

HIV: What the Primary Care Provider Needs to Know

Jennifer Adams, MD
Denver Health
General Internal Medicine and HIV Primary Care

September 28, 2010



HIV for PCP's

- PCP's often think they don't need to know much about HIV: "it's managed by specialists"
 - Making the diagnosis and linkage to care is your job
 - HIV patients will seek care in ER's, urgent care, specialty care and other settings
 - Incidence of new HIV infections in US unchanged in past decade but patients are living much longer so prevalence is increasing dramatically
 - HIV workforce is decreasing so generalists will be caring for patients with HIV more and more
 - Patients are developing chronic illnesses and complications of aging unrelated to their HIV
- The truth is, you need to know at least a little bit



Objectives

- Understand new HIV screening guidelines
- Correctly interpret the various HIV tests and know which one to order
- Recognize and diagnose acute HIV infection
- Counsel patients about appropriate post-exposure prophylactic treatment
- Recognize common anti-retroviral drug interactions

- We are not going to cover chronic management of HIV infection today



Case

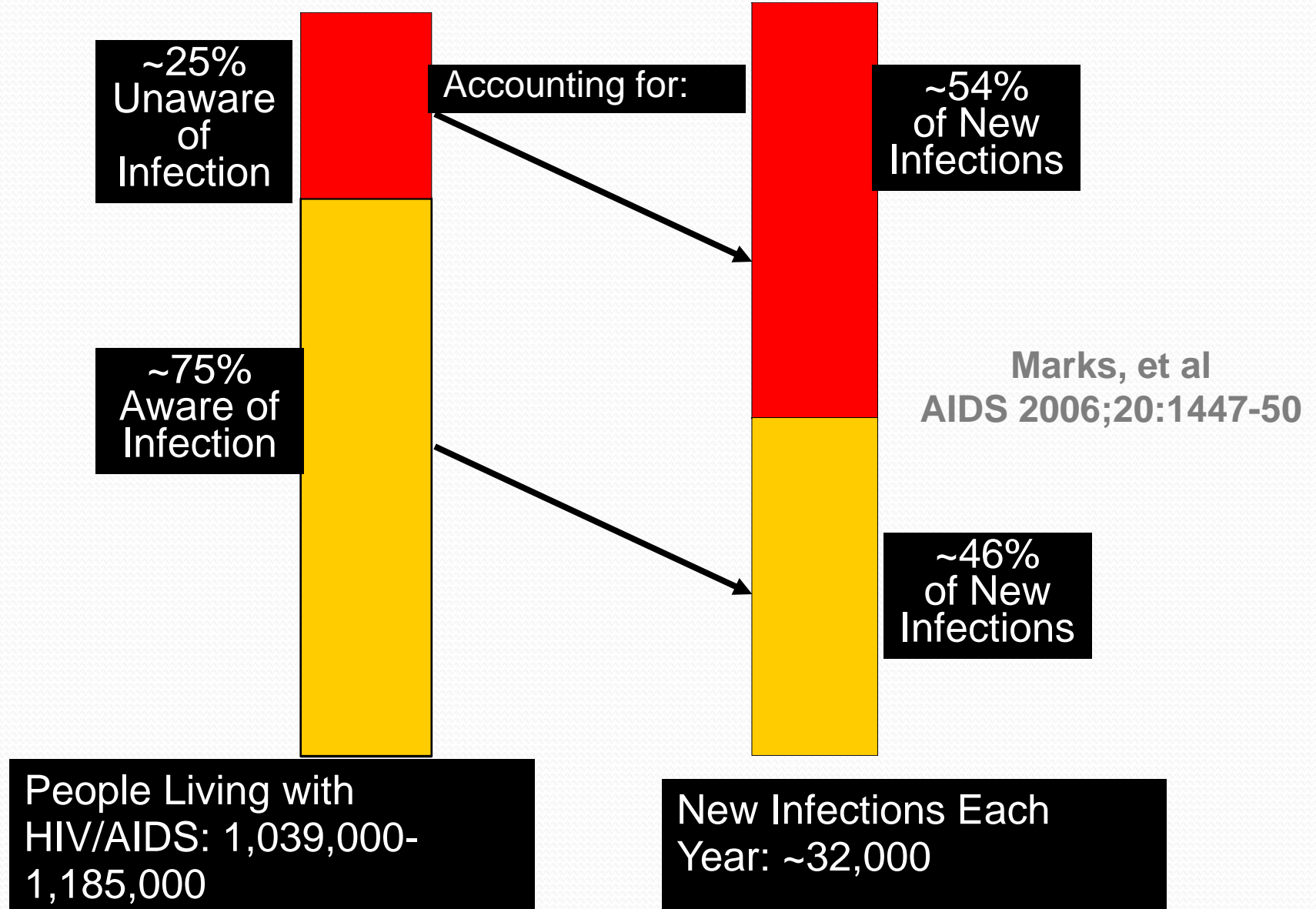
- 52 year old woman presents for a PAP. Also wants to discuss her knee pain, insomnia, and needs refills of her anti-hypertensive medications.
- You notice she's also due for diabetes and lipid screening, mammogram and colorectal cancer screening.
- Divorced mother of 2 teenagers. Monogamous with male partner for past 18 months.
- Denies recent STI's or drug use
- Has never been tested for HIV
- Is testing this woman for HIV a priority during this visit?



Screening

- HIV/AIDS is a leading cause of illness and death in the U.S.
- 1-1.2 million HIV-infected persons live in the U.S.
- 25% are unaware of their HIV infection
- HIV testing often is not done until late in the disease process: 39% of people are diagnosed with AIDS within 1 year of testing HIV+
- Perinatal HIV transmission continues, usually in women not offered testing during pregnancy; sometimes as result of infection during pregnancy

Awareness of Serostatus Among People with HIV and Estimates of Transmission

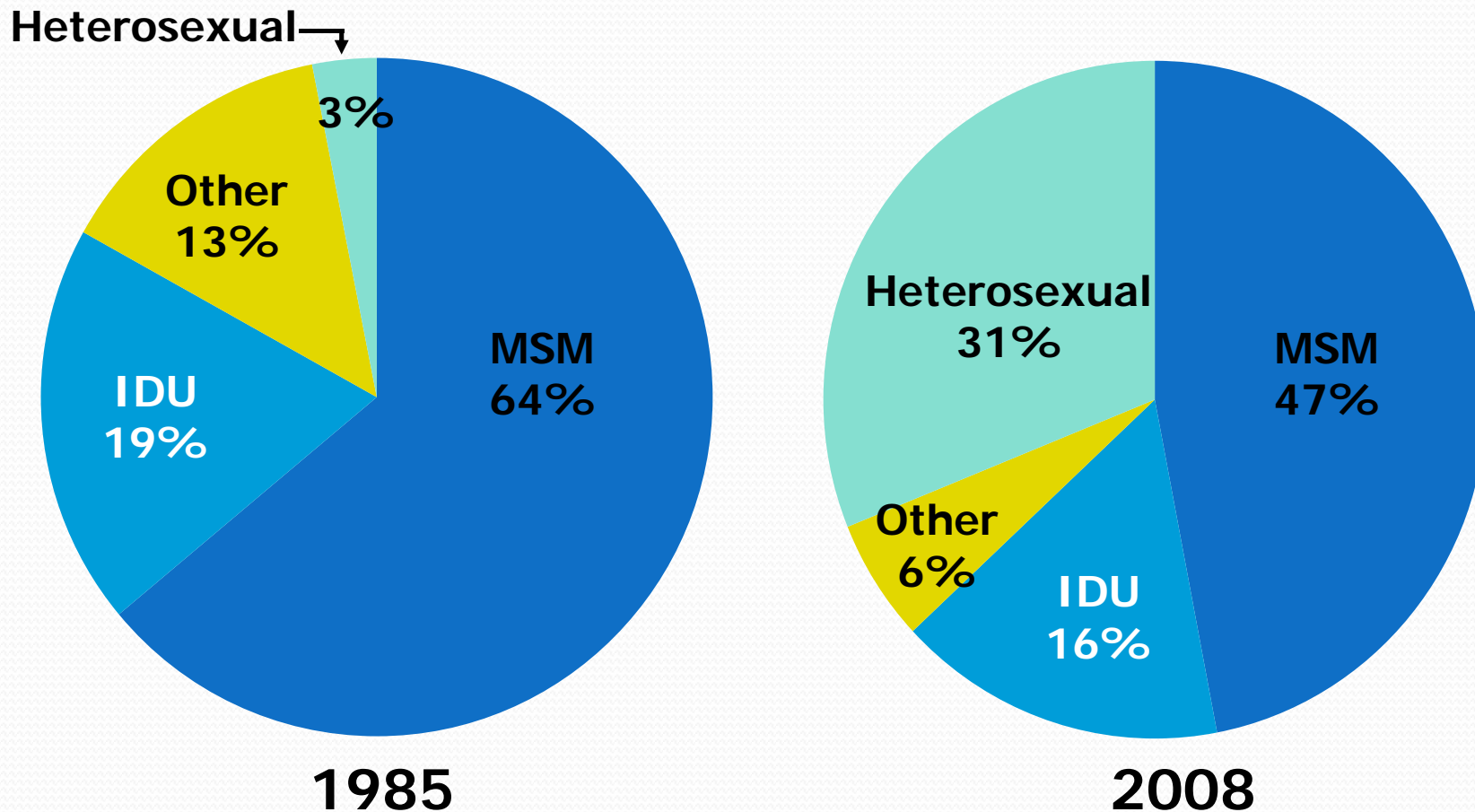




September 22, 2006: CDC Recommends Routine Screening

- Rationale for change:
 - Routine HIV screening will identify unrecognized HIV infection so that early treatment can be offered and interventions to reduce transmission can be implemented.
 - HIV screening is cost-effective, even in low-prevalence settings.
 - Among pregnant women, routine screening is much more effective than risk-based testing for detecting unsuspected HIV infection.
 - Making testing routine reduces stigma.

AIDS Diagnoses by Transmission Category, United States, 1985 & 2008



NOTE: Data are estimates. MSM=Men who have sex with men (gay and bisexual men); IDU=Injection drug use.
SOURCE: Kaiser Family Foundation, based on CDC, Presentation by Dr. Harold Jaffe, "HIV/AIDS in America Today", National HIV Prevention Conference, 2003; CDC, *HIV Surveillance Report*, Vol. 20, 2010.

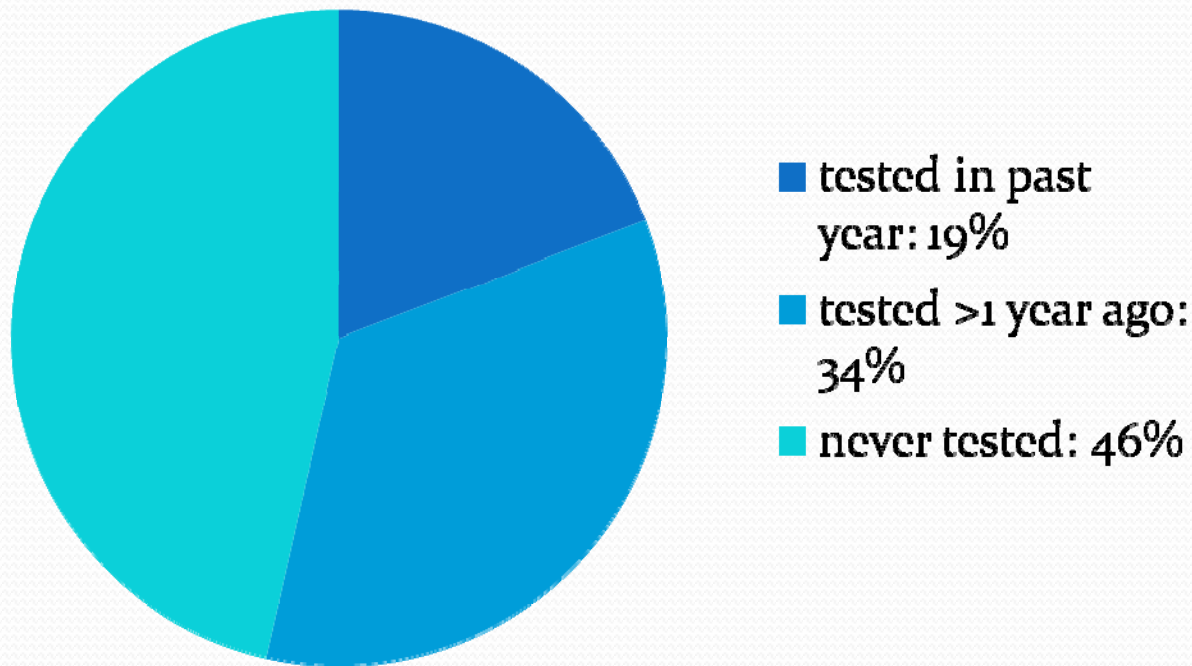
New Recommendations

- ROUTINE one time voluntary screening for patients age 13-64 in all health care settings
- OPT-OUT testing
- NO separate consent
- Pre-test counseling NOT required (but it's still a good idea)
- Additional screening recommended for patients treated for TB or other STI's, pregnant women, patients with ongoing risk factors for new infection
- Low prevalence areas should stop if < 1:1000 tests positive
 - Colorado's rate of HIV infection is 1.3%
 - 54.9% of patients diagnosed with HIV in Colorado live in Denver
- Remember, state laws and hospital policies trump guidelines
 - Colorado does not require written consent

Are the new recommendations working to identify new cases?

- Alternate 4 months sequences of opt-out testing and physician directed testing between 2007-2009 in the DH ED
- In opt-out phase, of approximately 28,000 eligible ER visits, 25% of patients were screened resulting in diagnosis of 25 infections (case rate of 0.15%)
 - 10 of these infections were not new but allowed linkage to care
- In physician directed phase, of approximately 29,000 eligible ER visits, 0.8% of patients were tested resulting in diagnosis of 5 infections (case rate of 0.01%)
 - One of these infections was not new
- Non-targeted opt-out testing was associated with more new diagnoses but at a lower rate than expected (RR 3.6)
- Average CD4 in opt-out group was 69, average CD4 in targeted testing group was 13 ($p=0.02$), only 4 cases in the opt-out phase had a CD4 >350

Percent of patients ages 18-64 who have been tested for HIV, 2010



Same survey in 2006 found that only 42% had never been tested!

Why aren't we doing a better job of screening?

- We don't have enough time
- We don't think our patients are at risk
- We don't think we're qualified to counsel patients about risks and benefits of screening
- We don't know what to do if someone tests positive!

Back to our case...

Back to our case...should she be screened?

- Yes, she should be screened today!
- One approach:
 - Normalize testing
 - Obtain verbal consent
 - Describe the possible test results
 - Make a plan to disclose results
- Now, what test are we going to use?

Complexities of HIV tests

- Different types of tests
 - Standard blood test: initial ELISA, confirmed with Western blot (sensitivity 99.3/specificity 99.7)
 - Oral test: swab collects oral mucosal exudate, tested for antibody (not looking for Ab in the saliva). Positive tests must be confirmed. Higher false positive rate
 - Rapid HIV antibody test: fingerstick or oral swab placed in developing solution. Results available in 20 minutes. Positive results must be confirmed.
 - Home testing: Same technology as standard blood test. Mail kit to lab and results are given over the phone.



Testing

- Any positive EIA or rapid test needs to be confirmed with a western blot
 - A positive EIA and negative WB = negative test
 - False positives can occur and will become more common as we scale up testing
- What causes a false positive test?
 - Cross reacting antibodies: pregnancy, other viral infections, collagen-vascular diseases, autoimmune diseases, malignancy, recent influenza vaccination

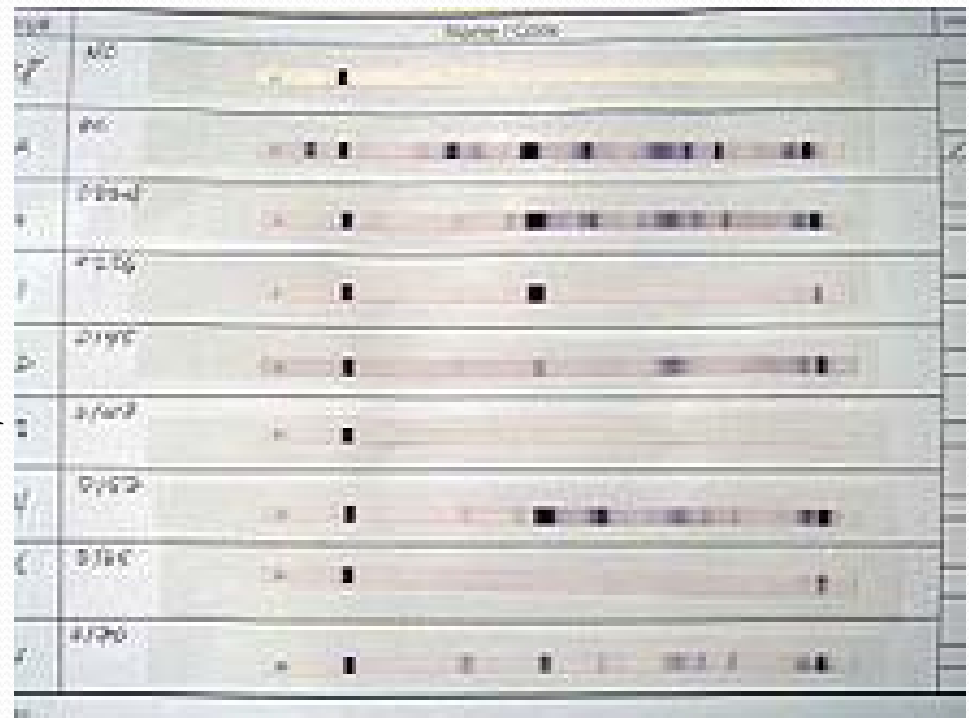


The Indeterminate Test

- Back to our patient:
- She's back for a follow up of her hypertension and for test results
- You're 20 minutes behind, but glance through her labs before entering her room
- Her HIV antibody is positive and her Western Blot is positive for the p24 and G160 antigens
- Does she have HIV?

The indeterminate test

- WB very specific
- Band patterns evolves over weeks to months
- Need a full compliment of bands to diagnose HIV
- 20% of healthy adults have an isolated p24 band
- Indeterminate test can indicate a false positive or early infection



Management of indeterminate results

- Back to our case....
- You need to tell her that she has an indeterminate result
- Bring her back for re-testing of the HIV Antibody and Western Blot in 4 weeks
- OR, consider viral load testing now if risk factors present, pregnant, patient anxiety, provider anxiety, risk for loss to follow up



Primary HIV Infection?

- 37 yo MSM
- C/o 1 week of malaise, night sweats, rash
- Exam: afebrile, maculopapular rash, diffuse adenopathy
- By the way, had unprotected insertive anal sex with an anonymous male partner 6 weeks ago. He's worried this is HIV.

Acknowledgement: case adapted from NW AETC slide set



What is the chance this is PHI?

- <1%
- 1-5%
- 6-10%
- 11-20%
- 21-40%
- >40%



Exposure Risks (average, per episode, involving untreated HIV-infected source patient)

Percutaneous (blood) ¹	0.3%
Mucocutaneous (blood) ²	0.09%
Receptive anal intercourse ³	0.3 - 3%
Insertive anal intercourse ⁴	0.06%
Receptive vaginal intercourse ⁵	0.1 – 0.2%
Insertive vaginal intercourse ⁶	0.03 – 0.14%

Primary HIV Infection: Signs & Symptoms

- Up to 90% of patients will be symptomatic
- Signs and symptoms typically begin 1-6 weeks post-exposure (2 weeks is most common)
 - Cases outside of this range have been reported
- Non-specific signs and symptoms: similar to EBV, influenza, hepatitis, streptococcal, syphilis
- High index of suspicion is critical

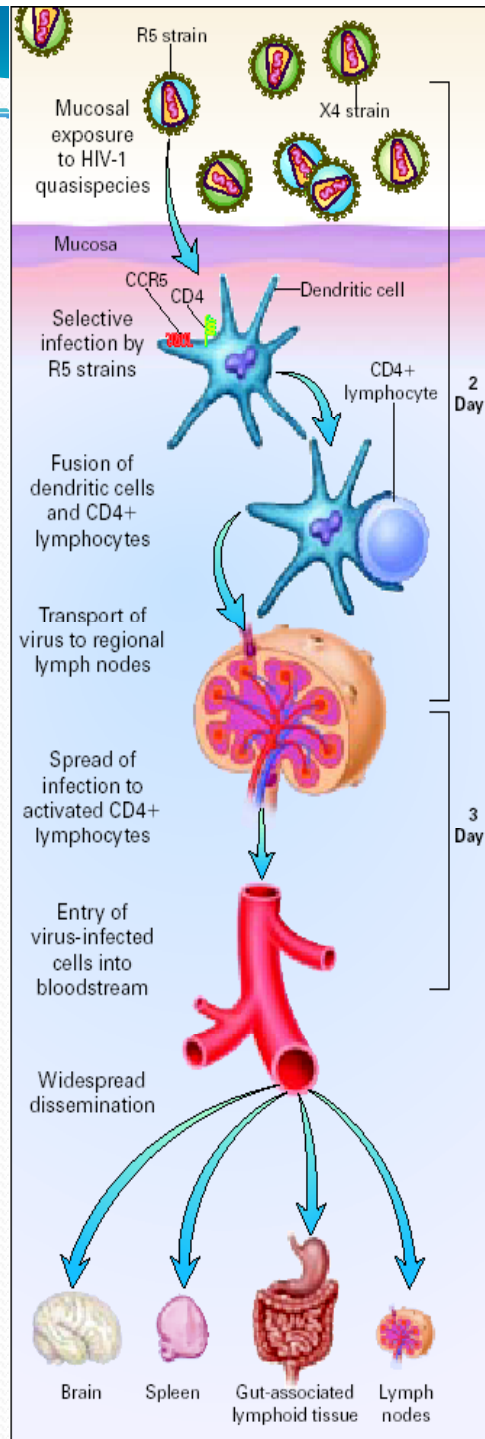
Kahn JO, Walker BD. N Engl J Med. 1998;339:33-39.
Schacker T, et al. Ann Intern Med. 1996;125:257-264.

Day 0

Day 0-2

Day 4-11

Day 11 on



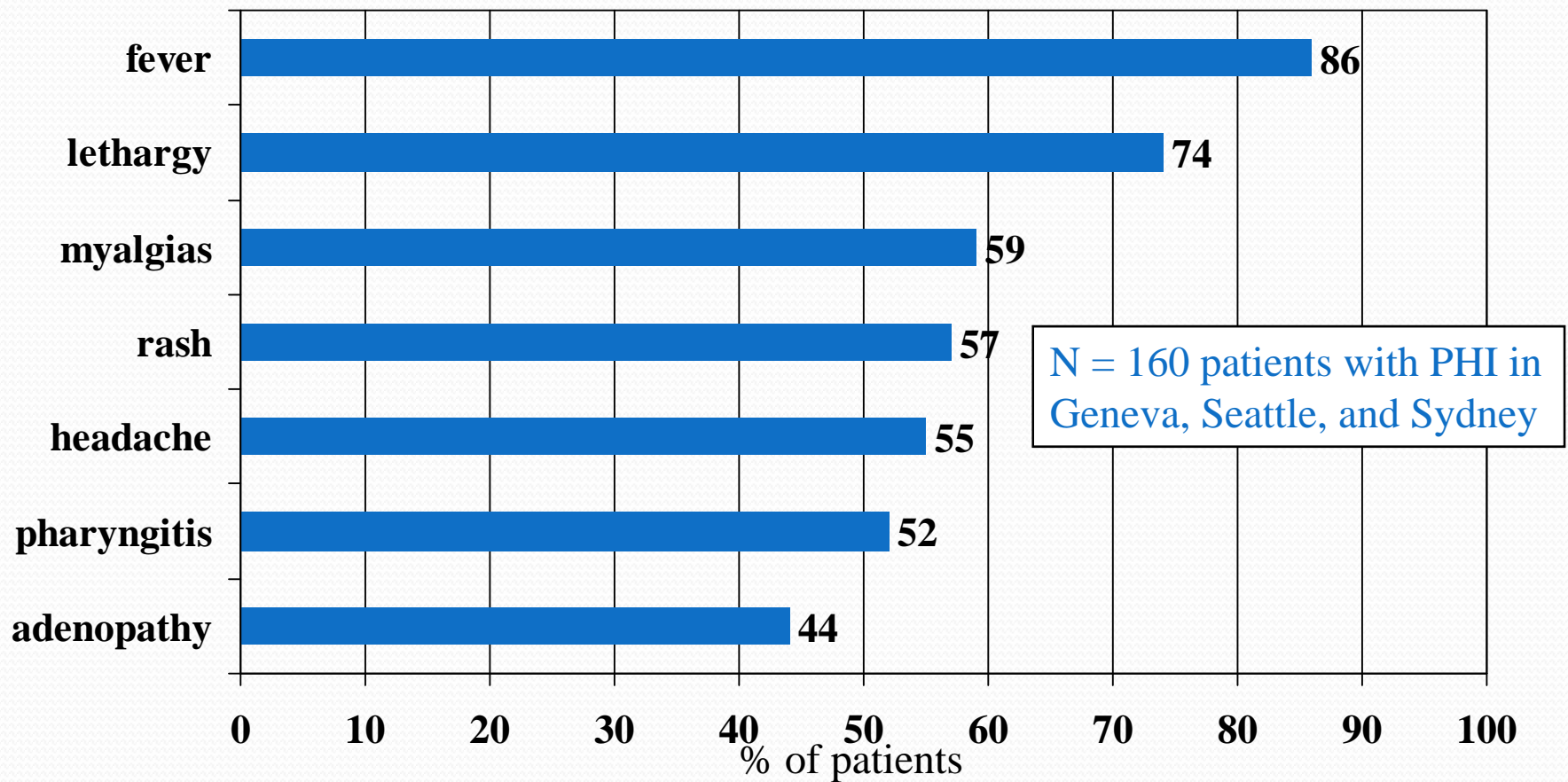
Exposure to HIV at mucosal surface or blood

Virus collected by dendritic cells, carried to lymph node

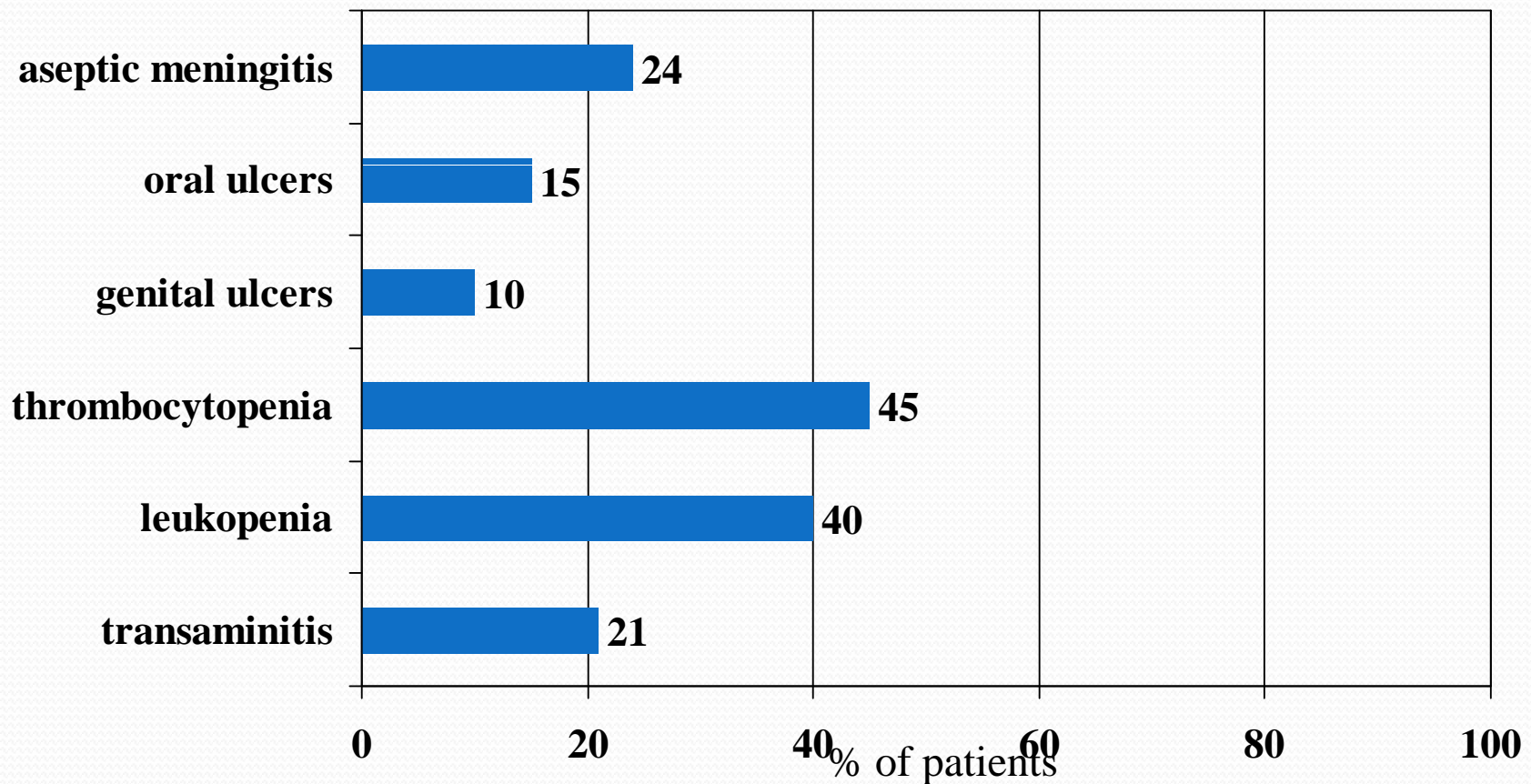
HIV replicates in CD4 cells, released into blood

Virus spreads to other organs

Primary HIV Infection: Common Signs & Symptoms



Primary HIV Infection: Other Signs & Symptoms



Kahn JO, Walker BD. N Engl J Med. 1998;339:33-39.

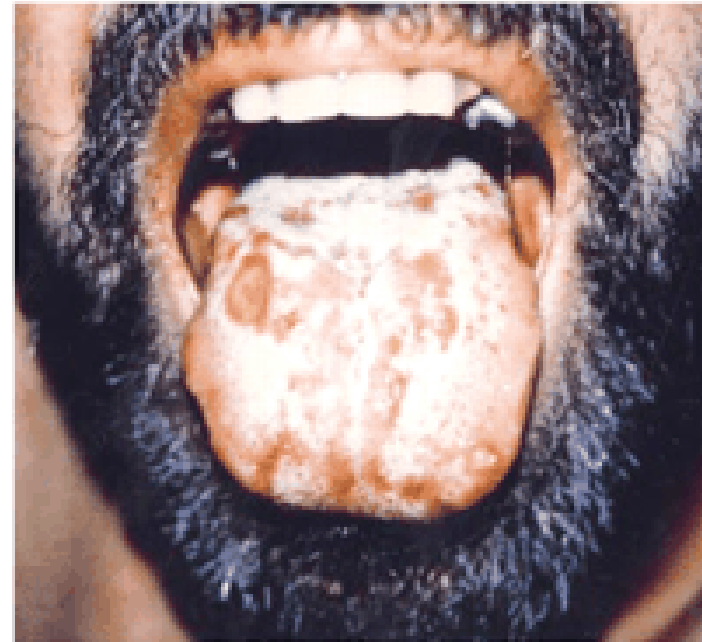
Primary HIV Infection

Rash



Trunk and face > limbs
Small pink macules

Mucosal Lesions



Oral ulcers, thrush

(Kahn, NEJM, 1998)



How often do patients with Primary HIV Infection seek care?

- Cohort of 46 adults with acute seroconversion
- 89% sought care in ER's, urgent cares, or primary care clinics for symptoms consistent with HIV seroconversion
- Diagnosis of acute HIV considered in only 26% of these patients

- **PHI often leads to medical evaluation, but HIV is under-diagnosed**



Back to our Patient

- Exposure Risk: unprotected insertive anal intercourse, unknown HIV status
- Time Course: onset of symptoms 5 weeks after exposure
- Signs and Symptoms: malaise, night sweats, rash, adenopathy

I would estimate his risk to be 1-5%

What tests would be most appropriate now?



His test results

- HIV RNA: 437 copies/ml
- HIV antibody: negative
- Mono spot: negative
- RPR: pending
- AST 112, ALT 67
- Normal CBC

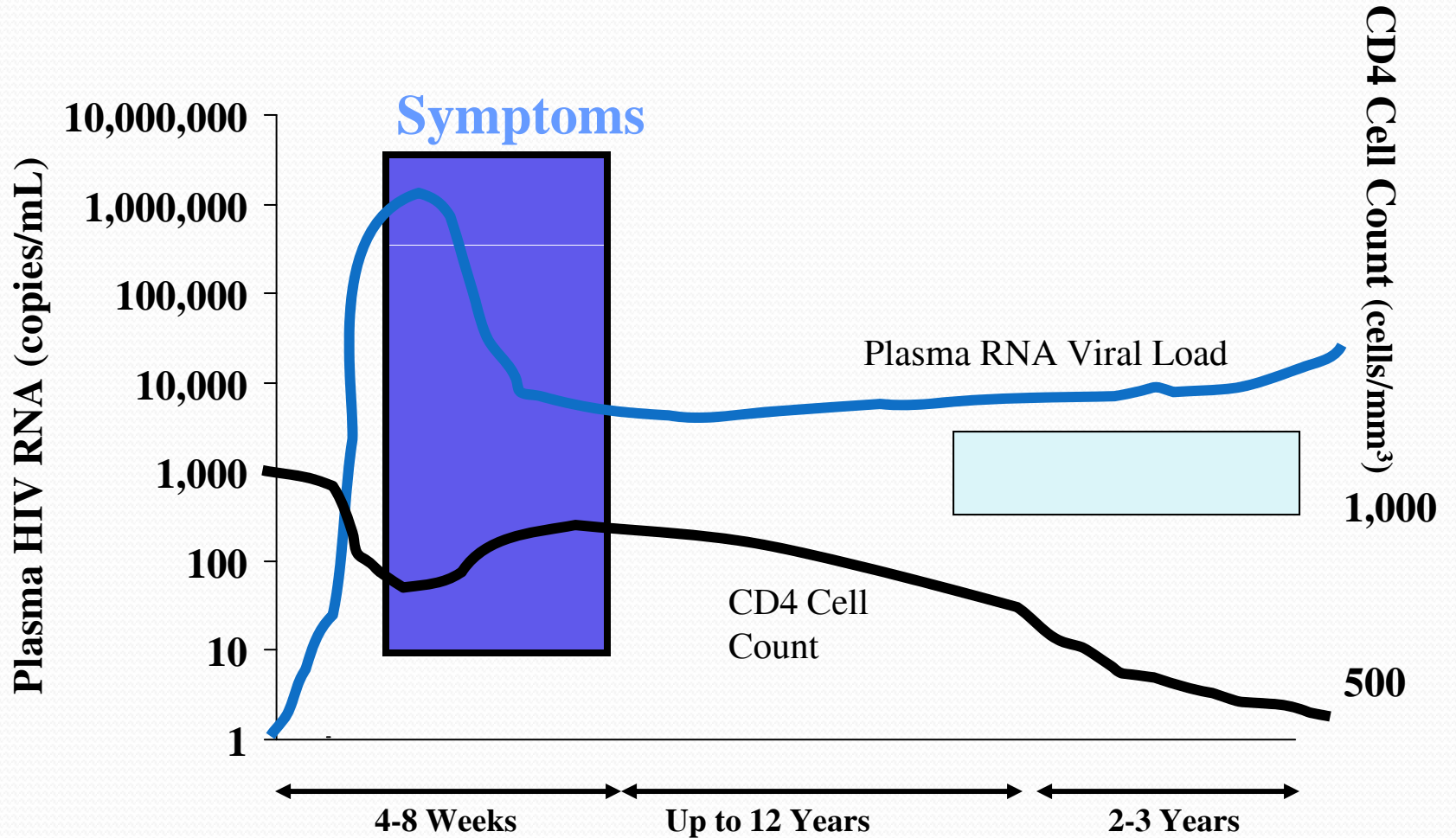
Does he have HIV?

yes

no

unsure

Primary HIV Infection



Diagnostic Testing: Viral Load

- More sensitive than HIV antibody³ for the diagnosis of PHI
- Positive one to three weeks before antibody test¹
- Typically high level, e.g. greater than 50,000-100,000 copies/mL^{2,3}
- False positives can occur
 - Most false positives are low level (<10,000 copies/mL)
 - HIV VL <10,000 copies/mL should probably be considered “indeterminate”

1. Busch MP, Satten GA. *Am J Med* 1997;102:Suppl 5B:117-24.

2. Kahn JO, Walker BD. *N Engl J Med*. 1998;339:33-39.

3. Daar ES et al. *Ann Intern Med*. 2001;134:25-29.

Follow up

- 6 weeks later
 - HIV RNA <50
 - HIV Ab negative
 - RPR 1:64



Why do we Care about Diagnosing PHI?

- Public Health:
 - Patients with PHI are likely to be highly infectious given very high viral loads
 - Diagnosis of HIV infection may lead to safer sex and needle practices
- Personal Health
 - 40% of patients with HIV not diagnosed until they are within one year of AIDS diagnosis
 - Antiretroviral therapy (ART) during PHI *may* alter the natural course of HIV disease



Linkage to Care

- Important next step for anyone diagnosed through screening, with primary infection, or known positive not currently in care
- Ideal if patient can be seen by HIV provider within 24-48 hours of their diagnosis
- PCP's responsibility to know what resources are available to connect patients with appropriate care



Post-Exposure Prophylaxis (PEP)

- Case 1: 28 yo F, Ob/Gyn resident presents to the urgent care clinic after needlestick in the OR 30 minutes prior. Unknown HIV status of the source patient.
- Case 2: 24 yo M, scratched his arm on unidentified sharp object yesterday when reaching into a trash can at a night club and drew blood.
- Case 3: 36 yo M, unprotected sex last night with male partner, unknown HIV status.
- Should these patients be offered PEP?



Possible HIV Exposures

- Potentially infectious:
 - Blood
 - Cerebrospinal fluid
 - Synovial fluid
 - Pleural fluid
 - Pericardial fluid
 - Peritoneal fluid
 - Amniotic fluid
 - Semen or vaginal secretions
- NOT infectious unless visibly bloody
 - Feces
 - Nasal secretions
 - Saliva
 - Sputum
 - Sweat
 - Tears
 - Urine
 - Vomitus

Risk of HIV Infection following Occupational Exposure to HIV-Infected Blood

- Approximately 0.3% following percutaneous exposure
- Approximately 0.09% following mucous membrane exposure
- As of 2004, only 57 documented cases in the US of occupational transmission
- Last reported case of occupational transmission in 2001
- Huge emotional impact of an occupational exposure

Risk of Other Blood Borne Infections from a Needlestick

- HIV 0.3%
- Hepatitis C 1.8%
- Hepatitis B (if not immunized)
 - Source EAg negative: 1-6% clinical hepatitis, 23-37% serologic infection
 - Source EAg positive: 22-31% clinical hepatitis, 37-62% serologic infection



NEJM, 1997: A CASE–CONTROL STUDY OF HIV SEROCONVERSION IN HEALTH CARE WORKERS AFTER PERCUTANEOUS EXPOSURE

- 33 case patients tested positive for HIV after occupational exposure, 665 patients tested negative for HIV after occupational exposure
- Enrolled patients reported to national surveillance databases between 1983-1994 in US, UK, France and Italy
- Case patients significantly less likely to have taken PEP
 - 80% reduction in transmission if any PEP regimen given within 2 hours of exposure
 - Most common PEP regimen was mono-therapy with AZT for a month

Factors Associated with Increased Risk of Transmission

- Deep injury (OR 15)
- Visible contamination of device with patient's blood (OR 6.2)
- Needle having been placed directly into vein or artery (OR 4.3)
- Source patient with terminal illness who died of AIDS within 2 months of the exposure (OR 5.6)
 - Interpreted now as VL >1500

Initiating PEP

- PEP should be started within hours of exposure
 - Monkey studies have shown no benefit if treated >72 hours after exposure
- PEP should be administered for 4 weeks, if tolerated
- Reevaluate within 72 hours of exposure, especially as additional information about the exposure or source patient becomes available
- If the source is found to be HIV negative, PEP should be discontinued
 - Window period with current HIV Ab assays is <3 weeks for most patients; 90% within 1 month; 95% within 3 months
 - Most acute HIV identifiable by symptoms
 - Never been a case of occupational transmission in the US involving a source patient in the window period

Which Drugs to Use?

- Consultation with an expert is recommended
- Regimens should be chosen to minimize potential drug toxicities and maximize the likelihood of adherence.
- Consider pregnancy in all women of child-bearing age.
- Consideration should be given to the history of the source person, including history of and response to ART, resistance tests, and disease stage
- If information on possible resistance is not immediately available, PEP (if indicated) should not be delayed; changes can be made later

Non-Occupational Exposures

- Testing of source usually not possible
- CDC guidelines: recommend PEP if source known to be HIV+ and within 72 hours of exposure. Case-by-case decision if HIV status of source is unknown
- Never been a documented case in US of transmission from a needle found in the community (2 cases of injuries from needles found in hospitals)
 - HIV thought to degenerate very quickly outside of the body
- Unclear how to manage people with ongoing risky exposures

Follow-Up of Exposed Patient

All exposed patients should receive the following, regardless of whether they receive PEP:

- Advise to use precautions (eg, avoid blood or tissue donations, breast-feeding, pregnancy, unprotected sex) to prevent secondary transmission
- HIV-antibody testing (EIA) to monitor for seroconversion: at baseline, 6 weeks, 12 weeks, and 6 months after exposure;
- HIV testing (what test?) if develops illness compatible with acute retroviral syndrome



Resources for Consultation

- Local experts
- National Clinicians' Postexposure Prophylaxis Hotline (PEPline)
 - 24-hour telephone consultation service: 888-448-4911

What do you want to do?

- Case 1: 28 yo F, OB/Gyn resident presents to the ER after needlestick in the OR 30 min prior. Unknown HIV status of the source patient.
- Case 2: 24 yo M, yesterday scratched his arm on unidentified sharp object when reaching into a trash can.
- Case 3: 36 yo M, unprotected receptive anal intercourse last night with male partner, unknown HIV status.



Our next case

- 38 yo F with well-controlled HIV, seen in urgent care for 1 week of epigastric pain and symptoms of reflux
- Current medications: OCP's, HAART (FTC/TDF, Atazanavir, Ritonavir)
- Labs are within normal limits
- Diagnosed with dyspepsia and GERD
- Prescribed Omeprazole and sent home, told to follow up with her PCP in a week
- 2 days later, you get a call from her HIV provider...

What went wrong?

- Drug interaction!
- PPI's significantly decrease serum levels of Protease Inhibitors and are contraindicated in treatment experienced patients
- Many of the commonly used drugs in primary care have significant interactions with antiretroviral therapy
 - Reported in 14-41% of patients on ARV's
- Can cause lower ARV concentration (ie. Resistance), or higher ARV concentration (ie. Toxicity)
- Can also effect efficacy and toxicity in the other drugs you're prescribing
- You need to look it up!

Some common drugs to be aware of:

- PPI's
- Inhaled/Nasal Steroids
- Statins
- Antifungals
- Antibiotics
- Oral contraceptives
- Warfarin
- Anticonvulsants
- Antidepressants
- Benzodiazepines
- Calcium channel blockers
- Alpha blockers
- Phosphodiesterase inhibitors
- Many herbals

Take Home Points for the HIV-savvy PCP

- Make screening for HIV routine in your practice
- Recognize symptoms that could be consistent with primary HIV and don't miss an opportunity to make the diagnosis
- Linkage to care is a priority for newly diagnosed patients with HIV
- Be prepared to discuss post-exposure prophylaxis with your patients
- Always consider drug interactions in patients on ARV's



Thank You