HIV Routine Testing and Prevention

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Session Objectives

- Describe routine testing principles
- Identify, counsel and provide HIV Pre-exposure prophylaxis (PrEP) to patients at high risk of HIV acquisition
- Identify, counsel and provide nonoccupational HIV Post-exposure prophylaxis (PEP) to patients at high risk of HIV acquisition
Case

- Ben is a 20 year old man who presents for vaccinations in preparation for a trip to Costa Rica.
- He has not been seen by a healthcare provider for 2 years.
- In addition to evaluation for his upcoming travel, should his provider offer an HIV test?

Goals of Routine Testing for HIV

- Improve Survival & Quality of Life
- Prevent New HIV Infections

Why Do We Need Routine HIV Screening?

- Many are unaware they have HIV infection – no symptoms
- Risk-based testing strategies fail to identify everyone who needs screening
- Late diagnosis of HIV remains a problem
  - In 2015 the estimated median interval from HIV infection to diagnosis was 3 years
Over 1.1 million people are living with HIV in the US.

One in seven are unaware of their infection.

Florida ranked 3rd in new HIV diagnoses in 2016.

Disproportionate Transmission of HIV in People Unaware of HIV Infection Status:

- **Aware**:
  - 75% of new HIV infections
- **Unaware**:
  - 25% of new HIV infections

Awareness of HIV Infection:

- **Unaware**: 25%
- **Aware**: 75%

New HIV Infections:

- **Unaware**: 54%
- **Aware**: 46%


HIV Testing:

- **59%** of homosexual men
- **42%** of people who inject drugs
- **29%** of gender and bisexual men

Many people at high risk for HIV aren’t getting tested every year.
How Do We Test For HIV Infection?

- HIV Antigen/Antibody Test (4th generation testing)
  - Can detect acute HIV infection
- HIV Antibody Test (3rd generation)
- Rapid HIV Test
  - Blood or sputum
  - Requires confirmation
- HIV viral load
  - Can detect acute HIV infection

Sequence of Appearance of Lab Markers of HIV-1 Infection

New CDC Recommendations for HIV Testing in Laboratories

Who Should We Screen? CDC 2006

- Routinely screen all patients aged 13-64 for HIV infection after notifying them that testing will be performed unless declined
- Opt-out testing
- Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings

Routine Screening for HIV Infection: CDC 2006

- Screen
  - All patients starting treatment for tuberculosis
  - All patients seeking treatment for STDs during each visit for a new complaint
  - Screen at least annually
  - Intravenous drug users and their sex partners
  - People who exchange sex for money or drugs
  - Sex partners of people with HIV infection
  - Men who have sex with men or heterosexuals who have or who their sex partners have had more than one sex partner since their most recent HIV test

Florida HIV Testing Statutes

- 381.004 HIV Testing
  - Obtaining Consent
    - "In a health care setting, the person to be tested shall be notified orally or in writing that the test is planned and that he or she has the right to decline the test. If the person to be tested declines the test, such decision shall be documented in the medical record. A person who has signed a general consent form for medical care is not required to sign or otherwise provide a separate consent for an HIV test during the period in which the general consent form is in effect."
Florida HIV Testing Statues 381.004

- “The person ordering the test or that person’s designee shall ensure that all reasonable efforts are made to notify the test subject of his or her test result. Notification of a person with a positive test result shall include information on the availability of appropriate medical and support services, on the importance of notifying partners who may have been exposed, and on preventing transmission of HIV. Notification of a person with a negative test result shall include, as appropriate, information on preventing the transmission of HIV. When testing occurs in a hospital emergency department, detention facility, or other facility and the test subject has been released before being notified of positive test results, informing the county health department for that department to notify the test subject fulfills this responsibility.”

http://www.leg.state.fl.us/Statutes/index.cfm?App_mode=Display_Statute&URL=0300-0399/0381/Sections/0381.004.html

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HIV Screening in Pregnant Women

- Universal Opt-out screening
- Address reasons for declining test
  - Document declinations in the medical records
- Timing of HIV test
  - Early during pregnancy
  - Repeat in third trimester, ideally < 36 weeks gestation
  - Rapid testing at time of delivery if indicated

CDC. MMWR 2006;55(RR14);1-17.
HIV Testing in Pregnancy
§ 384.31, F.S. & Rule 64D-3-042, F.A.C

- Florida Statute 384.31
  
  Testing of pregnant women; duty of the attendant.—Every person, including every physician licensed under chapter 458 or chapter 459 or midwife licensed under part I of chapter 464 or chapter 467, attending a pregnant woman for conditions relating to pregnancy during the period of gestation and delivery shall cause the woman to be tested for sexually transmissible diseases, including HIV, as specified by department rule. Testing shall be performed by a laboratory approved for such purposes under part I of chapter 483. The woman shall be informed of the tests that will be conducted and of her right to refuse testing. If a woman objects to testing, a written statement of objection, signed by the woman, shall be placed in the woman’s medical record and no testing shall occur.

What happens if the test is positive?

- Positive rapid tests require confirmation.
- Results should be communicated confidentially through personal contact
- Provide counseling
  - HIV is a manageable disease
  - Discuss HIV risk reduction
  - Discuss ways to handle the emotional consequences of a positive result
- Inform the patient that they might be contacted by health department staff

Partner Notification

- Partner notification is not legally mandated in the state of Florida
- Advise patients with a positive HIV test of the importance of notifying partners who may have been exposed and counsel on prevention of HIV transmission
- The Florida Department of Health can provide confidential partner notification services
HIV Prevention

- Voluntary male circumcision
- Blood safety
- Injection safety
- Microbicides
- Prevention of perinatal transmission
- Condom use
- Mutually monogamous sex with a partner who doesn’t have HIV
- Abstinence
- Treatment as Prevention
- Pre-exposure prophylaxis (PrEP)
- Post-exposure prophylaxis (PEP)
- Blood safety
- Injection safety
- Microbicides
- Prevention of perinatal transmission
- Condom use

What is PrEP?

A PERSON LIVING WITH HIV WHO HAS AN UNDETECTABLE VIRAL LOAD DOES NOT TRANSMIT THE VIRUS TO THEIR PARTNERS.
Pre-exposure Prophylaxis

PrEP IS AN HIV PREVENTION METHOD IN WHICH PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK OF BECOMING INFECTED

ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. AN HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.

Antiretroviral Mechanism of Action

Truvada® (TDF/FTC) PrEP

- FDA approval July 2012 for use in HIV PrEP
- Based on studies showing safety and efficacy in preventing HIV acquisition in the following groups
  - Men that have sex with men
  - Men and women in heterosexual HIV discordant relationships
  - Heterosexual men and women
  - Transgender women
  - People who inject drugs
PrEP Trials
Men and Transgender Women Who Have Sex With Men

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Participants</th>
<th>Risk Reduction</th>
</tr>
</thead>
</table>
| iPrEx | Randomized, double-blind, placebo controlled | Peru, Ecuador, Brazil, Thailand, S Africa, U.S. | 44% Overall
• 73% if took 90% of drug by self report/pill count
• 92% if detectable drug level |
| IPERGAY | Randomized, double-blind placebo controlled Event driven TDF/FTC | France & Canada | 86% |
| PROUD | Randomized, open label TDF/FTC daily vs placebo
• Immediate arm
• Delayed arm | England | 86% in immediate arm |

PrEP Trials
Heterosexual Men and Women

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Participants</th>
<th>Risk Reduction</th>
</tr>
</thead>
</table>
| Partners PrEP | Randomized, double-blind, placebo controlled Daily TDF or TDF-FTC or placebo | 4,758 HIV-discordant couples Kenya & Uganda | 75% with TDF-FTC
90% if drug detected
67% TDF |
| TDF2 | Randomized, double-blind placebo controlled Daily TDF:FTC or placebo | 1,219 heterosexual men and women Botswana | 62% |

PrEP Trials: Women

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Participants</th>
<th>Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprina 034</td>
<td>Double-blind, randomized, controlled TDF vaginal gel</td>
<td>S Africa</td>
<td>54% if high adherence</td>
</tr>
</tbody>
</table>
| FEM-PrEP | Double-blind, randomized, controlled TDF-FTC or placebo | 1511 Aged 18-35 S Africa
Kenya Tanzania | Stopped due to lack of efficacy
Low adherence |
| VOICE | Randomized, double blind TDF or TDF-FTC or TDF gel vs oral or topical placebo | Eastern and Southern Africa | Very high self reported adherence, but low drug levels detected
Stopped due to futility |
| ASPIRE | Double-blind, placebo controlled 25 mg dapivirine ring vs placebo | 3629 V Malawi, South Africa, Uganda, and Zimbabwe | 27% overall
61% in women over 25
10% if younger than 25 |
| Ring | Double-blind, placebo controlled 25 mg dapivirine ring vs placebo | 1,959 Uganda S Africa | 33% overall
37% if over 21
15% younger than 21 |
**PrEP: People Who Inject Drugs**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Participants</th>
<th>Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangkok Tenofovir</td>
<td>Double-blind, placebo-controlled trial Oral TDF or placebo</td>
<td>2,713</td>
<td>49% 70% in those with detectable plasma TDF level</td>
</tr>
</tbody>
</table>

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**Detectable Drug Prevents HIV Acquisition**

- A: Intracellular FTC/PrEp Level
  - Case (HIV positive)
  - Control (HIV negative)

- B: Intracellular TDF/PrEp Level
  - Case (HIV positive)
  - Control (HIV negative)

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**TDF/FTC (Truvada®) PrEP**

Adherence is critical

<table>
<thead>
<tr>
<th>Timing</th>
<th>Scheduled FTC/PrEp</th>
</tr>
</thead>
<tbody>
<tr>
<td>2x/week</td>
<td>90%</td>
</tr>
<tr>
<td>1x/week</td>
<td>50%</td>
</tr>
<tr>
<td>Every day</td>
<td>90%</td>
</tr>
</tbody>
</table>

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Who Should be Offered PrEP?

<table>
<thead>
<tr>
<th>Men Who Have Sex with Men</th>
<th>Heterosexual Women and Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-positive sexual partner</td>
<td>HIV-positive sexual partner</td>
<td>HIV-positive injecting partner</td>
</tr>
<tr>
<td>Recent heterosexual sex</td>
<td>Recent heterosexual sex</td>
<td>History of injecting or as condoms</td>
</tr>
<tr>
<td>High number of sex partners</td>
<td>High number of sex partners</td>
<td>Commercial sex worker</td>
</tr>
<tr>
<td>History of inconsistent or no condom use</td>
<td>History of inconsistent or no condom use</td>
<td>In high prevalence area or network</td>
</tr>
<tr>
<td>Commercial sex worker</td>
<td></td>
<td>Recent drug treatment (not currently injecting)</td>
</tr>
</tbody>
</table>

All AI recommendations

PrEP Steps
- Risk assessment
- Eligibility evaluation
- Monitoring
- Evaluation for indication to stop PrEP
Baseline Lab Evaluation
- Negative HIV Ab within a week of starting PrEP
- Serologic screen for Hepatitis B
  - Vaccinate if nonimmune
- Serologic screen for Hepatitis C
  - Consider annual screening for MSM, intravenous drug users
- Expert recommendation
  - Serologic screen for Hepatitis A if MSM
  - Immunize if negative
- Creatinine clearance > 60 mL/min
- Pregnancy test

Prescribing PrEP
- Truvada one tablet by mouth every day
- Dispense no more than 90 days
  - Patients must be evaluated for HIV every 90 days
    - Sooner if signs of acute HIV infection are present

Monitoring Lab Testing

<table>
<thead>
<tr>
<th>Lab Test</th>
<th>Every 3 months</th>
<th>At least every 6 months</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Ab</td>
<td>X</td>
<td></td>
<td>Consider HIV RNA PCR</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>STD screen</td>
<td></td>
<td>X*</td>
<td>Test at site of exposure</td>
</tr>
<tr>
<td>Pregnancy test for women</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Consider testing every 3 months
What if the HIV test is positive?

- Stop PrEP
- Not a fully suppressive regimen for HIV infection
- Two options for treatment
  - Hold off on ARV therapy until genotype results
  - Start a fully suppressive antiretroviral regimen and modify based on genotype results
- Order an HIV-1 RNA PCR, HIV-1 Genotype, CD4 count
- Link to an experienced HIV provider

**WHAT ARE RISKS OF PREP**

- Development of Resistance
  - Risk is low despite 2 drug therapy with PrEP
  - iPrEx
    - 48 people with HIV – none with significant resistance
  - Partner’s PrEP
    - 5 of 63 seroconverters developed resistance
    - M184V

Risk Compensation
- Behavioral disinhibition
- Not seen in most clinical trials

PrEP: Side Effects
- Headache
- Abdominal pain
- Poor appetite/weight loss
- Renal impairment, Fanconi syndrome
- Decreased bone density
- Lactic acidosis
- Hepatomegaly/steatosis
- Risk for hepatitis B exacerbation in those with chronic hepatitis B infection with Truvada® discontinuation

Discontinuing PrEP
- Positive HIV result
- Acute HIV signs or symptoms
- Non-adherence
- Renal disease
- Changed life situation: lower HIV risk

PrEP May Be Periodic


Case

Ben is a 25 year old man who has sex with men. He had 4 partners in the last month and while he used condoms, he wants to reduce his risk of HIV acquisition further. He asks about taking tenofovir alafenamide/emtricitabine (Descovy®) as he has heard it’s safer for the bones and kidneys. What do you tell him?

A. Currently, there isn’t sufficient data regarding efficacy of TAF containing regimens in PrEP
B. The only FDA approved regimen for PrEP includes TDF not TAF

Case

KS is a 35 year old man who is in a long term relationship with another man with whom he does not use condoms. His partner was diagnosed with acute HIV infection 1 week ago after a trip in which they both had sex with men of unknown HIV status. They did not use condoms.

KS and his partner last had unprotected sex 4 days ago.
KS had a negative HIV Ag/Ab test today
Would you start PrEP today?

A. Yes, this patient is clearly at high risk of HIV acquisition
B. No, I am concerned he could have been exposed to HIV too recently for the HIV Ag/Ab assay to pick up infection

Sequence of Appearance of Lab Markers of HIV-1 Infection

Main symptoms of Acute HIV Infection
Case

- Sam is a 42 year old man who has sex with other men. He wants to get on PrEP because he doesn’t want to have to use condoms to prevent acquisition of HIV infection.
- How would you counsel Sam?

Comprehensive Prevention Strategy

- Screen and treat all STDs
- HIV prevention counseling before and after testing
- Individual and couples risk reduction counseling
- Condoms with training and counseling

Case

- Martha is a 30 year old woman who has had multiple male sex partners in the last 6 months and started PrEP at the urging of her sister.
- She wants to know how many days it will take after starting PrEP to be protected.
Time to achieve protection with PrEP

- Rectal tissue 7 days
- Blood and cervicovaginal tissue 20 days
- However, these levels may not represent true clinical protection
  - Guidelines do not provide specific recommendations on time to protection
  - Critical to counsel on safer sex practices in combination with PrEP

HIV Post-Exposure Prophylaxis (PEP)

Non-Occupational PEP (nPEP)

Jake

CASE
Non-Occupational PEP

- Use of antiretrovirals to prevent HIV acquisition following high risk exposures to HIV infection outside of occupational settings
- nPEP is only for potentially exposed persons without HIV infection
- nPEP is recommended when source of body fluids is known HIV-infected and reported exposure presents a substantial risk for transmission

CDC. Updated Guidelines for Antiretroviral nPEP, 2016. Available at http://stacks.cdc.gov/view/cdc/38856

Non-Occupational PEP

- Provide any indicated prevention, treatment or supportive care for other exposure-associated health risks and conditions
  - Sexually transmitted infections
  - Traumatic injuries
  - Hepatitis B and C virus infection
  - Pregnancy

CDC. Updated Guidelines for Antiretroviral nPEP, 2016. Available at http://stacks.cdc.gov/view/cdc/38856

Non-Occupational PEP

- Don’t delay initiating nPEP if indicated and results of rapid HIV blood test results are unavailable
- Can stop nPEP if patient later determined to have HIV infection or source does not have HIV infection

CDC. Updated Guidelines for Antiretroviral nPEP, 2016. Available at http://stacks.cdc.gov/view/cdc/38856
Rationale

- Systemic infection does not appear to occur immediately
  - HIV initially affects target cells and takes time to cause systemic infection
  - Goal of prophylaxis is to attack the HIV virus prior to establishment of infection in immunologically protected sites

- PEP has been effective in occupational settings
  - 1997 study of healthcare workers exposed to HIV infected blood who took zidovudine within 4 hours of exposure reduced risk of HIV acquisition by 81%

- Perinatal prevention
  - Antiretroviral treatment of mother during pregnancy and delivery. PEP for baby has significantly decreased transmission of HIV

Animal Studies

- Macaque Studies
  - Inoculation of simian immunodeficiency virus (SIV)
    - Tenofovir decreased risk of seroconversion
      - Greatest reduction if started early and continued for 28 days
  - Intravaginal inoculation of HIV-2
    - Tenofovir prevented seroconversion in all 8 female macaques when started within 12 to 36 hours
nPEP Steps

1. What is the HIV status of the exposed person?
2. Does the source of the exposure have or is likely to have HIV infection?
3. What is the risk of HIV acquisition related to the exposure?
4. When the exposure occur?

Indications for Starting nPEP

1. Nonoccupational exposure to blood, genital secretions or other potentially infected body fluids from a person with known HIV infection
   - If HIV status is unknown, evaluate case-by-case, ideally with expert consultation
2. The exposure represents a substantial risk for HIV transmission
3. The person seeks care within 72 hours of exposure
Nonoccupational PEP for HIV Algorithm

- **Substantial risk for HIV Acquisition**
  - ≤ 72 hours since exposure
  - Source patient known HIV positive
  - nPEP recommended
- **Negligible risk for HIV Acquisition**
  - ≥ 73 hours since exposure
  - Source patient of unknown HIV status
  - nPEP not recommended
  - Case-by-case evaluation. Consider expert consultation.


Source patient known HIV positive

Source patient of unknown HIV status

nPEP recommended

nPEP not recommended

Case-by-case evaluation. Consider expert consultation.

Preferred nPEP Regimens

- **Tenofovir/emtricitabine (Truvada®)**
  - One tablet daily
  - Take with or without food
  - Do not use for PEP in patients with estimated creatinine clearance (CrCL) < 60 mL/min
  - Adverse effects
    - Flatulence
    - Headache
    - Renal insufficiency
    - Rarely, Fanconi syndrome

- **Dolutegravir (Tivicay®)**
  - 50 mg once daily
  - OR

- **Raltegravir (Isentress®)**
  - 400 mg twice daily

New York State DOH AIDS Institute: [www.hivguidelines.org](http://www.hivguidelines.org).

Raltegravir (Isentress®)
- Take with or without food twice daily
- Interactions with polyvalent cations
  - Avoid aluminum or magnesium containing antacids
  - Can take with calcium carbonate antacids
- Adverse effects
  - Diarrhea
  - Nausea
  - Headache
  - Rash (rare)

Dolutegravir (Tivicay®)
- Take with or without food once daily
- Interacts with polyvalent cations
  - Can take with calcium or iron supplements if taken with food
  - Take 2 hours before or 6 hours after other polyvalent cations
- Adverse effects
  - Headache
  - Insomnia
  - Rash/hypersensitivity reaction

Alternative nPEP or PEP in Renal Disease
- Alternative PEP
  - Tenofovir/emtricitabine (Truvada®) + darunavir (Prezista®) + ritonavir (Norvir®)
  - If creatinine clearance < 60 mL/min
    - Substitute zidovudine + lamivudine dose adjusted for degree of renal insufficiency for tenofovir/emtricitabine
What if the Source Has an Undetectable HIV viral load?

- Exposure to source with undetectable serum viral load does not eliminate the possibility of HIV transmission or need for PEP and follow-up testing
- Risk of transmission is thought to be very low, but not non-existent

Resistance in the Source Virus?

- If source patient is known or suspected to harbor drug-resistant HIV
  - Do not delay initiation of PEP
  - Consult with experts for PEP selection
  - Resistance testing at time of exposure is not practical, given length of time required for results
  - You can modify PEP regimen (with expert consultation) later if indicated

What if the Exposed Person is Pregnant?

- PEP is not contraindicated for pregnant women
- Pregnancy has been documented to increase susceptibility to HIV infection through sexual activity

CDC. Updated Guidelines for Antiretroviral Postexposure Prophylaxis (PEP) 2016. Available at http://stacks.cdc.gov/view/cdc/38485
Case

MR is a 35 year old man who has sex with men. He has had 5 sex partners in the last 6 months and comes for nPEP after a condom broke during anal receptive intercourse 2 hours ago. In addition to providing nPEP, what else should happen at this visit?

1. Discussion with patient re: PrEP after completion of nPEP
2. Provision of condoms
3. Discussion of safer sex practices
4. All of the above

Summary

- Engage and educate patients regarding available HIV prevention modalities
- Assess risk for acquisition of STDs and HIV
- Work with your patients to develop a realistic and effective prevention plan
- Provide PrEP and PEP as indicated for HIV prevention