HIV Screening, Testing, and Diagnosis for MSM in Primary Care

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Objectives

- Explain the HIV testing and consent process
- Summarize the debate over informed consent for HIV testing
- List different types of HIV tests available
- Explain diagnostic results from the different HIV tests
- Identify elements of effective screening for behavioral risk factors for MSM and other patients

… Do this *interactively*!
In the 2009 version of the movie Star Trek, what offense did Scotty commit to get posted on Delta Vega?

1. Drank too much scotch
2. Transported a grapefruit
3. Couldn’t find Admiral Archer’s prize beagle after transporting it from one planet to another
Who do you offer HIV testing to?

1. All of my patients
2. Patients who are at risk
3. Only my pregnant patients
4. I’m not always consistent
How do you provide HIV test results?

1. In person
2. In person if high-risk
3. By phone or letter
4. I’m not always consistent
HIV Screening
CDC 2006

• Screening
  – In all health care settings
  – Performed routinely for all patients aged 13-64 years
  – UNLESS prevalence of undiagnosed HIV infection is <0.1%

• Repeat Screening
  – Annually for those at high risk (IDU or partners, sex for money or drugs, sex partner of HIV+, multiple sex partners)

• Consent and Pretest Information
  – Screening should be voluntary on the part of the patient
  – Opt-out recommended
  – Document declination

CDC. MMWR 55(RR14), 2006
HIV Screening
USPSTF 2007

• Strongly recommends screening adolescents and adults at increased risk for HIV infection
  - Rating: A Recommendation (good evidence that screening will improve health outcomes, benefits substantially outweigh harms)

• No recommendation for or against routinely screening adolescents and adults who are not at increased risk for HIV infection
  - Rating: C Recommendation (fair evidence screening can improve health outcomes, but balance of benefits and harms too close to justify general recommendation)

April, 2007; www.ahrq.gov/clinic/uspstf/uspshivi.htm
HIV Screening

USPSTF 2007 Hi-Risk Definitions

- MSM after 1975
- Unprotected sex with multiple partners
- IDU
- Sex for drugs or money
- Hi-risk partner
- STD treatment
- Blood transfusion 1978-1985
- OR upon request
- OR seen in high-risk or high-prevalence setting
  - Includes adolescent clinics with high prevalence of STDs
  - High-prevalence setting defined as $\geq 1\%$ prevalence

April, 2007; www.ahrq.gov/clinic/uspstf/uspshivi.htm
HIV Screening
ACP and HIVMA 2009

• Recognition of CDC and USPSTF
  – agreement on screening for HIV in high-risk groups and settings
  – disagreement on low-risk groups and settings

• ACP/HIVMA recommends that clinicians
  – adopt routine screening for HIV and encourage patients to be tested
  – determine the need for repeat screening on an individual basis
Current Massachusetts Law and Regulation

- MGL C. 111, §70F requires written consent to conduct an HIV antibody or antigen test (or to release the results of such test), distinct from other consent
- Applies specifically to health care providers and health care facilities
- Laboratory regulation (105 CMR 180.300 § C) requires procedures for ensuring consent before test may be performed on a specimen
- Additional requirements tied to MDPH contracts: pre-/post-test counseling, disclosure of results, specimen transport, data management, etc.
Is Informed Consent a Barrier?

- High rates of late to care; evidence of missed opportunities
- Besides genetic testing, no other biologic testing requires this level of consent
- Informed consent is an artifact of an earlier era where stigma and discrimination were common
- Consent reinforces the stigma related to HIV and HIV testing
- Obtaining consent is a procedural burden and barrier to higher volumes of tests
- Physicians should be free to order any test that in their clinical judgement is medically indicated
Is Informed Consent Still Needed?

- HIV is still a highly stigmatized disease
- HIV continues to affect the most vulnerable patients
- Obtaining consent prevents patients from being tested without their knowledge
- Obtaining consent creates an educational moment
- Obtaining consent begins a process of engagement that will be necessary to link HIV+ patients to care
- The administrative burden of obtaining consent can be significantly reduced
Massachusetts Bills Filed
2011 Legislative Session

• “An Act to Increase Routine Screening for HIV”
  – Bills filed in House (H02906, Byron Rushing) and Senate (S01108, Patricia Jehlen)
  – Remove written consent for HIV testing and replace it with verbal consent documented in the patient medical record
  – Also state health insurance needs to cover routine HIV screening
  – “Every health care provider who delivers primary medical care services or infectious disease services to an adolescent or adult patient shall offer an HIV test to the patients unless the health care provider determines there is evidence of prior HIV testing or the patient is being treated for a life-threatening emergency.”
What lab do you send HIV screening tests to?

1. My clinic runs the test on-site
2. A local hospital lab
3. A commercial lab
4. The state lab
What type of HIV screening test do you do?

1. 4\textsuperscript{th} generation Ag/Ab combo assay
2. 3\textsuperscript{rd} generation assay
3. A rapid test
4. I’m not sure
Laboratory-based HIV Algorithm

• From late 1980s
• Initial screening test, generally EIA
• Supplemental test, WB or IFA, performed following repeatedly reactive EIA
• Results reported as Positive, Negative, or Indeterminate

Slide courtesy of B. Werner/APHL-CDC
Current Algorithm

A (HIV Immunoassay)

A+  
A (in duplicate)

A++ or + -

A- (Negative for HIV-1 antibodies)

B (HIV-1 WB or HIV-1 IFA)

Positive
Positive for HIV-1 antibodies

Negative
Negative for HIV-1 antibodies

Indeterminate
Inconclusive for HIV-1 antibodies; request redraw in 2-4 weeks; requires medical follow-up for further evaluation and testing

Slide courtesy of B. Werner/APHL-CDC
Limitations of the Current Algorithm

• Antibody tests do not detect infection in ~10% of infected persons at highest risk of transmission

• Western blot confirmation is less sensitive during early infection than many widely used screening tests

• Delays inherent with centralized screening reduce the “effective sensitivity” because infected persons may not learn their test results and become lost to follow up
Detection of HIV by Diagnostic Tests

Symptoms
- p24 Antigen
- HIV RNA
- HIV EIA* (3rd generation, IgM-sensitive EIA)
- Western blot

Weeks Since Infection

*4th generation, Ag/Ab Combo EIA
*3rd generation, IgM-sensitive EIA
*2nd generation EIA
*viral lysate EIA

Modified from After Fiebig et al, AIDS 2003; 17(13):1871-9

Slide courtesy of B. Werner/APHL-CDC
4th Generation Combination EIA

Plasma/serum → Coated well: HIV antigen, p24 antibody

HIV antibody → p24 antigen

Enzyme-detection:
- HIV antigen
- p24 antibody

Detects HIV antibody or p24 antigen if present

Slide courtesy of B. Branson
3rd Generation “Sandwich” EIA

Antigen coated well: Recombinant proteins or synthetic peptides

Plasma/serum

HIV antibody

IgG

IgM

Enzyme-detection

HIV antigen

Detects HIV IgM or IgG if present

Slide courtesy of B. Branson
1\textsuperscript{st} and 2\textsuperscript{nd} Generation “Indirect” EIA

Plasma/serum (1 h/37°C)

Antigen coated well
1\textsuperscript{st} - Viral lysate
2\textsuperscript{nd} – Recombinant proteins or synthetic peptides

IgG HIV antibody

Enzyme-detection

enzyme

anti-human IgG

Detects HIV IgG if present

Slide courtesy of B. Branson
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Analyte</th>
<th>Specimen Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>FDA Approval</th>
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</thead>
<tbody>
<tr>
<td>Unigold Recombigen HIV</td>
<td>Trinity Biotech</td>
<td>HIV-1</td>
<td>Whole blood, Serum, Plasma</td>
<td>100%</td>
<td>99.7%</td>
<td>Dec. 2003</td>
</tr>
<tr>
<td>OraQuick ADVANCE HIV-1/2</td>
<td>Orasure Technologies</td>
<td>HIV-1, HIV-2</td>
<td>Whole blood, Oral fluid, Plasma</td>
<td>99.6% BL 99.3% OF</td>
<td>100% BL 99.8% OF 99.9% plasma</td>
<td>June 2004</td>
</tr>
<tr>
<td>Multispot HIV-1/HIV-2</td>
<td>BioRad Labs</td>
<td>HIV-1, HIV-2</td>
<td>Serum, Plasma</td>
<td>100%</td>
<td>99.9%</td>
<td>Nov. 2004</td>
</tr>
<tr>
<td>INSTI HIV-1</td>
<td>bioLytical Labs</td>
<td>HIV-1</td>
<td>Whole blood, Plasma</td>
<td>99.8%</td>
<td>99.0%</td>
<td>Nov. 2010</td>
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<tr>
<td>Reveal G3 Rapid HIV-1</td>
<td>MedMira</td>
<td>HIV-1</td>
<td>Serum, Plasma</td>
<td>99.8%</td>
<td>99.1% serum 98.6% plasma</td>
<td>Oct. 2006</td>
</tr>
</tbody>
</table>

Slide courtesy of B. Werner/APHL
Uni-Gold Recombigen

Multispot HIV-1/HIV-2

Reveal G3

OraQuick Advance

Clearview Complete HIV 1/2

Clearview HIV 1/2 Stat Pak

FDA-approved discriminatory test

CLIA-waived specimen type

Slide adapted from B. Branson
**FDA Approved Laboratory-based Screening Assays**

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>HIV-1/HIV-2 Capabilities</th>
<th>Specimen Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Date of FDA Approval</th>
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</thead>
<tbody>
<tr>
<td><strong>EIA</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Genetic Systems™ rLAV EIA</td>
<td>Bio-Rad <a href="http://www.bio-rad.com">www.bio-rad.com</a></td>
<td>HIV-1</td>
<td>Serum, Plasma, DBS</td>
<td>100%</td>
<td>99.9%</td>
<td>June 1998</td>
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<tr>
<td><strong>CIA</strong></td>
<td></td>
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<tr>
<td>Architect HIV-1/2 Ag/Ab Combo</td>
<td>Abbott Laboratories <a href="http://www.abbottdiagnostics.com">www.abbottdiagnostics.com</a></td>
<td>HIV-1 p24 Ag HIV-1 Ab HIV-2 Ab</td>
<td>Serum, Plasma</td>
<td>100%</td>
<td>99.77%</td>
<td>June 2010</td>
</tr>
<tr>
<td><strong>NAAT (FDA approved for screening for acute infections and confirmation of HIV-1 infections)</strong></td>
<td></td>
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</tr>
</tbody>
</table>

*Slide courtesy of B. Werner/APHL-CDC*
Sequence of Test Positivity Relative to WB

15 Seroconverter panels - 50% Positive Cumulative Frequency

Modified from Owen et al J Clin Micro 2008

Slide courtesy of B. Werner/APHL-CDC
HIV-2 Infection

• HIV-2 positive individuals frequently linked through travel or country of origin to HIV-2 endemic areas
• HIV-2 infected individuals have been found in low prevalence areas of US
• HIV-1/2 differentiation is important to clinical care and treatment
• HIV-2 infected individuals may be misdiagnosed as HIV-1 positive due to high cross reactivity – “cryptic HIV-2”
• HIV-2 cannot be detected with HIV-1 viral load assays

Slide courtesy of B. Werner/APHL-CDC
Characteristics of Proposed HIV Diagnostic Algorithm

- Detect acute as well as established HIV infections
- Differentiate HIV-1 from HIV-2
- Get timely results to facilitate initiation of care - more same day reporting
- Eliminate indeterminate and inconclusive results whenever possible

Slide courtesy of B. Werner/APHL-CDC
Proposed Laboratory Algorithm

A HIV-1/HIV-2 Ag/Ab Immunoassay *

A+ Repeat in duplicate † → A(- -) Negative for HIV-1 and HIV-2 Ab and HIV-1 p24 Ag **

A1(± ± or ± -)

B HIV-1/HIV-2 Ab Differentiation Immunoassay

B HIV-1 (+) HIV-2 (-) Positive for HIV-1 Ab ‡
B HIV-1 (-) HIV-2 (+) Positive for HIV-2 Ab ‡
B HIV-1 (+) HIV-2 (+) Positive for HIV Ab $‡$
B HIV-1 (-)/HIV-2 (-) or inconclusive

C Individual HIV-1 NAT

C+ Positive for HIV-1 RNA ‡¶
C- Negative for HIV-1 RNA #

* A could be an IgM sensitive antibody immunoassay if the Ag/Ab combination immunoassay is not available.
† Repeating A+ is assay dependent.
‡ Refer to care and follow up testing.
§ HIV positive; further testing required to rule out dual infection.
¶ Acute HIV-1 infection.
# Consider HIV-2 DNA testing if clinically indicated.
** If early acute infection is suspected, NAT can be performed.

Slide courtesy of B. Werner/APHL-CDC
Alternative Algorithms

• Individual or pooled NAT on seronegative specimens
• Traditional algorithm with supplemental NAT option
• Algorithms for oral fluid and dried blood spot (DBS) specimens
• Presumptive positive algorithm for POC or laboratory – sequential Ab immunoassays

WB useful for diagnostic dilemmas and testing vaccine recipients
HIV Testing Algorithm Information

• HIV Testing Algorithms: A Status Report
  [http://www.aphl.org/hiv/statusreport](http://www.aphl.org/hiv/statusreport)

• 2010 HIV Diagnostics Conference, including presentations of data identified as needs for algorithms in the status report and draft of proposed new algorithm
  [http://www.hivtestingconference.org](http://www.hivtestingconference.org)

• CLSI document, M53-P, under review
  – “Criteria for Laboratory Testing and Diagnosis of HIV-1 Infection; Proposed Guideline”
  – Includes algorithms utilizing assays available outside the US as well as those FDA approved
Interpreting HIV Test Results

• Newer tests detect infection earlier

• Know which tests your lab uses

• New algorithms for confirmation using combinations of tests are being evaluated
Awareness of Serostatus Among People with HIV and Estimates of Transmission

- ~25% Unaware of Infection
- ~75% Aware of Infection

People Living with HIV/AIDS:
1,039,000-1,185,000

Accounting for:

New Sexual Infections Each Year:
~32,000

~54% of New Infections
~46% of New Infections

Marks, et al
AIDS 2006;20:1447-50
After people become aware they are HIV-positive, the prevalence of high-risk sexual behavior is reduced substantially.

Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the U.S. Marks G, et al. JAIDS. 2005;39:446
Role of Acute/Early HIV Infection

• Xiradou *AIDS 2004*: Acute = 11% of new infections
  – 35% from casual partners; 6% from steady partners
• Yorke *JAIDS 2004*: Transmissions in symptomatic stage dominate in established epidemics
• Brenner *JID 2007*: Recent infection accounted for 50% of onward transmissions in Quebec
• Pinkerton *AIDS 2007*:
  – 8.6% of new infections from Acute
  – 48.5% from nonacute, serostatus unaware
  – 42.9% from nonacute, serostatus aware

Slide courtesy of B. Werner/APHL
Likelihood of HIV Transmission

What holds you back from inquiring about sexual risk behaviors with your patients?

1. It’s uncomfortable to ask these questions
2. I’m not sure how best to phrase questions
3. Don’t ask – don’t tell – I’m not sure what to do about the answers
4. I’ve known the patient forever – I don’t think they’re at risk
5. The patient will think I’m stereotyping them as someone who is at risk
6. There just isn’t enough time
7. There is no way to get reimbursed for this type of care
Framework for Asking about Behavioral Risk

- Reinforce confidentiality
- Establish rapport
- Be tactful
- Be clear
- Check your assumptions…
- Be non-judgmental

Ask, Screen, Intervene
Risk Screening Techniques

- Open the conversation
- Open-ended Questions
- Closed-ended Questions
- Permission Giving Statements
Risk Screening:
What Should We Ask?

GENERAL QUESTIONS

- Determine whether the patient has been having sex...
  OPEN-ENDED: “To provide the best care, I ask all my patients about their sexual activity – so, tell me about your sex life.”

- Statements about sex practices and drug-related behaviors may need clarification...
  OPEN-ENDED: “I don’t know what you mean, could you explain..?”
Risk Screening: What Should We Ask? WHO

- Determine number and gender of partners, current and past...
  
  OPEN-ENDED: “Tell me about your partners”

- Ask about HIV status of sex and/or injection partners...
  
  OPEN-ENDED: “Talk to me about the HIV status of your partners”
**Risk Screening:**

**What Should We Ask?** WHAT, WHERE

- **Ask about various types of sexual activity…**
  OPEN-ENDED: "Tell me about how you have sex"

- **Determine where patient meets sex and/or injection partners (e.g., venues)…**
  OPEN-ENDED: "Where do you meet your partners?"

*Don’t forget:* Internet, bars, bathhouses, circuit parties, public venues, travel, and sex abroad
Risk Screening: What Should We Ask? PREVENTION METHODS

◆ Ask about condoms/barrier contraception…
  OPEN-ENDED: “What’s your experience been with condom use?”

◆ Ask about drug-injection equipment…
  OPEN-ENDED: “How do you know your works are clean?”
Identifying Risk: Benefits

- **Clinician Perspective**
  - Assists in clinical intervention/exam
  - Provides focus for an in-depth risk assessment and direction for risk reduction or referral
  - May identify persons with acute HIV infection who may be more infectious

- **Patient Perspective**
  - Opportunity to ask questions
  - May affect self-motivation for behavior change
  - Patients *want* to have these discussions yet often will not initiate on their own
Asking about Behavioral Risk…

- Screening
  - Risk Factors
  - STIs

In-Depth Risk Assessment

Ask  Screen  Intervene
Knowledge = Power