>
<th>Expected Maximum Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body fat redistribution</td>
<td>3-6 months</td>
<td>2-5 years</td>
</tr>
<tr>
<td>Decreased muscle mass/strength</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Softening of skin/decreased oiliness</td>
<td>3-6 months</td>
<td>Unknown</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>1-3 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Decreased spontaneous erections</td>
<td>1-3 months</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Male sexual dysfunction</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Breast growth</td>
<td>3-6 months</td>
<td>2-3 years</td>
</tr>
<tr>
<td>Decreased testicular volume</td>
<td>3-6 months</td>
<td>2-3 years</td>
</tr>
<tr>
<td>Decreased sperm production</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Thinning and slowed growth of body/facial hair</td>
<td>6-12 months</td>
<td>&gt;3 years</td>
</tr>
<tr>
<td>Male pattern baldness</td>
<td>No regrowth, loss stops 1-3 months</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

WPATH Standards of Care, Version 7.
## Feminizing Treatment Cost

<table>
<thead>
<tr>
<th>Medication</th>
<th>Average Cost (per month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vivelle-Dot (patch)</td>
<td>$85</td>
</tr>
<tr>
<td>Climara (patch)</td>
<td>$41</td>
</tr>
<tr>
<td>Estradiol (oral)</td>
<td>$8</td>
</tr>
<tr>
<td>Estrogen valerate (IM)</td>
<td>$150</td>
</tr>
<tr>
<td>Spironolactone (oral)</td>
<td>$35</td>
</tr>
<tr>
<td>Finasteride (oral)</td>
<td>$75</td>
</tr>
<tr>
<td>Progesterone (oral)</td>
<td>$63</td>
</tr>
<tr>
<td>Medroxyprogesterone</td>
<td>$10</td>
</tr>
<tr>
<td>Depo-Provera</td>
<td>$85</td>
</tr>
</tbody>
</table>
Masculinizing Hormones

Testosterone

- **Route of Administration**
  - IM
  - SQ
  - Transdermal

- **Contraindications**
  - Pregnancy
  - Uncontrolled coronary artery disease
## Masculinizing Treatment Options

<table>
<thead>
<tr>
<th></th>
<th>Intramuscular/Subcutaneous Injection(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent</strong></td>
<td>Tesosterone Cypionate</td>
</tr>
<tr>
<td></td>
<td>Testosterone Enanthate</td>
</tr>
<tr>
<td><strong>Brand Name</strong></td>
<td>Depo-Tesosterone</td>
</tr>
<tr>
<td></td>
<td>Delatestryl</td>
</tr>
<tr>
<td><strong>Pre-oophorectomy</strong></td>
<td><strong>Starting Dose</strong></td>
</tr>
<tr>
<td></td>
<td>50-100 mg weekly (or 100-200 mg q 2 weeks)(^2)</td>
</tr>
<tr>
<td><strong>Max Dose</strong></td>
<td>125 mg weekly (or 250 mg q 2 weeks)(^3)</td>
</tr>
<tr>
<td><strong>Post-oophorectomy</strong></td>
<td><strong>Decrease dose by 3/4</strong></td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Agent</th>
<th>Transdermal Gel[^5]</th>
<th>Transdermal Topical Solution</th>
<th>Transdermal Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Name</td>
<td>AndroGel[^6]/Testim[^7]</td>
<td>Axiron[^8]</td>
<td>Androderm (2 or 4 mg/patch)</td>
</tr>
<tr>
<td>Starting Dose</td>
<td>50mg daily</td>
<td>30 mg (1 pump) to each underarm (60 mg/day)</td>
<td>2-4 mg daily</td>
</tr>
<tr>
<td>Max Dose</td>
<td>100 mg daily</td>
<td>120 mg/day</td>
<td>10 mg daily</td>
</tr>
<tr>
<td>Post-oophorectomy</td>
<td></td>
<td>Decrease dose by ¾</td>
<td></td>
</tr>
</tbody>
</table>
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 |
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
## Testosterone Effects

<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>

WPATCH Standards of Care, Version 7
## Testosterone Treatment Cost

<table>
<thead>
<tr>
<th>Medication</th>
<th>Average Cost (per month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone cypionate (IM)</td>
<td>$105</td>
</tr>
<tr>
<td>Testosterone enanthate (IM)</td>
<td>$87</td>
</tr>
<tr>
<td>AndroGel (packets)</td>
<td>$340</td>
</tr>
<tr>
<td>AndroGel (Pump)</td>
<td>$358</td>
</tr>
<tr>
<td>Testim (tubes)</td>
<td>$378</td>
</tr>
<tr>
<td>Axiron (pump)</td>
<td>$331</td>
</tr>
<tr>
<td>Androderm (patch)</td>
<td>$378</td>
</tr>
</tbody>
</table>
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
319-334-7444 (option 1)

www.uihealthcare.org/lgbt/
Resources

- Center of Excellence for Transgender Health
  - [http://transhealth.ucsf.edu](http://transhealth.ucsf.edu)

- WPATH Standards of Care
  - [http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351](http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351)

- Endocrine Society Guidelines