Treating HIV in Transgender Patients: A Clinical Update

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Transgender Populations

- Transgender (trans): people whose gender identity differs from assigned birth sex
  - Trans women – current female/feminine identity
  - Trans men – current male/masculine identity
- Genderqueer: identify as neither entirely male nor female; or identify as combination of male and female
- Cisgender (cis): non-transgender

- 25 million transgender people worldwide
- 1.4 million transgender people in United States
  - Approximately 0.6% of the population

Caveat: prevalence depends on definition
  - eg, medical therapy, diagnosis of GD, self-report


Transgender Men

- Systematic review (2012-2015)
- 6 U.S. prevalence studies
  - 5 Laboratory-tested: 0.5% - 4.3% (n=1)

Laboratory Confirmed HIV Prevalence

Potential HIV risk among TMSM

- Testosterone associated with shifting sexual desires
- Increased sexual frequency
- Greater likelihood of cis-male sexual partnerships

Poteat et al. JAIDS 2016, Dadasovich et al. CHS 2016
Transgender Women

- Global meta-analysis of laboratory-confirmed HIV (2000-11)
  - 22% prevalence in the United States
  - 34-fold greater than the general population
- Systematic review and data synthesis (2012-2015)
  - Highest: 40% among trans women of color
  - Lowest: 4.5% in youth (16-24 years old)
  - Incidence estimate: 2.9 per 100 person-years

Alexis Rivera, transgender activist
Died from HIV at age 34 (2012)

Baral et al. TLOD 2013, Poteat et al. JAIDS 2016

HIV Care and Viral Suppression

- Transgender N=3,900

Gender Affirmation and HIV Care

- Top 5 Health Concerns of HIV+ trans people, in order
  1. Gender-affirming and non-discriminatory care
  2. Hormone therapy and side effects
  3. Mental health care, including trauma
  4. Personal care, eg. nutrition
  5. Antiretroviral therapy and side effects

- TW whose HIV primary care provider is also their hormone prescriber, more likely to:
  - Have an undetectable viral
  - Have an HIV primary care visit in the previous 6 months

Deutsch 2015 (preliminary self-report data presented at NHPC); Positively Trans Survey, n = 157
Dimensions of Gender Affirmation

Social Gender Affirmation
- Preferred Name
- Preferred Pronoun

Psychological Gender Affirmation
- Felt Gender is Respected and Validated
- Resist Internalized Stigma and Transphobia

Medical Gender Affirmation
- Pubertal Blockers
- Hormone Therapy
- Gender Confirmation Surgery

Legal Gender Affirmation
- Legal Name Change
- Legal Gender Marker Change

Gender-Affirming Clinical Settings

- Do not assume gender identity or sexual orientation
- Use gender-neutral forms of address, until sure of gender
  - Eg. Ma’am, Sir, Mr./Mrs./Ms.
- Use 2-step process to determine gender identity at intake
  - Determining which pronoun to use (eg. he, she, they)?
    - Ask politely and privately
    - What is the presenting gender?
    - Echo the language you hear
    - Use the correct pronoun consistently

- Anatomical terms – what words to use
  - Avoid terms like “post-op” and “pre-op”
  - Ask about anatomy, only if you need to know

Ascertaining Gender Identity

1. What is your current gender identity?
   - Male
   - Female
   - Transgender Male/Transman/FTM
   - Transgender Female/Transwoman/MTF
   - Genderqueer
   - Additional category (please specify):
     - Decline to answer

2. What sex were you assigned at birth?
   - Male
   - Female
   - Decline to answer
Case 1: Chantelle
- 26 year old trans woman presents with newly diagnosed HIV, requests hormones and sildenafil
- PMH: no significant illness or hospitalizations
- Medications: None
- LABS:
  - CD4 count 175
  - Viral load 80,000
  - Other labs normal
- PHYSICAL EXAM:
  - Bilateral breast buds
  - Feminine body contour
  - Otherwise unremarkable

What are her HIV-related needs?
What are her primary care needs?
What questions do you have?

Initial Visits: Medical History
- Document history of gender interventions
  - Social transition (tucking, binding, etc.)
  - Hormone dose, duration, prescription and "street"
  - Use of needles for hormone injection (shared)
  - Silicone injections or other fillers, "pump parties"
  - Gender affirming surgeries
- Review gender-related goals
  - Legal, physical, social etc.
- Address psychosocial issues
  - Depression, PTSD, substance use history
  - Employment, sex work history, safety
  - Assess social support system (eg. disclosure, "passing")
Initial Visits – Best Practices

• Transgender patients probably have had previous negative healthcare experiences
  • Developing trust and rapport may take longer than usual. Use principles of trauma-informed care
  • Pay attention to pronouns, names, gender markers
• Avoid genital/rectal exams on first visit, if possible
  • History of sexual abuse and trauma is common
  • Discuss choice of language to describe anatomy
  • Facilitate sensitive sexual health services
    • Use gender neutral terms, avoid possessive pronouns
    • Seek permission for any exam, creative collaboration

Sexual History: Example Questions

□ Tell me about your recent sexual relationships.
  □ How many partners have you had in last 3 months?
  □ What are the genders of your partners?
□ What kinds of sex are you having?
  □ Which behaviors might expose you to others fluids?
  □ Which behaviors might expose others to your fluids?
  □ How do you protect yourself? (Your partners?)
  □ How often do you use barriers? Tell me about the times that you don’t use barriers. Tell about the times you do.
□ What words do you like to use for your body parts?

Preventive Care: Anatomy-based screening

□ Prostate screening
  □ All trans women with prostate per current guidelines
□ Testicular exams
  □ All trans women with testes per guidelines
□ Breast exams and mammography
  □ Based on amount of estrogen exposure and age
□ Anal and/or neovaginal pap smears, HPV screening
  □ Based on sexual behavior and type of neovagina
□ STD screening based on sexual behavior
  □ Screen all sites of exposure, screen more often if at high risk
Medical and Surgical Interventions

Feminizing (MTF)
- Hormones (estrogen)
- Androgen blockers
- Breast augmentation
- Labiaplasty
- Vaginoplasty
  - Penile inversion
  - Sigmoid colon
- Orchiectomy
- Tracheal shave
- Facial feminization

Masculinizing (FTM)
- Hormones (testosterone)
- Chest masculinization
- Hysterectomy, salpingo-oophorectomy
- Metoidioplasty
- Phalloplasty
- Vaginectomy
- Scrotoplasty
- Urethroplasty
- Testicular prostheses

Evidence-Based Guidelines, July 2016
Masculinizing Hormones

- **Testosterone**
  - Intramuscular injections (cypionate, enanthate, undeconate)
  - Gels, patches, implants
  - Goal: testosterone in normal male range

- **Expected Effects**
  - Facial/body hair, deepening voice, amenorrhea, clitoral enlargement, vaginal atrophy, increased libido, reduced fertility
  - Fertility decreases after menses cease, pregnancy may be possible

- **Adverse Effects**
  - Acne, oily skin, migraines, weight gain, fluid retention, polycythemia
  - Hepatotoxicity, worsening of lipid profile

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**Case 3: Ray**

- 45 year old trans man with stable HIV presents for follow-up visit 9 months after starting testosterone. Continues to menstruate.

**LABS:**
- CD4 count: 600
- Viral load <50
- Other labs normal

**PHYSICAL EXAM:**
- Unremarkable, including normal pelvic exam

**MEDS:**
- Stribild
- Testosterone enanthate 200mg every 2 weeks

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**Feminization**

- What questions do you have?
- What is in your differential?
- What needs to be done about menses?
Common Feminizing Regimens

**Usually estrogen + androgen blocker**

**Estrogens**
- Estradiol valerate (IM)
- Estradiol patch (preferred for those > 45y)
- Conjugated estrogen*

**Androgen blockers†**
- Spironolactone
- Finasteride
- Dutasteride
- Cyproterone acetate

**Goal:** maintain estrogen level < 200 pg/mL
**Goal:** maintain testosterone level < 55 ng/dL

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**Expected Effects of Feminizing Therapy**

<table>
<thead>
<tr>
<th>Expected Effect</th>
<th>Onset</th>
<th>Maximum</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>variable</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>Improved male pattern baldness (no regrowth)</td>
<td>1-3 months</td>
<td>1-2 years</td>
</tr>
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**Feminizing Therapy: Adverse Effects**

**Estrogens**
- Venous thrombosis/pulmonary emboli (ethinyl estradiol)
- Hypertriglyceridemia
- Elevated blood pressure
- Gallbladder disease
- Macroprolactinoma

**Spironolactone**
- Hyperkalemia
- Hypotension

**Flutamide**
- Hepatic toxicity
Soft Tissue Fillers

- Loose fillers (industrial silicone, other substances)
- Injected into breasts, face, hips, buttocks
- Risk of bloodborne pathogens, migration, inflammation, emboli, disfigurement, and death
- Use associated with AIDS diagnosis
- Unknown impact on HIV disease progression


Case 2: Monica

- 36 year old trans woman recently switched from TDF/FTC/EFV to TDF/FTC/DRV/RTV. Complains of new hot flashes.

LABS:
- CD4 count 520,
- Viral load < 50
- Other labs normal

PHYSICAL EXAM:
- BP 160/90 (x 2 visits)
- Otherwise unremarkable

MEDS:
- TDF/FTC/DRV/RTV
- Delestrogen 20mg IM q 2wks
- Spironolactone 100 mg BID

- What meds should be avoided when treating her hypertension?
- What is in the differential diagnoses for her hot flashes?

Estrogen and Antiretroviral Agents

- Available data based on oral contraceptives (ethinyl estradiol)
- No published data available on interactions with 17-beta estradiol or conjugated estrogen
- Where interactions with oral contraceptives exist:2
  - No clinically significant effect on ART levels
  - Fosamprenavir trough levels reduced with ethinyl estradiol
  - Some NNRTIs and PIs reduce levels of estrogen
- HIV+ trans women who believed ART had negative effects on hormones were 3 times more likely to take higher-than-prescribed doses of hormones
- Consider monitoring estradiol levels when initiating/changing ART

**Pre-exposure prophylaxis**

**Clinical Trials**

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Participants</th>
<th>Number</th>
<th>Drug</th>
<th>Modified ITT efficacy of % reduction in acquisition of HIV infectiona</th>
<th>Adherence-adjusted efficacy based on drug detection in bloodb</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrEP</td>
<td>Men who have sex with men and transgender women</td>
<td>2,499</td>
<td>FTC-TDF</td>
<td>44 (15-63)</td>
<td>92 (40-99)</td>
</tr>
<tr>
<td>PrEP</td>
<td>Partners PrEP</td>
<td>474</td>
<td>TDF</td>
<td>67 (44-81)</td>
<td>86 (67-94)</td>
</tr>
<tr>
<td>PrEP</td>
<td>Bangkok Thailan Study</td>
<td>2,411</td>
<td>TDF</td>
<td>49 (10-72)</td>
<td>74 (17-94)</td>
</tr>
<tr>
<td>PrEP</td>
<td>Fem-PrEP Heterosexually active women</td>
<td>2,120</td>
<td>FTC-TDF</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>PrEP</td>
<td>Voice Heterosexually active women</td>
<td>5,029</td>
<td>FTC-TDF</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

- Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up HIV test.
- The percentage of reduction in HIV incidence among those with tenofovir detected in blood, compared with those without detectable tenofovir.
- Finding not statistically significant.

**Pre-exposure prophylaxis for cis male same sex activity**

**Pre-exposure prophylaxis for heterosexual couples**

**Pre-exposure prophylaxis for injection drug users**

**Adherence challenges for heterosexual cis women**

**Pre-exposure prophylaxis and transgender men**

- No published data on PrEP in transgender men
- PrEP effective for receptive anal sex after 7 days of use with a minimum adherence of 4 pills per week
- CDC recommends 20 days of daily use for all other acts, e.g., vaginal intercourse
- No data on PrEP in transgender men, including TMSM
- Efficacy of PrEP in TMSM may be affected by anatomy and hormonal milieu

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http://www.cdc.gov/hiv/basics/prep.html
PrEP in Transgender Women: iPrEx

- Trans women: 339/2499 (14%)
- Lack of efficacy: HR 1.1
  - TDF detected in no trans women at seroconversion
  - No seroconversions observed in trans women with TDF levels consistent with > 4 pills/week
  - TDF levels not linked to behavioral risk

<table>
<thead>
<tr>
<th>Clinical Trials with women</th>
<th>PrEP Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEx (trans women)</td>
<td>18%</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>24%</td>
</tr>
<tr>
<td>VOICE</td>
<td>29%</td>
</tr>
</tbody>
</table>

Key Messages

- Gender affirmation improves engagement in care
  - Use preferred pronouns and name
  - Defer unnecessary questions and exams
  - Build rapport before performing genital exams

- Guidelines are available to guide hormone therapy
  - Providing hormone therapy may improve ART adherence
  - Estrogen may reduce fosamprenavir levels
  - PI's and NNRTI's may reduce estrogen levels → monitor

- PrEP can be an important tool for trans people
  - Adherence support is essential
  - Limitations of medical knowledge

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