HIV Prevention 2016

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* I have no financial relationships to disclose.

* I will not discuss off-label use and/or investigational use in my presentation.

* Slides provided by various sources including AETC, CDC, DHHS, and Dr. Paul Sax
Josh is a 28-year-old male who is presenting to your office for an urgent visit.

He reported that he was having sex with a guy the night before without a condom (insertive anal).

He is concerned that the guy has not been tested for HIV before.

Josh was tested for HIV three months ago and the result was negative.

He uses condoms most of the times except when he drinks alcohol.
What is the best next step?

1. Avoid prescribing PEP since the patient did not have unprotected receptive anal intercourse
2. Place a STAT order for infectious disease consultation so the patient can be seen within a week
3. Prescribe PEP immediately
4. Repeat HIV testing in 2 weeks (window period). If test is negative, then prescribe PEP
# Exposure Risks
(average, per episode, involving HIV-infected source patient)

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Risk Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous (blood)</td>
<td>0.3%</td>
</tr>
<tr>
<td>Mucous membrane exposure</td>
<td>0.09%</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>0.3 - 3%</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>0.06%</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>0.1 – 0.2%</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>0.03 – 0.14%</td>
</tr>
<tr>
<td>Receptive oral (male)</td>
<td>0.06%</td>
</tr>
<tr>
<td>Female-female orogenital</td>
<td>4 case reports</td>
</tr>
<tr>
<td>IDU needle sharing</td>
<td>0.67%</td>
</tr>
<tr>
<td>Vertical (no prophylaxis)</td>
<td>24%</td>
</tr>
</tbody>
</table>
Risk of Infection

- Blood and visibly bloody body fluids
- Semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid
- Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they are visibly bloody
If the decision is made to administer post-exposure prophylaxis, it should be started as early as possible after an exposure, **ideally within 2 hours**

Post-exposure prophylaxis is not indicated if the patient presents for care more than 72 hours after an exposure

**HIV testing (serology and RNA)** should be performed at baseline

Before offering post-exposure prophylaxis, patients should also be evaluated for the following criteria:

- the nature of the exposure
- whether the HIV status of the source is known
- whether the exposure occurred within 72 hours prior to presentation
- whether the patient is committed to future risk reduction
What is the recommended PEP regimen?

1. Zidovudine/lamivudine plus boosted darunavir
2. Tenofovir/emtricitabine plus raltegravir
3. Tenofovir/emtricitabine
4. Zidovudine/lamivudine plus boosted lopinavir
Tenofovir + emtricitabine [Truvada] (QD) plus either raltegravir (BID) or dolutegravir (QD) are recommended as the preferred initial PEP regimen because of:

- its excellent tolerability
- proven potency in established HIV infection
- ease of administration

Zidovudine and efavirenz are no longer recommended in the preferred PEP regimen because of significantly high rates of treatment-limiting side effects.
PrEP treatment should be continued for ___ days. HIV testing should be repeated at ___ weeks and ___ months.

1. 28 days; 4 weeks and 3 months
2. 28 days; 4 weeks and 6 months
3. 42 days; 4 weeks and 3 months
4. 42 days; 4 weeks, and 6 months
You are evaluating a 23 year-old male at your office for a primary care visit

He has no active complaints. He is sexually active with men and had six partners over the past year

He has a history of syphilis diagnosed two-years ago and was treated with IM penicillin

Six months ago, you counseled him on the importance of consistent condom use

He reports that he currently uses condoms ~80% of the times. No recent STD since last visit. He drinks alcohol occasionally and no illicit drug use
What would you recommend for Michael?

1. HIV screening
2. HIV and STD screening
3. HIV, STD screening and discuss the importance of persistent condom use
4. Offer daily Truvada (TDF/FTC) plus HIV, STD screening and discuss the importance of persistent condom use
# Understanding PrEP

**Example: Birth Control**

<table>
<thead>
<tr>
<th>Oral Contraceptive (“The Pill”)</th>
<th>Pre-Exposure Prophylaxis (PrEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevents pregnancy if taken before sex. <strong>Does not work as morning-after pill.</strong></td>
<td>Prevents HIV infection pre-exposure. <strong>Will not work if already exposed.</strong></td>
</tr>
<tr>
<td>Does not always start working immediately.</td>
<td>Does not start working immediately.</td>
</tr>
<tr>
<td>Must take daily – cannot skip doses.</td>
<td>Must take daily – cannot skip doses.</td>
</tr>
<tr>
<td>Only helps prevent pregnancy, will not prevent STIs (should still use condoms).</td>
<td>Only helps prevent HIV – will not prevent other STIs (should still use condoms).</td>
</tr>
<tr>
<td>Very effective at preventing pregnancy, but not 100% effective.</td>
<td>Very effective at preventing HIV infection, but not 100% effective.</td>
</tr>
<tr>
<td>Should be taken by anyone who is sexually active (at risk for becoming pregnant)</td>
<td>Should be taken by anyone who could be exposed to the HIV virus (at risk for HIV)</td>
</tr>
</tbody>
</table>
If PrEP is taken daily, it can reduce sexually acquired HIV infection by up to...

1. 50-60%
2. 60-80%
3. 80-90%
4. >90%
I feel that patients on PrEP will...

1. Increase their risk behavior
2. Decrease their risk behavior
3. No change in behavior
4. I don’t know
Which statement best applies to you?

1. I have not prescribed PrEP
2. I have prescribed PrEP for 1-5 patients
3. I have prescribed PrEP for >5 patients
For those who said they have not prescribed PrEP, was it because...

1. I need more information about PrEP
2. It takes too much time
3. None of my patients could afford it
4. Other
My top concern about PrEP is...

1. Not enough research on long term effects of PrEP
2. Financial concerns – who is paying for it?
3. STDs will increase due to increase in risk behavior
4. Patients will not be adherent
5. Not enough education for providers
6. On demand PrEP is not effective in women
7. Other
Only Infectious Disease Specialists can prescribe anti-viral medications

1. True
2. False
3. Don’t know
How does PrEP work?
Pre-Exposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men - The iPrEX Trial

* Randomized clinical trial - 4905 subjects
* Truvada (TDF/FTC) was shown to decrease the risk of HIV transmission by 42% in MSM who also received comprehensive preventive services
* The risk was decreased by 92% in patients with detectable drug levels

Table 2. Adverse Events.*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>FTC–TDF (N = 1251)</th>
<th>Placebo (N = 1248)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>no. of events</td>
<td>no. of patients (%)</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>867 (69)</td>
<td>2630</td>
<td>877 (70)</td>
</tr>
<tr>
<td>Any serious adverse event</td>
<td>60 (5)</td>
<td>76</td>
<td>67 (5)</td>
</tr>
<tr>
<td>Any grade 3 or 4 event</td>
<td>151 (12)</td>
<td>248</td>
<td>164 (13)</td>
</tr>
<tr>
<td>Grade 3 event</td>
<td>110 (9)</td>
<td>197</td>
<td>117 (9)</td>
</tr>
<tr>
<td>Grade 4 event</td>
<td>41 (3)</td>
<td>51</td>
<td>47 (4)</td>
</tr>
<tr>
<td>Elevated creatinine level</td>
<td>25 (2)</td>
<td>28</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Headache</td>
<td>56 (4)</td>
<td>66</td>
<td>41 (3)</td>
</tr>
<tr>
<td>Depression</td>
<td>43 (3)</td>
<td>46</td>
<td>62 (5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>20 (2)</td>
<td>22</td>
<td>9 (&lt;1)</td>
</tr>
<tr>
<td>Unintentional weight loss (≥5%)</td>
<td>27 (2)</td>
<td>34</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>46 (4)</td>
<td>49</td>
<td>56 (4)</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>15 (1)</td>
<td>16</td>
<td>11 (&lt;1)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (&lt;1)‡</td>
<td>1</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>Discontinuation of study drug</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanently</td>
<td>25 (2)</td>
<td>26</td>
<td>27 (2)</td>
</tr>
<tr>
<td>Permanently or temporarily</td>
<td>79 (6)</td>
<td>99</td>
<td>72 (6)</td>
</tr>
</tbody>
</table>

* A listing of all laboratory abnormalities and clinical adverse events of grade 2 or higher that were reported in ≥25% or more subjects (1%) is provided in Tables S9 and S10 in the Supplementary Appendix. FTC–TDF denotes emtricitabine and tenofovir disoproxil fumarate.
† P values were calculated by the log-rank test.
‡ This death was due to a motorcycle accident.
Sexual behavior by perceived treatment group

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0081997
Truvada (TDF/FTC) was shown to decrease the risk of HIV transmission by 75% in uninfected individuals in stable heterosexual serodiscordant relationship who also received comprehensive preventive services.

- Tenofovir alone decreased the risk by 67%.
- The risk was decreased by 90% in patients with detectable TDF and FTC levels.
- 8 patients were infected with HIV before randomization. Resistant HIV to the study medications developed in 2 cases.
- No participants who acquired HIV after randomization developed resistance.

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

* Randomized clinical trial - 414 subjects
* Truvada (TDF/FTC) before and after sexual activity was shown to decrease the risk of HIV transmission by 86% in MSM who also received comprehensive preventive services
* Median of 15 pills/month

FDA Approval

FDA approves Truvada for prevention of HIV/AIDS
Indications:

* On May 14, 2014, the US Public Health Service and the CDC released the first comprehensive guidelines for PrEP.
* PrEP is indicated in patients who are HIV-negative and have one of the following risk factors:
  1. HIV-positive partners
  2. MSM with recent unprotected sex or STD
  3. Intravenous drug users (IDU) who reported sharing needles or equipment, or have recently starting substance use treatment program (high-risk for relapse).
  4. Heterosexual men or women who infrequently use condoms and have sex with high-risk partners
Estimated percentages and numbers of adults with indications for preexposure prophylaxis (PrEP), by transmission risk group — United States, 2015

**MSM**
- Not Indicated for PrEP: 1,499,903 (75%)
- Indicated for PrEP: 492,000 (25%)
  - 1 in 4

**IDU**
- Not Indicated for PrEP: 506,600 (81%)
- Indicated for PrEP: 115,000 (19%)
  - 1 in 5

**HETEROSEXUAL**
- Not Indicated for PrEP: 156,000,000 (99.60%)
- Indicated for PrEP: 624,000 (0.40%)
  - 1 in 200

Case Continued:
You decided to start Michael on PrEP. What tests should you order next?

1. HIV testing, hepatitis B antigen and Cr clearance
2. HIV testing, CD4, liver function test and Cr clearance
3. HIV testing, liver function testing, and Cr clearance
4. HIV testing, CD4 and liver function testing
* HIV testing, hepatitis B antigen and Cr clearance are key tests before starting PrEP

* Other tests include:
  - STD panel (RPR, GC/CD)
  - Hepatitis A serology in MSM (for immunity)
  - Hepatitis B serology (for immunity)
  - Hepatitis C serology
  - Pregnancy testing (in women)
How often should you repeat HIV testing?

1. Every 30 days
2. Every 3 months
3. Every 6 months
4. Once a year
Testing and Retesting to Confirm Negative HIV Status

Are there signs or symptoms of HIV-1 infection, OR is recent exposure to HIV suspected?

NO

DO NOT initiate TRUVADA for PrEP
Wait 1 month to ensure HIV-1 has not been contracted

Confirm negative HIV-1 status
If appropriate, consider prescribing TRUVADA for PrEP

YES

Confirm that HIV-1 has not been contracted using a highly sensitive, FDA-approved test
If appropriate, consider prescribing TRUVADA for PrEP

RE-CONFIRM NEGATIVE HIV-1 STATUS AT LEAST EVERY 3 MONTHS

https://start.truvada.com/hcp/confirm-negative-hiv1-status
Reducing HIV Risk Behaviors

- Trusting and confidential **environment**
- **Ongoing dialogue** with the patient regarding their risk behavior
- **PrEP is not always effective** in preventing HIV infection particularly if used **inconsistently**
- Consistent use of PrEP together with other prevention methods (consistent condom use, discontinuing drug injection or never sharing injection equipment) confers very high levels of protection
Beginning PrEP Medication Regimen

* Prescribe 1 tablet of Truvada (TDF [300mg] plus FTC [200mg]) daily.

* In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.

* Provide risk-reduction and PrEP medication adherence counseling and condoms.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>At Least Every 3 Mos</th>
<th>After 3 Mos and at Least Every 6 Mos Thereafter</th>
<th>At Least Every 6 Mos</th>
<th>At Least Every 12 Mos</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ HIV test</td>
<td>▪ Assess renal function</td>
<td>▪ Test for bacterial STIs</td>
<td>▪ Evaluate need to continue PrEP</td>
</tr>
<tr>
<td></td>
<td>▪ Medication adherence counseling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Behavioral risk reduction support</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>▪ Adverse event assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ STI symptom assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Pregnancy test (where appropriate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HBsAg+</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ HBV DNA by quantitative assay* (every 6-12 mo)</td>
<td></td>
</tr>
</tbody>
</table>
PrEP in Clinical Practice: What Are the Barriers to PrEP Uptake?

<table>
<thead>
<tr>
<th>Users</th>
<th>Providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unaware of HIV risk, PrEP availability, or how to access it</td>
<td>• Unaware of intervention</td>
</tr>
<tr>
<td>• No or delayed access to clinical preventive care</td>
<td>• Uncertain how to deliver the intervention</td>
</tr>
<tr>
<td>• Uninsured or unable to pay</td>
<td>• Wary of complexity and time involved</td>
</tr>
<tr>
<td>• Adherence challenges</td>
<td>• Discomfort with assessing candidacy</td>
</tr>
<tr>
<td>• Concern about disclosure and stigma</td>
<td>• Uncertain how to bill for intervention</td>
</tr>
</tbody>
</table>
Reasons to stop PrEP:
* Evidence of HIV infection
* Pregnancy
* Adverse events
* Chronic non-adherence
* Patient choice

On Discontinuing PrEP: Hepatitis B antigen, HIV

If resuming PrEP after stopping, repeat standard pre-PrEP evaluation
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* Randomized clinical trial-414 subjects
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New data on PrEP - 2016

* MTN-020/ASPIRE & IPM-027: Efficacy and Safety of Dapivirine Vaginal Ring. Protection 27-37%
* ÉCLAIR: Cabotegravir LA (injectable) in HIV-Negative Men at Low Risk for HIV Infection
* HPTN-069/A5305: Maraviroc-Based PrEP for MSM
**Conclusions**

- PEP is recommended after possible/confirmed HIV exposure within 72 hours
- Recommended PEP regimen is truvada (TDF/FTC) and raltegravir/dolutegravir for 28 days
- PrEP is recommended as one prevention option for sexually active MSM, heterosexual men and women, IDU at substantial risk of HIV acquisition
- Adherence is a key factor in PrEP efficacy
- Before prescribing PrEP, HIV infection must be excluded, and the patient should be assessed for comorbidities that may present health risks
- The recommended PrEP regimen is fixed-dose TDF/FTC
- Patients prescribed PrEP should return for follow-up visits at least every 3 months
Questions
Evaluations

* Please complete Presentation Evaluations.