Cases from the HIV Primary Care Clinic

William R. Short, MD, MPH
Associate Professor of Medicine
Perelman School of Medicine at the
University of Pennsylvania
Philadelphia, PA
Learning Objectives
Upon completion of this presentation, learners should be better able to:

- Implement best practices for providing HIV primary care

Faculty and Planning Committee Disclosures
Please consult your program book or the Conference App.

Off-Label Disclosure
This case discussion may contain discussion of off-label uses of approved agents.

CDC 2015 STD Tx Guidelines https://www.cdc.gov/std/treatment/
Case 1

- 48-year-old male with no PMH presents with generalized fatigue and weight loss of about 20 lbs over the past 2-3 months (unintentional)
- He was seen in ED for evaluation
- No additional medical history and he takes no medication
- He has never had an HIV test
- HIV screening test (4th generation) drawn and positive

Physical Examination
3 Types of candidiasis
As part of his examination, he has a dilated retinal examination and you see this:
Question: What is your recommendation?

A. Start Ganciclovir
B. Suggest intraocular Ganciclovir implant
C. Start Acyclovir
D. Start treatment with ART
E. Something else

CMV Retinitis
2014 CDC Recommendations: HIV Diagnostic Testing Algorithm

- **New recommendations offer faster diagnosis**
  - As much as 3 to 4 weeks sooner than previous approach

- **Sequence of tests recommended**
  - Use of EIA testing with a confirmatory Western blot **no longer recommended**
  - Initial screening tests to detect HIV p24 antigen and HIV antibody should be used
  - If positive, confirmatory HIV-1/HIV-2 antibody differentiation immunoassay

EIA = enzyme immunoassay antibody.

Sensitive HIV-1/2 immunoassay (e.g., fourth-generation Ag/Ab assay)

- Reactive (+)
  - HIV-1/HIV-2 differentiation immunoassay
    - HIV-1 (+) HIV-1 antibodies detected
      - Initiate care (and viral load)
    - HIV-2 (+) HIV-2 antibodies detected
      - Initiate care
  - Negative (-)
    - Negative for HIV-1 and HIV-2 antibodies and p24 Ag

RNA

- RNA+ Acute HIV-1 infection
  - Initiate care
- RNA (-) Negative for HIV-1
  - Initiate care


Question:
Which test should you order in ALL newly diagnosed people with HIV?

A. CMV IgG
B. HIV tropism
C. HIV genotype (reverse transcriptase/protease)
D. HIV genotype (reverse transcriptase/protease/integrase)
E. HIV phenotype
Lab Evaluation: Routine Tests

- Chemistries, BUN/Cr, liver function tests
- CBC/diff
- Fasting lipids and glucose
- G6PD: blacks; males from Mediterranean, India, Southeast Asia
- Urinalysis (U/A)

Labs: Screening for Infection

- Serologic testing for infections that can reactivate:
  - Cytomegalovirus IgG (only if at low risk so that counseling can be provided if test is negative)
  - Toxoplasma IgG

- Hepatitis serologies (A, B, C)

- Tuberculin skin test (TST) or interferon-gamma release assay (IGRA)
  - TST >5 mm is positive in HIV+ patients
  - If negative and patient’s CD4 count is <200, repeat TST or IGRA after immune reconstitution
**STI Screening**

- For sexually active individuals:
  - Screen for syphilis, gonorrhea (GC) and chlamydia (CT) at first evaluation
  - Screen at least annually (more frequently if exposures)
  - For MSM:
    - Urethral (urine NAAT) screen for GC/CT if insertive intercourse
    - Screen for rectal and pharyngeal STI if receptive intercourse
  - If multiple or anonymous partners, more frequent screening, e.g. every 3-6 months

https://www.cdc.gov/std/prevention/screeningreccs.htm

**Lab Evaluation: HIV-specific Tests**

- **CD4 count**: best predictor of risk of opportunistic infection or cancer¹
  - CD4 count < 200: toxoplasma, PCP, PML, Cryptosporidiosis, oral and esophageal candidiasis, Kaposi sarcoma, NHL
  - CD4 count <50: risk of MAC, CMV, primary CNS lymphoma

- **HIV RNA (“viral load”)**
- **HIV resistance testing**
- **HLA-B5701: if considering abacavir²**
  - Positive in 8% of US whites. ≈2% of US African-Americans and Hispanics¹
  - If B5701+, do not prescribe abacavir (50% chance of hypersensitivity reaction)

HIV Drug Resistance Testing

<table>
<thead>
<tr>
<th>Patient</th>
<th>Resistance Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly Diagnosed or Treatment Naive</td>
<td>Genotype (RT and PR)</td>
</tr>
<tr>
<td></td>
<td>(Integrate genotype only if suspicion based on history)</td>
</tr>
<tr>
<td>Virologic Failure to 1st or 2nd Lines of Therapy</td>
<td>Genotype</td>
</tr>
<tr>
<td></td>
<td>(Integrate geno. if failing INSTI)</td>
</tr>
<tr>
<td>Suspected Complex Resistance</td>
<td>Phenotype and Genotype</td>
</tr>
<tr>
<td>Considering CCR5 antagonist</td>
<td>DNA tropism</td>
</tr>
</tbody>
</table>

Interpretation of genotypes:
- www.iasusa.org/content/hiv-drug-resistance-mutations
- Stanford HIV Drug Resistance: http://hivdb.stanford.edu/


Transmitted Drug Resistance

McClung RP, et al. CROI 2019 #3337
Case 1

- 48-year-old male presents with newly diagnosed HIV
- Labs: CD4: 90 cells/ul
  HIV RNA: 150,000 copies/ml
- All other labs are normal
- HLA-B5701: negative
- Genotype: wildtype
- No additional medical history and she takes no medication

Question:

**CD4 count: 90, HIV RNA 150,000. OI Prophylaxis?**

A. None  
B. Trimethoprim/sulfamethoxazole  
C. Azithromycin  
D. Trim/sulfa + azithromycin  
E. Ganciclovir
Pneumocystis pneumonia (PCP) prophylaxis (trim/sulfa DS daily) if:
- CD4 count < 200 (CD4% < 14)
- history of thrush
Toxoplasmosis gondii prophylaxis if:
- CD4 Count < 100 AND Toxo IgG +
Mycobacterium avium complex prophylaxis (azithromycin 1200mg weekly) if:
- CD4 count < 50

Source: http://aidsinfo.nih.gov/guidelines

Question: Which regimen would you start?

1. TDF / 3TC / low dose (400mg) EFV (generic)
2. ABC/ 3TC / DTG
3. TAF/ FTC + DTG
4. TAF / FTC/ ELV / cobi
5. TAF/ FTC / BIC
6. TAF / FTC + RAL (once daily)
7. TAF / FTC / RPV
8. TAF/ FTC /DRV/cobi
9. Something else
Case 2

- 30-year-old female presents with newly diagnosed HIV
- Asymptomatic
- Labs: CD4: 600 cells/ul
  HIV RNA: 2500 copies/ml
- All other labs are normal
- She would like to have a child in the future

Question: Would you start her on ART?

1. Yes
2. No
3. Not sure
Question: Which regimen would you start?

1. TDF / 3TC / low dose (400mg) EFV (generic)
2. ABC / 3TC / DTG
3. TAF / FTC + DTG
4. TAF / FTC / ELV / cobi
5. TAF / FTC / BIC
6. TAF / FTC + RAL (once daily)
7. TAF / FTC / RPV
8. TAF / FTC / DRV / cobi
9. Something else

Reproductive Cycle of Women

The Women’s Health Continuum: A Lifespan Approach

Puberty
Preconception
Pregnancy
Postpartum
Newborn
Interconception
Menopause
Postreproduction

Potential origins of adult diseases before, during, and after conception and pregnancy

https://www.slideshare.net/bixbycenter/gregory41006
Pre-Pregnancy planning

- Any patient encounter with a nonpregnant women of reproductive potential is an opportunity to counsel about wellness and healthy habits, which may improve reproductive and obstetric outcomes
- One Key Question Initiative:
  - Would you like to become pregnant in the next year?
- Prenatal Vitamin with folic acid (400mcg is adequate)

ASRM & ACOG, Committee opinion no. 762, January 2019

Pre-Pregnancy planning

- Immunization status assessed annually for TDaP. MMR, Hepatitis B, and Varicella.
  - Vaccines for Rubella and varicella should not given at least 28 days before pregnancy or PP.
  - TDaP given again 27-36 weeks during each pregnancy
- All patients should receive annual Influenza vaccine.
- Hold HPV vaccine during pregnancy.

ASRM & ACOG, Committee opinion no. 762, January 2019
Antiretroviral Pregnancy Registry Study (www.APRegistry.com)

<table>
<thead>
<tr>
<th>ARVs</th>
<th>Defects/Live Births (+200 reported 1st trimester exposures)</th>
<th>Prevalence % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>35/1183</td>
<td>3.0 (2.1, 4.1)</td>
</tr>
<tr>
<td>Didanosine</td>
<td>20/437</td>
<td>4.7 (2.9, 7.1)</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>70/2998</td>
<td>2.3 (1.8, 2.9)</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>154/5069</td>
<td>3.0 (2.6, 3.3)</td>
</tr>
<tr>
<td>Stavudine</td>
<td>218/81</td>
<td>2.6 (1.6, 3.9)</td>
</tr>
<tr>
<td>Tenofovir DF</td>
<td>85/2715</td>
<td>2.3 (1.8, 2.9)</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>134/4186</td>
<td>3.2 (2.7, 3.8)</td>
</tr>
<tr>
<td>PIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>29/1309</td>
<td>2.2 (1.5, 3.2)</td>
</tr>
<tr>
<td>Indinavir</td>
<td>7/289</td>
<td>2.4 (1.9, 4.9)</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>30/1421</td>
<td>2.1 (1.4, 3.0)</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>29/1122</td>
<td>2.1 (1.9, 3.3)</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>72/3200</td>
<td>2.2 (1.8, 2.6)</td>
</tr>
<tr>
<td>Darunavir</td>
<td>13/406</td>
<td>2.6 (1.4, 4.4)</td>
</tr>
<tr>
<td>NNRTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>28/1040</td>
<td>2.3 (1.5, 3.4)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>32/1148</td>
<td>2.6 (1.9, 3.5)</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>3/352</td>
<td>0.9 (0.2, 2.5)</td>
</tr>
<tr>
<td>INSTI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raltegravir</td>
<td>9/212</td>
<td>2.9 (1.4, 5.6)</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>6/228</td>
<td>3.5 (1.5, 6.0)</td>
</tr>
<tr>
<td>Elvitegravir</td>
<td>9/223</td>
<td>2.2 (0.8, 5.4)</td>
</tr>
</tbody>
</table>

Birth Defect Rates

<table>
<thead>
<tr>
<th>ARVs (overall)</th>
<th>Population-Based Data (CDC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>


GYN History

- She had a pap smear done at diagnosis and a repeat in one year that were both normal.
- She has a routine pap with cotest this visit and the results are as follows:
  - Negative cytology but + HRHPV but not 16/18
- What are your next steps?
Cervical Cancer Screening in Women with HIV

• < 30 years
  – Cervical pap at time of HIV diagnosis
  – If normal, repeat every 12 months
  – If 3 consecutive paps are normal, then every 3 yrs
  – Co-testing (pap and HPV) not recommended
  – Refer for colposcopy if ASCUS on pap and reflex HPV test positive or if pap result is LSIL or worse


Cervical Cancer Screening in Women with HIV

• >= 30 years
  – Pap alone or pap with HPV co-testing
    Pap alone:
    – At time of HIV diagnosis; then annually
    – If 3 consecutive paps normal, then every 3 yr
    Pap with HPV co-testing:
    – If pap and HPV co-testing negative, screen every 3 yr
    – If pap normal and HPV positive, repeat testing in 1 yr; if HPV type 16 or 18 positive, refer for colposcopy
    – If ASCUS and reflex HPV positive, refer for colposcopy
    – For LSIL or worse, refer for colposcopy

Case 3
- 28-year-old male presents with HIV who transfers his care to your practice
- He moved from Florida and he was last seen 9 months ago
- Labs: CD4: 500 cells/ul
  - HIV RNA: < 20 copies/ml
- He has no other Past Medical History
- He is on FTC/TAF/BIC (started about 9 months prior)
- He is sexually active with one male
- His RPR is 1:4 with + FTA-Abs (asymptomatic)
- He denies a history of syphilis

Time Line
Untreated Syphilis

1° Chancr
2° Rash, fever, neuro symptoms
Latent No symptoms
3° Gumma, bone, cardiac, nerve disease

*Early* syphilis if < 1 yr

Workowski KA, et al. MMWR Recomm Rep. 2015;64:1-137
Syphilis

- *T. pallidum*
- Incubation period: 9-90 days
- Primary: painless chancre with regional adenopathy
  - Resolves within weeks
- Secondary (2-6 months from initial infection):
  - Skin: Rash, Alopecia, Condyloma lata
  - Systemic: Flu-like symptoms
  - CNS: aseptic meningitis; Bell’s palsy; uveitis
  - Other: protean manifestations can manifest in any organ system
  - Rash resolves over weeks
- Tertiary syphilis: Cardiac / aortitis, gummas, neurologic sequelae
- Neurosyphilis: can occur at any stage (including oto / ophtho involvement)
- Latent (asymptomatic): Early (< 1 year asymptomatic) vs Late (>1 year or unknown duration)

Workowski KA, et al. MMWR Recomm Rep. 2015;64:1-137

Oral chancre
Extragenital chancre

Have high index of suspicion for any oral lesions on buccal, pharyngeal mucosa, on tongue or lips/perioral area
Secondary syphilitic rash

Condylomata lata
Condylomata lata

Treatment of Syphilis

- **Primary, Secondary, Early latent:**
  - Benzathine penicillin G 2.4 million units IM once
  - If PCN-allergic: Doxycycline 100 mg po bid for 14 days
- **Late Latent:**
  - Benzathine penicillin G 2.4 million units IM weekly for 3 consecutive weeks
  - If PCN-allergic: Doxycycline 100 mg po bid for 28 days
- **Neuro or ocular:**
  - IV PCN G 18-24 million units q4H x 10-14 days
- **HIV, Pregnant, neurosyphilis -> if PCN-Allergic:** desensitize

Workowski KA, et al. MMWR Recomm Rep. 2015;64:1-137
**Expected Response to Syphilis Therapy**

- Primary or secondary syphilis[^1]: ≥ 4-fold decline in nontreponemal serologic titers by 6-12 mos of follow-up
  - 15% to 20% of pts treated for primary or secondary will not achieve this at 1 yr posttreatment[^2,3]
- Latent syphilis (early, late, or unknown duration)[^1]: ≥ 4-fold decline in initially high (≥ 1:32) nontreponemal serologic titers by 12-24 mos of follow-up
- Neurosyphilis:
  - Repeat LP in 6 months to ensure WBC and protein improving


---

**Interpretation of Changing Syphilis Titers**

- Call health department to get prior titers and treatment records
- Meaningful change is 2 dilution (or 4-fold) change in titer
  - eg,
    - 1:2 -> 1:4 or 1:1, no meaningful change
    - 1:2 -> 1:8, meaningful change
- Remember to think about the prozone phenomenon!

[^1]: Workowski KA, et al. MMWR Recomm Rep. 2015;64:1-137
Thank you!!