Transgender Women, Hormone Therapy, and HIV

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Disclosure

I have no real or perceived vested financial interests that relate to this presentation nor do I have any relationships with pharmaceutical companies, biomedical device manufacturers, and/or other corporations whose products or services are related to pertinent therapeutic areas.

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Objectives

1. Describe key elements of primary medical care for transgender women with HIV
2. List commonly used medications for gender affirmation among transgender women
3. Identify common drug-drug interactions in the care of transgender women with HIV

Definitions

- Transgender or Trans
  - Umbrella term to describe people who identify with a gender that differs from their natal sex
- Trans woman
  - Currently identifies as a woman
- Trans man
  - Currently identifies as a man

This presentation will focus on trans women who bear the heaviest burden of HIV
Case 1: Mariana

- 35-year-old trans woman is referred to you after testing positive for HIV during a recent visit to the county sexually transmitted diseases (STD) clinic.

- She has lived as a woman for the last twenty years. She has received only intermittent medical care, relying on underground estrogen and silicone injections to maintain a feminine appearance. She has not had any genital surgery.

- CD4 count of 209 cells/mm³
- HIV RNA 156,000 copies/ml
- She is otherwise healthy
- She is interested in both hormonal therapy and antiretrovirals

Fears about health care
Consequences of Poor Access to Care

- **Illicit hormone use**
  - Internet, international, veterinary supply, “herbal”
  - Doses are guessed at and usually are too high
  - Sharing vials of hormones and/or syringes

- **Illicit soft tissue filler use**
  - Injection of silicon gel, oils, and other substances
  - Risks include
    - Infections/sepsis from unsterile technique
    - Blood borne pathogens from contaminated syringes
    - Inflammation, granulomas and scarring
    - Disfigurement due to shifts of silicone
    - Immediate death due to emboli

- **Delayed HIV testing**
  - 45-65% of HIV-positive trans women unaware of status

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Gardner et al., 2011; Herbst, 2007; Houston Area Ryan White Planning Council, 2013; Melendez, 2005

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**HIV Treatment Cascade**

- **Overall**
  - 100% infected, 80% diagnosed, 62% linked to care, 36% on treatment, 28% undetectable

- **Trans women**
  - 100% infected, 50% diagnosed, 38% linked to care, 24% on treatment, 18% undetectable
HIV Prevalence

- **First published meta-analysis (2008)**
  - 28% among all trans women
  - 56% among AA trans women
  - Most studies among street-based sex workers

- **Recent global meta-analysis (2012)**
  - 22% in the United States
  - OR = 34 (CI: 31-38) compared to general population

Herbst 2008, Baral 2012

Improving the Cascade for Trans Women

- **Barriers to Engagement & Retention in HIV Care**
  - Avoidance due to stigma and past negative experiences
  - Prioritization of hormone therapy
  - Concerns about interactions between HIV meds and hormones

- **Facilitators of Engagement & Retention in Care**
  - Providers knowledgeable about trans-related medical issues
  - Able to provide and integrate hormone therapy and HIV care
  - All staff respectful and sensitive to trans issues (eg. IDs)

- **Correlates of Adherence and Viral Load**
  - Less stress due to trans discrimination (adherence and VL)
  - Adherence to hormone therapy (adherence)

Sevelius, Ann Behav Med, 2014; Sevelius, AIDS Care, 2014
CASE 2: Chantelle

40 year old HIV-positive trans woman has requested hormones from you. She wants to ‘go all the way’ with feminization but she desires continued erectile function until she can have genital surgery.

- PMH: Hypertension, Hyperlipidemia, Type 2 DM – all well controlled
- SH: Smokes 1PPD and daily marijuana, occasional beer, no current relationship, inconsistent condom use with casual partners.
- Meds: HCTZ, Pravastatin, Metformin, TDF/FTC, ATV/r
- Labs: CD4 400, HIV RNA <74, Other labs unremarkable

Responsibilities of Hormone Prescribers

1. Perform an initial evaluation
2. Discuss the expected effects of medications, including sexual and reproductive
3. Confirm that patients have the capacity to understand the risks and benefits and make an informed decision
4. Provide ongoing medical monitoring
5. Communicate as needed with other providers
6. If needed, provide patients with a brief written statement indicating that they are under medical supervision and care that includes feminizing or masculinizing hormone therapy
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Key Concepts for Hormone Therapy

- Getting gender care and HIV care at the same place may improve adherence to both
- Several hormone protocols are readily available
  - Endocrine Society, UCSF, Callen-Lorde
- Higher doses result in faster changes, but same end result with higher risk
  - Heredity limits tissue response
- Second puberty
  - It takes just as long to complete as the first
  - Only reverses some of the effects of the 1st puberty
Common Medications for Feminization

- **Anti-androgens**
  - Spironolactone
  - Finasteride

- **Estrogens**
  - Conjugated Equine Estrogen (CEE)
  - Estradiol (oral, injectable, patch)

- **Progesterone**
  - Use is controversial
  - Some find it helps with early breast development
  - Adverse effects: weight gain, irritability, hyperlipidemia, liver disease, etc.


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### Anti-Androgens

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Starting Dose</th>
<th>Average Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone (Aldactone)</td>
<td>50 mg/day</td>
<td>100 mg/day</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>Finasteride (Proscar)</td>
<td>1 mg/day</td>
<td>5 mg/day</td>
<td>5mg/day</td>
</tr>
</tbody>
</table>

Hembree 2009; WPATH SOC 2011; Callen Lorde Protocols 2012.
Anti-Androgens: Spironolactone

- **Benefits**
  - Modest breast development
  - Softening of facial and body hair
  - Enable feminization on a lower dose of estrogen

- **Risks**
  - Hyperkalemia
  - Hypotension
  - Drug Interactions

- **Contraindications**
  - Renal insufficiency
  - Serum potassium > 5.5
  - ACE/ARB therapy

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What to prescribe: Estrogens

<table>
<thead>
<tr>
<th>Hormone Name</th>
<th>Starting Dose</th>
<th>Average Dose</th>
<th>Max Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-β Estradiol oral (Estrace)</td>
<td>2 mg/day</td>
<td>4 mg/day</td>
<td>6 mg/day</td>
</tr>
<tr>
<td>17-β Estradiol Valerate IM (Delestrogen)</td>
<td>20mg IM q 2wks</td>
<td>20-40 IM q 2wks</td>
<td>40mg IM q 2wks</td>
</tr>
<tr>
<td>17-β Estradiol cypionate IM (Depo-Estradiol)</td>
<td>2.5mg IM q 2wks</td>
<td>5.0 mg IM q 2wks</td>
<td>10mg IM q 2wks</td>
</tr>
<tr>
<td>17-β Estradiol patch</td>
<td>0.1-0.2 mg/day</td>
<td>0.2-0.3 mg/day</td>
<td>0.3 mg/day</td>
</tr>
<tr>
<td>CEE (Premarin)</td>
<td>1.25-2.5mg/day</td>
<td>5 mg/day</td>
<td>10 mg/day</td>
</tr>
</tbody>
</table>

Ethynyl estradiol (OCPs) NOT recommended due to higher embolic risk at feminizing doses

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Hembree 2009; WPATH SOC 2011; Calen Lorde Protocols 2012;
### Expected Effects and Timing of Feminizing Hormone Therapy (SOC7)

<table>
<thead>
<tr>
<th>Expected 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>Softer 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>Erectile 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/reduced growth face/body hair</td>
<td>6-12 months</td>
<td>&gt; 3 years</td>
</tr>
<tr>
<td>Improvement in male pattern baldness (no regrowth)</td>
<td>Loss stops 1-3 months</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

### Risks associated with Estrogen Therapy

<table>
<thead>
<tr>
<th>Level</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely increased risk</td>
<td>Venous thromboembolic disease</td>
</tr>
<tr>
<td></td>
<td>Hypertriglyceridemia</td>
</tr>
<tr>
<td></td>
<td>Gallstones</td>
</tr>
<tr>
<td></td>
<td>Elevated liver enzymes</td>
</tr>
<tr>
<td></td>
<td>Weight gain</td>
</tr>
<tr>
<td>Likely increased risk when additional risk factors present</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Possible increased risk</td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Hyperprolactinemia or prolactinoma</td>
</tr>
<tr>
<td>Possible increased risk when additional risk factors present</td>
<td>Type 2 Diabetes Mellitus</td>
</tr>
<tr>
<td>No increased risk or inconclusive</td>
<td>Breast cancer</td>
</tr>
</tbody>
</table>
Contraindications to Estrogen

- **Absolute**
  - History of estrogen-dependent cancer
  - Thrombotic event and/or hypercoagulable condition
  - End-stage chronic liver disease

- **Relative**
  - Smoking
  - Uncontrolled hypertension
  - Uncontrolled diabetes
  - Desire to maintain fertility
  - History of clotting disorder, DVT, PE
  - Liver disease
  - Hyperprolactinemia
  - Untreated or treatment resistant depression
  - Migraine

Risks Reduction (VTE)

- Use minimum effective dose
- Add aspirin if > 40 yo
- **STOP SMOKING**
- Use transdermal patch if smoker >40yo
- Stop 2 weeks before surgery or immobilization
Summary: common feminizing regimen

Estradiol 2 mg to 6 mg daily

and

Spironolactone 100-200 mg divided BID or
Finasteride 5 mg daily

plus aspirin 81-325 mg daily if over age 40

Laboratory Monitoring

- Check potassium at baseline and 1-2 months after starting or increasing dose of spironolactone
- Check testosterone, liver enzymes, fasting lipids, and glucose at baseline and 1 month after starting or increasing estrogen, then every 3-6 months.
- Check prolactin at baseline and repeat if symptoms
- Goals
  - Achieve desired clinical response at lowest dose
  - May seek testosterone in female range, but unnecessary if goal achieved at a higher range
  - It’s not essential to check estradiol levels.

Hembree 2009; WPATH SOC 2011; Cullen Lorde Protocols 2012;
Follow-Up Care

- Subjective
  - Assess and document feminization
  - Review medication use (including illicit and OTC)
  - Monitor mood and social impact of transition
    - Identify social needs (ID documents, etc.)
  - Counsel re: silicone, sexual activity, smoking/CVD risk

- Objective
  - STD screening and preventive care, as indicated
  - Clinical breast exam +/- mammography (unclear when)
  - Bone density, as indicated by other risks
  - Prostate screening even after genital surgery

CASE 3: Janet

21 yo HIV trans woman on antiretrovirals and feminizing hormone therapy comes to clinic complaining of poor appetite, loss of interest in her usual activities.

She had unwanted side effects when she was on paroxetine in the past and wants to see if St. John’s Wort will improve her mood.

- PMH: Major depression, Chronic Hepatitis B
- SH: Binge drinks at parties on weekends, non-smoker
- Meds: Estradiol 6 mg QD, Spironolactone 100mg BID, TDF/FTC, DRV/r
- Labs: CD4 620, VL 100, AST 68, ALT 100
Cytochrome (CYP) P450 metabolism

- **Common inducers (they reduce drug levels)**
  - Smoking
  - St. John’s Wort
  - All Protease Inhibitors
  - NNRTI’s

- **Common inhibitors (they raise drug levels)**
  - Grapefruit
  - Statins
  - Azoles (anti-fungals)

- **Mixed inducer/inhibitor**
  - Efavirenz
Drug Interaction

Estradiol levels are **DECREASED** by:

- Cigarette smoking
- Nelfinavir
- Nevirapine
- Ritonavir
- Lopinavir
- Rifampin
- Progesterone
- Dexamethasone
- Naphthoflavone
- Telaprevir
- Sulfamidine
- Carbamazepine
- Phenytoin
- Phenobarbital
- Phenylbutazone
- Benzoflavone
- Sulfinpyrazone

www.hivwebstudy.org

Drug Interaction

Estradiol levels are **INCREASED** by:

- Isoniazid
- Fluvoxamine
- **Fluoxetine**
- Sertraline
- Paroxetine
- Diltiazem
- Verapamil
- Cimetidine
- Astemizole
- Itraconazole
- Ketoconazole
- Fluconazole
- Miconazole
- Clarythromycin
- Erythromycin
- Grapefruit

www.hivwebstudy.org
Janet

- She was advised against taking St. Johns Wort and was not restarted on paroxetine due to past side effects and potential drug interactions with estradiol.

- She's started on citalopram and her mood improves

- However, her follow-up labs: CD4 600 and VL 800

- She admits to skipping doses of ARVs because they give her hot flashes.

### ARVs and Hormonal Contraceptives

**DHHS Guidelines**

<table>
<thead>
<tr>
<th>Ritonavir-boosted Protease Inhibitors</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td>↑ norgestimate</td>
</tr>
<tr>
<td>Darunavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td>↓ norethindrone</td>
</tr>
<tr>
<td>Fosamprenavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td>↓ norethindrone</td>
</tr>
<tr>
<td>Lopinavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td>↓ norethindrone</td>
</tr>
<tr>
<td>Saquinavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td></td>
</tr>
<tr>
<td>Tipranavir/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓</td>
<td>EE</td>
<td>no Δ norethindrone</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protease Inhibitors without Ritonavir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Fosamprenavir</td>
</tr>
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<td></td>
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</tbody>
</table>
ARVs and Hormonal Contraceptives

<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Efavirenz</th>
<th>Etravirine</th>
<th>Nevirapine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>↔ EE</td>
<td>↑ EE</td>
<td>↓ EE</td>
</tr>
<tr>
<td></td>
<td>↓ Levenorgestrel</td>
<td>No ∆ Norethindrone</td>
<td>No ∆ Norethindrone</td>
</tr>
<tr>
<td></td>
<td>↓ Norelgestromin</td>
<td></td>
<td>No ∆ DMPA</td>
</tr>
<tr>
<td>Use alternative methods.</td>
<td>No dose adjustment necessary</td>
<td>Use alternative methods</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>Norelgestromin &amp; levonorgestrel are active metabolites of norgestimate.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CCR5 Antagonist</th>
<th>Maraviroc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No ∆ EE or levonorgestrel</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Integrase Inhibitor</th>
<th>Raltegravir</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No clinically significant effect</td>
</tr>
</tbody>
</table>

Estrogens & Antiretrovirals

- **DHHS evidence based on oral contraceptives**
  - Oral contraceptives use ethinyl estradiol at contraceptive doses
  - Hormones for transgender patients usually are 17-β estradiol or conjugated equine estrogen (CEE)

- **Most drug interactions decrease estrogen levels**
  - If estrogen is continued and antiretrovirals are stopped, this may lead to dangerously high estrogen levels with associated risk of adverse effects
Janet

- She was switched from TDF/FTC, DRVr to TDF/FTC, RTG
- She reports that she pairs her twice daily hormones with her twice daily ARVs and does not have trouble remembering to take them.
- Her repeat viral load is <75

Drug Interactions - Take Homes

- Amprenavir and Fosamprenavir are the only antiretrovirals that should not be co-administered with estrogen due to risk of virologic failure.
- No interactions between androgen blockers and antiretrovirals, but lower doses may be adequate.
- Some HIV medications change the levels of estrogens, therefore estrogen dose adjustment may be necessary.
- Patients may prioritize hormone therapy over HIV treatment and discontinue ARVs if they notice a problem.
Medical Resources

- World Professional Association for Transgender Health
  - (SOC 2001, update expected in September 2011)
    - http://www.wpath.org/publications_standards.cfm

- Tom Waddell Clinic (2006 Protocols)

- Endocrine Society (Clinical Practice Guidelines 2009)

- British Columbia

- New England Journal of Medicine (Gooren 2011)

- Transgender COE (Primary Care Protocols 2011)
  - http://www.transhealth.ucsf.edu/tcoe?page=protocol-00-00

Expert Advice at Your Fingertips

HIV/AIDS Clinical Consultation
1-800-933-3413
Mon-Fri 8am to 8pm EST
www.ucsf.edu/hivcntr