HIV in Primary Care

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San Francisco General Hospital
UCSF

HIV Warm Line

• Phone: 1-800-933-3413
• Hours: 6am-5pm (PST), M-F

HIV PEP LINE

• Phone: 888-448-4911
• 24 hours/day
Overview

• HIV testing recommendations

• Update on Pre-exposure prophylaxis (PREP) & Post-exposure prophylaxis

• Antiretroviral therapy: When to start & what the non-HIV specialist needs to know about antiretrovirals

Relevance to General Internal Medicine

• Unacceptably high rates of ongoing HIV transmission in US (50,000/yr) and underdiagnosis (20% undiagnosed)
• Routine testing in outpatient and inpatient settings recommended and increasingly implemented
• Non-HIV providers frequently test and thus diagnose patients with HIV
• HIV diagnosis commonly made in the setting of a first opportunistic infection, which necessitates early ART start (within 2 weeks)
Case #1

- 35 year old heterosexual African-American man comes to you for a new patient visit, needs an physical and wants to establish care

- While he doesn’t espouse any notable HIV risk factors other than occasional “less than perfect” condom use, you offer him an HIV test in accordance with the CDC & USPTF guidelines recommending HIV testing to all adults

- He is surprised; “OK, fine by me, but no one ever told me I should get a test before. I really don’t think I am at risk. Isn’t AIDS going away in the US?”
Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Race/Ethnicity, 2011—United States and 6 Dependent Areas

Males
N = 39,495

- American Indian/Alaska Native: 2%
- Asian: 2%
- Black/African American: <1%
- Hispanic/Latino*: 42%
- Native Hawaiian/other Pacific Islander: <1%
- White: 30%

Females
N = 10,512

- American Indian/Alaska Native: 1%
- Asian: 1%
- Black/African American: <1%
- Hispanic/Latino*: 17%
- Native Hawaiian/other Pacific Islander: <1%
- White: 63%

Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
*Hispanic/Latinos can be of any race.

HIV “Cascade of Care”

- Diagnosed
- Linked to Care: 82%
- Retained in Care: 66%
- Prescribed ART: 37%
- Virally Suppressed: 33%
- Virally Suppressed: 25%

CDC 2012
Routine, not risk based testing

- **CDC 2006**
  - Age 13-64 at least once (unless prevalence <0.1%) and all pregnant women
  - Yearly testing for those at high risk
  - Opt out screening (assent inferred unless patient declines), written consent not required

- **US Preventative Task Force (USPTF) 2013**
  - Screen all ages 15-65
  - All Pregnant women
  - <15 and >65 if at increased risk
  - Repeat testing if remain at risk


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**Most current HIV tests positive within 30 days of infection**

Adapted from Pilcher JID 2010; 201(S1):S7–S17
Diagnosis of Acute HIV infection

• ~50% of acute HIV infection will be symptomatic 2-4 weeks after exposure
  – Fever, headache, sore throat, lymphadenopathy, rash

• If suspected, send HIV RNA (and HIV antibody, if not recently tested)
  – If only low level HIV viremia, repeat test
• Several “4th Generation HIV” tests now FDA approved: Antibody and viral antigen
  – BioRad GS HIV Combo Ag/Ab
  – ARCHITECT HIV Ag/Ab Combo


Case #1

• Much to his surprise, and yours, his antibody test comes back positive
• His CD4+ Count is 500, with an HIV RNA viral load of 50,000 copies/ml
• When the shock has subsided, he asks you, “What does this mean, Doc? How long do I have to live?”
Counseling in new HIV infection

1) HIV+ patients can expect to live long healthy life when engaged in medical care
   – HIV has become a chronic disease, similar to diabetes or heart disease

2) Current HIV medications do not cause physical changes and stigma of older medication

3) Sex and parenthood without HIV transmission are both possible
   – Discuss your patient’s reproductive hopes and reassure that sex can be a part of their lives

Pre-exposure prophylaxis: PrEP

• Preexposure prophylaxis (PrEP) is giving an HIV-negative individual a pill (daily, or coitally?) to prevent HIV infection
Recent Breakthroughs in HIV Prevention

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART for prevention</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td>HPTN 052, Africa, Asia, Americas</td>
<td></td>
</tr>
<tr>
<td>PREP for discordant couples; Partners PREP, Uganda, Kenya</td>
<td>73 (49-85)</td>
</tr>
<tr>
<td>PreP for heterosexual men and women; TDF, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>57 (38-66)</td>
</tr>
<tr>
<td>PreP for MSMs; IPT, EX, America, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td>Treatment sexually transmitted infections; Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td>Microbicide gel/topical PreP; CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td>HIV vaccine; RV144, Thailand</td>
<td>31 (1-51)</td>
</tr>
</tbody>
</table>

Condoms (88%)

FDA approves Truvada for PREP 7.2012

- Truvada (tenofovir/emtricitabine fixed dose combination) approved in combination with safer sex practices “to reduce the risk of sexually-acquired HIV infection in adults at high risk”

- PREP risks
  1) Drug Resistance: seroconverters and those with undiagnosed HIV at baseline developed drug resistance
  2) Drug toxicity: renal and bone
- Covered by most private insurance
CDC Guidance: Jan 2011 and Aug 2012

- Document negative HIV Ab test and test for acute HIV with HIV RNA if symptomatic prior to initiation
- Confirm pt is at “substantial, ongoing, high risk for acquiring HIV infection”
-Prescribe no more than 90 days at a time
-Link known HIV positive partners to care
- Caution during pregnancy; Don’t use while breastfeeding
- Monitoring
  - q2-3 mo. HIV testing, counseling and condoms
  - q6 mo STD screening
  - Creatinine at 3 months, then q6mo


Phase III PrEP Studies: Concerns about efficacy in women

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>POPULATION</th>
<th>LOCATION</th>
<th>Active arm(s)</th>
<th>EFFICACY (mITT-analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEx</td>
<td>2499 MSM and TGF</td>
<td>South America, USA, Thailand, South Africa</td>
<td>FTC/TDF</td>
<td>42% (95% CI 18-60) 48 vs. 83</td>
</tr>
<tr>
<td>TDF-2</td>
<td>1219 heterosexual men and women</td>
<td>Botswana</td>
<td>FTC/TDF</td>
<td>63% (95% CI 21-83) 9 vs. 24</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>4758 serodiscordant heterosexual couples</td>
<td>Kenya and Uganda</td>
<td>FTC/TDF TDF</td>
<td>73% (95% CI 49-85) 67% (95% CI 44-81) 13 FTC/TDF, 17 TDF, 52 placebo</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>2120 heterosexual women</td>
<td>Kenya, Tanzania, Zimbabwe, South Africa</td>
<td>FTC/TDF</td>
<td>No difference 33 FTC/TDF vs. 35 placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stopped early due to lack of efficacy</td>
</tr>
<tr>
<td>VOICE</td>
<td>5000 heterosexual women</td>
<td>Uganda, Zimbabwe, South Africa</td>
<td>FTC/TDF TDF Vaginal TDF gel</td>
<td>Oral and vaginal TDF arms stopped early</td>
</tr>
</tbody>
</table>
Post Exposure Prophylaxis (PEP)

- Can be administered up to 72 hours after exposure - the sooner the better
- Recommended 28 day course
- Basic Regimen vs Expanded regimen, depending on extent of exposure

MMWR 2005, MMWR 2007

PEP: Non Occupational exposure

- Don’t forget PEP after sexual exposure!
- Risk of infection varies by type of exposure
  - Receptive Anal Intercourse - 2%
  - Receptive Vaginal intercourse – 0.01%
  - Bite or assault <0.01%
- Also consider for exposure of mucous membranes/non-intact skin to blood/fluids from HIV infected individual
- Recommended within 72 hours of exposure

Pinkerton, Arch Internal Med 2004
# Post Exposure Prophylaxis- Percutaneous

<table>
<thead>
<tr>
<th>Exposure</th>
<th>HIV+ Class 1</th>
<th>HIV+ Class 2</th>
<th>Unknown HIV status/source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less severe (solid needle, superficial)</td>
<td>2 Drug PEP</td>
<td>Expanded ≥ 3 drug PEP</td>
<td>No PEP/ Consider 2 drug PEP</td>
</tr>
<tr>
<td>More severe (large-bore hollow needle, deep puncture, visible blood on device, needle from patient’s artery or vein)</td>
<td>Expanded ≥ 3 drug PEP</td>
<td>Expanded ≥ 3 drug PEP</td>
<td>No PEP/ Consider 2 drug PEP</td>
</tr>
</tbody>
</table>

**HIV Class 1:** asymptomatic HIV infection or known low viral load (<1,500 copies/ml)

**HIV Class 2:** symptomatic, AIDS, acute HIV, or known high viral load

**MMWR 2005**

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## Other considerations for PEP

- Baseline and follow-up testing for HIV, HBV, HCV
- Pregnancy test/morning after pill
- Testing/treatment for sexually transmitted disease
- Anti-emetics to accompany ART
- Counseling

- If unsure which to start, start basic without delay then add 3rd agent if indicated
- If highly resistant source case- start ART and get help

**PEP line: 888-448-4911**
Back to the Case: 
Next steps for in new HIV diagnosis

• Evaluation and staging of patient

• Prophylaxis for opportunistic infections if needed

• ART: when and what to start

Initial Laboratory Testing

• Confirmation of HIV

• HIV Viral load- *Can be LOW/Undetectable in “Elite Controllers”*

• HIV Genotype (testing for HIV drug resistance)
  – Recommended for all patients at time of diagnosis
  – Transmitted drug resistance up to 17.5% in 2009-2011

• Screening for other STDs: GC, CT, Syphilis

• Hepatitis serologies

• Opportunistic infection (OI) screening:
  Toxoplasmosis IgG, latent TB evaluation, consider MAC culture if CD4+ < 50 cells/mm³

• G6PD
### Prophylaxis for Opportunistic infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>Indication</th>
<th>Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>CD4⁺ &lt;200</td>
<td>TMP/SMX (Dapsone, Atovaquone)</td>
</tr>
<tr>
<td>Toxoplasmosis (if IgG +)</td>
<td>CD4⁺ &lt;100</td>
<td>TMP/SMX (Dapsone+ Pyrimethamine)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>PPD &gt;5mm or positive IGRA, contact with TB</td>
<td>Isoniazid x 9 months</td>
</tr>
<tr>
<td>Mycobacterium Avium (MAC)</td>
<td>CD4⁺ &lt; 50</td>
<td>Azithromycin 1200 mg weekly</td>
</tr>
</tbody>
</table>

### HIV Primary Care- ART related testing

- **HLA-B5701**
  - Allele associated with development of Abacavir hypersensitivity
    - NPV 100%
    - PPV 50%
  - More prevalent in Caucasian populations
  - Send if considering Abacavir as part of ART

- **“Tropism” testing**
  - Tests for which coreceptor HIV uses to enter cells, CCR5 (“R5”) or CXCR4 (“X4”)
  - If considering CCR5 antagonist (Maraviroc, Vicriviroc)
  - *Not standard testing for antiretroviral naïve individuals*

Mallal 2002, Mallal 2008
Case #1

• You have counseled your patient about what an HIV diagnosis means in 2013, safer sex, and performed initial staging.

• He asks you, “When do I have to start HIV medicines?”

When would you start this patient on ART?

1. Now- no reason to wait
2. When his CD4 cell count is < 350
3. Now only if he has other comorbidities (CAD, kidney disease, hepatitis), otherwise wait
4. When he has his first opportunistic infection

35 yo man with CD4+ 500, HIV RNA 50,000, no other comorbidities
Who should receive ART?

- HIV complications not just infectious...
  - include liver, cardiac, renal disease due to chronic ongoing immune activation secondary to HIV replication

- Risk of these events higher in those off ART compared to on ART at all CD4 strata

- Lower rates of progression in patients started on ART immediately vs. delayed

- Public health benefit of reduced transmission

April 2, 2010
City Endorses New Policy for Treatment of H.I.V.
By SABIN RUSSELL

In a major shift of HIV treatment policy, San Francisco public health doctors have begun to advise patients to start taking antiviral medicines as soon as they are found to be infected, rather than waiting — sometimes years — for signs that their immune systems have started to fail.

US DHHS guidelines 2013

- Consider ART in all HIV infected patients
- ART recommended for prevention of transmission

All patients with HIV infection should receive ART, regardless of CD4 count
WHAT ART TO START

Class Examples
• Nucleos(t)ide Reverse Transcriptase inhibitors (NRTI’s or “Nukes”) Tenofovir, Truvada (tenofovir+emtricitabine), abacavir
• Non-nucleoside reverse transcriptase inhibitors (NNRTI’s) Efavirenz, Nevirapine, Rilpivirine
• Protease Inhibitors Darunavir, Atazanavir, Ritonavir (used for “boosting”)
• Integrase Inhibitors Raltegravir, Elvitegravir
• CCR5 Inhibitors Maraviroc
• Fusion Inhibitors T-20
Non-ritonavir booster Cobicistat
What ART to start

• **Preferred:**
  - Raltegravir
  - Darunavir/ritonavir + tenofovir/emtricitabine
  - Atazanavir/ritonavir or
  - Efavirenz/truvada/emtricitabine (Atripla)

• **Alternative:**
  - Abacavir containing regimens
  - Other protease inhibitors: Lopinavir/ritonavir (Kaletra), fosamprenavir, saquinavir
  - Nevirapine based regimens

DHHS Guidelines, 2/2013

What to avoid

• Monotherapy or dual therapy
• Generally avoid AZT, D4T, and DDI as less toxic, effective alternatives available
• 3 NRTIs alone
• AZT + D4T: antagonistic
• DDI + D4T: overlapping side effects
• DDI + tenofovir: blunted CD4 response
• Unboosted protease inhibitors
Top 10 Antiretroviral Toxicities

Toxicities of the NRTIs

• 1) Lactic acidosis and hepatic steatosis (higher incidence with thymidine analogues AZT & D4T)

• 2) Lipoatrophy - AZT, D4T, DDI

• 3) Tenofovir- Can cause and exacerbate renal failure
NNRTI Toxicities

4) Efavirenz (*Sustiva*)
   - First Trimester Teratogen
   - CNS effects (Dizziness, nightmares, worsening of pre-existing psychiatric disorders)
   - +++ Drug interactions- lowers many drug levels

5) Nevirapine (*Viramune*)
   - Rash and Hepatotoxicity (may be severe and life-threatening)
   - Avoid starting in men with CD4+ > 400, women CD4+ > 250

Protease Inhibitor (PI) Toxicities

6) Dyslipidemia
7) Insulin resistance
8) GI intolerance: nausea & diarrhea
9) Hepatic toxicity

10) Key PI Drug-drug interactions
    - Statins: simvastatin and lovastatin contra-indicated – can use atorvastatin at low dose
    - Avoid rifampin (rifabutin is alternative)
    - Watch with warfarin and anti-convulsants
    - *NO PPI with ATAZANA VIR*
Considerations in choosing ART

• One pill/once daily:
  – Efavirenz/tenofovir/emtricitabine (Atripla)
  – Rilpivirine/tenofovir/emtricitabine (Complera)
  – Elvitegravir/cobicistat/tenofovir/emtricitabine (Stibild)

• Food requirements
  – Empty stomach: Efavirenz
  – Fatty meal: Rilpivirine & Elvitegravir

• Transmitted drug resistance

• Concomitant medical conditions: renal impairment, hepatitis B, other medications
• Desire for pregnancy

Monitoring on therapy

• Goal is undetectable HIV RNA
  – Usually achieved by 16-24 weeks on therapy
  – If not responding, discuss adherence and consider resistance testing

• Monitor renal/hepatic function as well as lipids and fasting glucose

• CD4+ count should rise, but some individuals experience slow/no response despite virologic suppression (“immunologic failure”)
Case #2

65 year woman with DM, hyperlipidemia, CAD admitted to medicine service for cough, shortness of breath, “rule out pneumonia”

- Chest X Ray- no focal infiltrate, but patient with 4L oxygen requirement, not improving on antibiotics
- You obtain a rapid HIV test as part of routine hospital care as she has never been tested
  – HIV Ab +, confirmatory western blot positive

- Respiratory sample confirms Pneumocystis jiroveci pneumonia (formerly carinii) - PCP

Case #2

- You start PCP therapy and steroids and her respiratory status slowly improves

- Your patient asks, “How soon can I start HIV therapy?”
When to start ART in Acute Opportunistic Infection?

1. After full 4 weeks course of PCP treatment is completed
2. After patient is discharged and is established in outpatient HIV care
3. Now
4. No one knows for sure

Start in setting of opportunistic infection

• Starting ART within 2 weeks of an opportunistic infection (including TB) reduces AIDS progression and death
  – ART now commonly started in hospital during treatment for OI

• Exceptions to this rule: CNS opportunistic infections
  – TB meningitis: no clear benefit to early ART, increased adverse events
  – Cryptococcal meningitis: improved mortality when ART deferred 4-5 weeks.
Summary

• HIV epidemic has not declined in US in recent years with at-risk populations increasing in prevalence
• Routine HIV screening in primary care is cost effective
• ART initiation higher CD4+ counts and treating earlier in course of opportunistic infection therapy
• Hospital setting may be preferred site of ART initiation for many OI’s
• Internists will increasingly diagnose HIV, initiate ART, and provide PREP and PEP

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Thank you!