CASE #1

A 27 year old previously healthy man presents to an urgent care center with fever, sore throat, lymphadenopathy, severe fatigue and a diffuse erythematous rash. His symptoms have been present for approximately 48 hours and his history reveals unprotected receptive anal intercourse with another man 12 days prior to the onset of his symptoms. He had a negative HIV antibody test approximately 6 months ago. His physical examination shows a temperature of 39.0 C, no exudative pharyngitis, the presence of cervical and axillary lymphadenopathy, and a generalized morbilliform rash. All laboratory tests are pending.

Which of the following is the most likely diagnosis?

A. Syphilis
B. Acute HIV Infection
C. Shingles
D. Measles
E. Drug Hypersensitivity
F. None of the Above
Primary (Acute) HIV Infection

- Symptomatic in 30-90% of newly infected individuals
- Symptoms occur 2-6 weeks after exposure to HIV
- Median duration of symptoms 15-28 days

Laboratory Studies with Acute HIV

- Positive HIV-1 RNA Assay and Negative HIV Antibody Test
Natural History of Untreated HIV Infection

Cumulative HIV Cases in the U.S.

1.18 million people with HIV/AIDS in the United States
- 50,000 new HIV infections each year in the past decade
(approximately 40% of these are acquired from people who didn’t know they were infected)
Late Diagnosis of HIV in Oregon

- Only 41% of Oregon adults have ever been tested for HIV
- During 2008 – 2012, 39% of Oregonians newly diagnosed with HIV infection had severe enough immune suppression to meet AIDS criteria within 12 months of diagnosis
- These individuals likely had been infected for ≥7 years
- These individuals reported missed opportunities for testing, often because they didn't recognize or report their HIV risks.

HIV Testing: Now part of primary care

HIV screening is recommended for patients aged 13-64 years in all health-care settings.

Persons at high risk for HIV infection should be screened for HIV at least annually.

Cost effective in patients up to 75 years old if sexually active and local HIV prevalence > 0.1%

What is PrEP?

WHAT IS PREP?
What is Pre-Exposure Prophylaxis, or PrEP?

- A prevention strategy in which individuals at highest risk of HIV infection take a medication regularly (along with continued behavioral risk-reduction strategies) to prevent HIV infection.
- Truvada (tenofovir/emtricitabine) was approved for HIV PrEP by the FDA in July 2012 and is a fixed dose combination of tenofovir and emtricitabine.
- Tenofovir/emtricitabine is modestly effective at reducing Herpes Simplex (HSV) acquisition and has reduced the rate of Hepatitis B acquisition in certain populations.

Truvada is tenofovir/emtricitabine (TDF/FTC) and is currently the only medication approved by the FDA for PrEP

HIV Drug Targets

Both tenofovir disoproxil fumarate and emtricitabine are nucleoside reverse transcriptase inhibitors (NRTIs).

Tenovir-Emtricitabine as PrEP for HIV Prevention

Estimated Protection from PrEP, All Participants

Tenofovir-Emtricitabine as PrEP for HIV Prevention

Estimated Protection in All Participants (Dark Bar) vs Adherent Participants (Light Bar)


What is PrEP?

Who Should Be Offered PrEP?

CDC Guidelines for PrEP: 2017

Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults; therefore,

- PrEP is recommended as one prevention option for sexually-active adult MSH (men who have sex with men) at substantial risk of HIV acquisition. (IA)
- PrEP is recommended as one prevention option for adult heterosexual men and women who are at substantial risk of HIV acquisition. (IA)
- PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition. (IA)
- PrEP should be discussed with heterosexual-active women and men whose partners are known to have HIV infection (HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy. (B)

Who should be offered PrEP?

<table>
<thead>
<tr>
<th>Among Who Have Sex with Men</th>
<th>transgender women and men</th>
<th>Persons Who Inject Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>high risk sexual partner</td>
<td>high risk sexual partner</td>
<td>high risk sexual partner</td>
</tr>
<tr>
<td>recent sexual partner</td>
<td>recent sexual partner</td>
<td>recent sexual partner</td>
</tr>
<tr>
<td>commercial sex work</td>
<td>commercial sex work</td>
<td>commercial sex work</td>
</tr>
</tbody>
</table>

Avoid PrEP in the following:

**Contraindications**
- HIV Positive
- Estimated creatinine clearance (eGFR/CLcr) < 60ml/min
- Possible recent HIV exposure
  - (If patient presents within 72 hours of possible HIV exposure, offer nPEP, then consider PrEP)

**Caution**
- Hepatitis B (HBV) infection: Can flare up when stopping the medications used for PrEP; check the Hepatitis B Antibody/Antigen (HBsAb/Ag) prior to initiation of PrEP
- Prolonged Flu-like illness: Consider evaluation for acute HIV infection with HIV RNA PCR before initiation of PrEP
- In patients with conditions such as diabetes mellitus or hypertension, there may be an increased risk of kidney disease; consider more frequent creatinine monitoring
- Difficulty with adherence
- Pregnancy or breastfeeding
- Osteoporosis
- Adolescents

Interpreting Tests for Hepatitis B

<table>
<thead>
<tr>
<th>Test Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIVAb(+)</td>
<td>Immune due to natural infection</td>
</tr>
<tr>
<td>HIVAb(+)</td>
<td>Immune due to hepatitis B vaccine</td>
</tr>
<tr>
<td>HIVAb(-)</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

If you have questions about PEP, call the helpline:
Clinician Consultation Center PEPline
http://nccc.ucsf.edu/clinician-consultation
1-888-448-4911
Knowledge Test

Who would NOT be a good candidate for PrEP?

A. Someone who engages in condomless vaginal or anal sex with a partner of unknown HIV status who is known to be at substantial risk of HIV infection.
B. Someone who is HIV positive.
C. Someone who has a creatinine clearance of 65 ml/min.
D. Someone who injects drugs and shares needles or equipment.

PrEP Screenings and Labs

What is PrEP?

Recommended HIV Screening Prior to PrEP Initiation

At a minimum, document a negative screening test within 1 week before initiating (or reinitiating) PrEP

(A) Blood (serum) lab-based testing, or
(B) Rapid, point-of-care, fingerstick blood testing*

If negative or indeterminate screening result in a patient with recent signs and symptoms of acute HIV

(A) Repeat screening test in 1 month and defer PrEP decision, or
(B) Send HIV RNA PCR (preferred)

*Oral rapid tests should not be used to screen for HIV infection when considering PrEP because they can be less sensitive than blood tests
**Additional Labs prior to PrEP initiation**

**Initial visit:**
- HIV test (ideally 4th generation HIV Ag/Ab)
- Creatinine (renal function)
- Gonorrhea/Chlamydia PCR (include rectal, pharyngeal and urine screening in MSM)
- Syphilis (RPR)
- Hepatitis B (HBsAb/Ag)
- Hepatitis C (HCV Ab)
- Pregnancy test for women of child-bearing age
- Provide Hepatitis B (HBV) & Human papillomavirus (HPV) immunizations as indicated

**Counseling**

**Topics to discuss at PrEP visits:**
- Importance of daily adherence, link dosing to daily routine
- STI and HIV prevention (condom use/risk reduction)
- Safer injection drug use practices
- Need for regular follow-up visits and lab tests
- Reproductive goals and contraception
- Symptoms of acute HIV infection
- Risks of stopping and/or restarting PrEP, and need to notify provider
- Insurance and medication assistance
- Refill policies and procedures

**Side Effects of TDF/emtricitabine**

- **Nausea and headache:** 10% of patients, which usually resolve within 1 month
- **Renal dysfunction:** Small risk, typically reversible if PrEP is discontinued
- **Bone mineral density decrease:** PrEP associated with 1% decrease; however, no increased risk of fractures
Prescribe

- When initial work-up and counseling are completed:
- **Prescribe:** Truvada (tenofovir disoproxil fumarate/emtricitabine 300/200mg) 1 tab PO daily, #30, 2 refills for a **MAXIMUM 90 day supply**

Lab Screenings and Visits

**Week 1**
- Call, check if prescription filled
- Assess adherence and side effects

**Month 1**
- Consider HIV test (ideally 4th generation HIV Ag/Ab)
- Assess adherence and side effects

Lab Screenings and Visits

**At least every 3 months:**
- HIV test (ideally 4th generation HIV Ag/Ab)
- Pregnancy test
- Assess adherence
- Evaluate need to continue PrEP (sexual history)
- Provide only 3-month refill
Lab Screenings and Visits

**At least every 6 months:**
- Gonorrhea/chlamydia and syphilis (more frequently depending on risk)

**Renal Function**
- Creatinine at baseline
- Creatinine at 3 months
- Creatinine every 3-6 months (more frequent if patient has renal risk factors)

**At every visit:**
- Provide risk reduction counseling and assess for signs/symptoms of acute HIV infection

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Summary of Recommended Laboratory Evaluation
Baseline and Routine Monitoring for Patients taking PrEP

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Baseline</th>
<th>Every 3 months</th>
<th>At least every 6 months</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV screening assay</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>Consider need for HIV RNA PCR</td>
</tr>
<tr>
<td>HBV antibody panel and HCV antibody</td>
<td>✔</td>
<td></td>
<td></td>
<td>Offer HBV vaccination if not immune</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>Avoid PrEP if CrCl &lt;60 mL/min</td>
</tr>
<tr>
<td>General STI screen</td>
<td>✔</td>
<td></td>
<td></td>
<td>Include oral/rectal/urethral GC/CT screen if risk</td>
</tr>
<tr>
<td>Pregnancy test for women*</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The safety of PrEP in pregnancy has not been established

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Counseling

**Key messages in efficacy:**
- When taken daily with excellent adherence, PrEP is over 90% effective for preventing HIV (CDC)
- Maximum drug levels are reached in rectal tissues after 7 days and in blood and vaginal tissues after 20 days
- If planning to stop PrEP, continue PrEP for 28 days after last potential HIV exposure
- If patient has chronic Hepatitis B, monitor LFTs if PrEP discontinued
- PrEP does not prevent gonorrhea, chlamydia, syphilis, genital warts, herpes, or Hepatitis C
PrEP in Practice

Is there a risk of drug resistance to Truvada if a person acquires HIV while on PrEP?

<table>
<thead>
<tr>
<th>Trial</th>
<th>%</th>
<th>% HIV-1 Detectable/HIV-1 Resistance/ HIV-2 Detectable/HIV-2 Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEx</td>
<td>124</td>
<td>0/36</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>1040</td>
<td>4/71</td>
</tr>
<tr>
<td>TDF2</td>
<td>601</td>
<td>0/30</td>
</tr>
<tr>
<td>TDF/FTC 27</td>
<td>552</td>
<td>4/71</td>
</tr>
<tr>
<td>TDF/FTC 22</td>
<td>1038</td>
<td>1/23</td>
</tr>
<tr>
<td>TDF/FTC 21</td>
<td>378</td>
<td>4/14 (1.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>7062</td>
<td>5/24 (0.07%)</td>
</tr>
</tbody>
</table>

*The 22 week analysis, outcome levels of risk of resistance to be examined*

Does use of PrEP increase sexual risk-taking?

- In both iPrEx and Partners PrEP, condomless sex was less common over time
- BUT subjects did not know if they were on PrEP or placebo
Is PrEP Worth the Cost?

Cost- About $13,600 annually (about $1,130 monthly)

- Preventing one new HIV infection will save the healthcare system an estimated $357,498 in lifetime HIV care costs.
- Most health insurance providers cover Truvada for PrEP (patient just pays co-pay for doctor's visit, and lab tests and drug co-pay)
- Remember, there are varying degrees of benefit for all prescription drugs
- Insurance may require prior authorization
- Resources at end of this presentation to help patient pay for PrEP, including contacts for PrEP Navigators.

IPERGAY TRIAL-"on demand" PrEP

- Placebo controlled trial in MSM-France and Canada
- 400 enrolled, 199 TDF/FTC and 201 placebo
- 2 pills 2-24 hrs prior to sex, then 1 tab/day x 2 days
- HIV infection in 2 TDF/FTC and 14 in placebo (86% reduction)

PrEP in the Future

- Tenofovir-containing pills are not feasible for everyone. There is an encouraging pipeline of new PrEP prevention products that will deliver additional options.
Resources

- Clinical Consultation Center PrEPline: 855.488.7737 or [http://nccc.ucsf.edu/clinician-consultation](http://nccc.ucsf.edu/clinician-consultation)
- PrEP Calculator for MSM risk and assessment: [https://ictrweb.johnshopkins.edu/ictr/utility/prep.cfm](https://ictrweb.johnshopkins.edu/ictr/utility/prep.cfm)

Medication Assistance Programs:

- Gilead Financial Support: [https://start.truvada.com/paying-for-truvada](https://start.truvada.com/paying-for-truvada)
- Patient Access Network: [www.panapply.org](http://www.panapply.org)
- Patient Advocate Foundation Co-Pay Relief: [https://www.copys.org](https://www.copys.org)

Regional Contacts:

- Mountain West AIDS Education and Training Center
  - Oregon Program: dayna@reg.org or 971.200.5266
  - Can offer providers further education on HIV and PrEP
- Cascade AIDS Project
  - PrEP Coordinators: prep@cascadeaids.org or 503.223.5907
  - Can help patients navigate insurance and prescription assistance programs available for PrEP

PEP (post-exposure prophylaxis)

- Occupational (needlestick, scratch, blood splash, etc)
- Non-occupational (high risk sex, IDU, others)
- Both PEP and nPEP utilize 3 drugs active against HIV (only 2 drugs for PrEP)
Exposure Risk (per episode, with infected source)

<table>
<thead>
<tr>
<th>Exposure Pathway</th>
<th>Risk Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous (blood)</td>
<td>0.3%</td>
</tr>
<tr>
<td>Mucocutaneous (blood)</td>
<td>0.09%</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>1 - 2%</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>

HIV Prevalence Rates

- U.S. Population: 0.45%
  ~ 1.2 million cases
- VA: 0.41%
  - 25,271 cases
- Multnomah County: 0.40%
  - 2,797 cases
- Portland VA Medical Center: 0.40%
  - 305 cases

Potentially infectious for HIV

- blood
- spinal fluid
- pleural fluid
- pus
- semen
- vaginal secretions
- amniotic fluid
- pericardial fluid
- synovial fluid

NOT infectious

- urine
- feces
- saliva
- nasal secretions
- gastric fluid
- sputum
- tears
- sweat
- vomitus
nPEP Evaluation Algorithm

HIV nPEP Regimens-2016 guidelines

The preferred regimen for otherwise healthy adults and adolescents:
- Tenofovir disoproxil fumarate (tenofovir DF or TDF) (300 mg) once daily plus
  raltegravir (RAL) 400 mg twice daily or dolutegravir (DTG) 50 mg daily. [V1-A2ci]
  [VII-C]
  Avoid dolutegravir in pregnancy.

- Alternative regimen for otherwise healthy adults and adolescents is
  tenofovir DF (300 mg) with emtricitabine (FTC) (200 mg) once daily plus
  darunavir (DRV) (800 mg) and ritonavir (RTV) (100 mg) once daily. [VII-C]

Treatment recommended for 28 days.
If CD4 <350, use abacavir/lamivudine with INSTI or PI.
See guidelines for treatment in children.

Follow-up labs nPEP

<table>
<thead>
<tr>
<th>Test</th>
<th>Source</th>
<th>Exposed person</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Ag/Ab setting*</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Hepatitis B serology, including Hepatitis B surface antigen</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Hepatitis C serology test</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Urine pregnancy*</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Pregnancy*</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Renal ultrasound</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>CD4 and CD8 counts</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Plasma viral load</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>Serum alanine transaminase, aspartate transaminase</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>HIV viral load</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>HIV reverse transcriptase RNA</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td>HIV nef transactivator RNA</td>
<td>Baseline</td>
<td>-6 weeks after exposure</td>
</tr>
<tr>
<td><strong>UCSF Clinician Consultation Center for PEP</strong></td>
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<td>------------------------------------------------</td>
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</tr>
<tr>
<td>HOURS OF OPERATION FOR OCCUPATIONAL PEP CONSULTATION ARE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 a.m. – 8 p.m. ET (seven days a week).</td>
<td></td>
<td></td>
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<tr>
<td>HOURS OF OPERATIONS FOR NON-OCCUPATIONAL PEP CONSULTATION ARE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 a.m. – 8 p.m. ET Monday – Friday, and 11 a.m. – 8 p.m. ET on weekends &amp; holidays.</td>
<td></td>
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<tr>
<td>(888) 448-4911</td>
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