HIV Challenges in 2012: Diagnosis, Testing and Other Hot Topics

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Disclosures
I have nothing to disclose.

Objectives: HIV Testing
- Brief review of HIV epidemiology
- Identify major reasons for testing and impediments in 13-64 year olds
- Describe different HIV tests, their pros and cons
- Describe procedures necessary to implement HIV testing of all teens in your medical practice
Changing HIV Epidemic in US

- Protease Inhibitors (PI) introduced in 1996
- Much improved Rx since then (16 ys)
- “AIDS” in 1995 – 1998:
  - Incidence declined 38%
  - Deaths declined 63%
- New “HIV” infections stable since 2000, too
- But … increased in MSM, esp Afr-Americans

CDC data, publ in PLoS ONE 8/3/11
Current Interventions and Issues in US

- **Rx**: HAART is widely available
- **Vaccine**: No prospect for many years
- **Prevention**: Behavioral messages don’t reach the most vulnerable populations
- **Transmission**: In 2006, ~50% of new HIV was acquired from undiagnosed people
- **By the numbers, 2010**: ~230,000 of HIV+ people are unaware of HIV dx (21%)
- **Among MSM**: 44% unaware of dx

 CDC Recommendations in 2006

- Expand testing to “ID” unaware pts
  - Bring them into care earlier
  - Reduce transmission to others
- Use voluntary “opt-out” screening in all healthcare settings
- Target: HIV testing all 13-64 year olds

Prevention with Early Rx: 2011

- Large NIH-funded study done in 9 countries
- 1,763 sero-discordant couples: 1+ / 1-
- HIV+ partners had CD4 counts of 350-500
- Randomized 1:1 to Early vs Delayed Rx
  (Delayed = Rx when CD4 drops < 350)
- 1st prevention EP: Partner converts to +
- 1st clinical EP: TB, SBI, WHO4 event or death

MMWR 2006

**Prevention with Early Rx: Results**

- 28 transmissions virologically linked to HIV + partner (+11 acquired from others):
  - 1 of 28 in Early Rx group: HR 0.04, P<0.001
- Early Rx: Fewer clinical endpoints, HR 0.59
- Conclusion: Early Rx reduces both sexual transmission of HIV and clinical events
- Thus: Personal and public health benefits!


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**Minimal elements of HIV test counseling**

- “HIV is the virus that causes AIDS”
- “You are being tested for HIV as part of routine screening”
- “I will advise you on the next steps, if necessary, based on your test results”
- “You can opt to decline or defer the test”
- “Any questions?”
- Plan when/where to disclose in person.
  - You can cancel and call with negative results.

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**“Opt-out” testing in healthcare settings**

- Before: Offer testing to people who you think are at risk, but you really don’t know
- Now: Opt-out removes insensitivity and judgment assoc with risk-based screening
- High-risk behaviors may stay undetected
- Patients may not acknowledge risks
- Prevention counseling NOT required
- Where? Settings where prevalence ≥ 0.1%
- Others? All patients with TB, new STIs

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**Sample chart documentation**

- HIV Screening Test (check off)
  - Offered, patient accepted
  - Patient declined because:
    - has already been tested
    - is not ready
    - does not consider self at risk
  - Not offered: practitioner does not consider patient to be at risk
  - Not offered, lack of time

Futterman, CCO 2010
Minimal plan for + disclosure

- Know what to say and how to say it
- Connect to advocates or counselors
- Plan referral to HIV specialist
- Remember HIPAA & state laws
- Mandatory public health reporting
- Now: Include prevention counseling

More about disclosure

- It takes time. Sit down.
- Need to be patient and to listen.
- See syllabus for suggested content.
- Ideally, have support people available.
  - Peer advocate or social worker.
- Plan MD hand-off smoothly, carefully.

Repeat Screening Indications

- Sexually active teen patients: annually (+?)
- Known high-risk patients: at least annually
  - IDU, partners of IDU, sex for money/drugs
  - Partners of HIV, MSM
  - Heterosexuals with >1 partner since last test
- Before any new sexual relationship
- Sources of an occupational exposure
- Use clinical judgment for others

Barriers to HIV Testing

- Conflicting state or local laws
- Misinformation re: pre-test counseling
- Stigma assoc with HIV diagnosis
- Fear of HIV discrimination
- Cost of tests (~$4 std. vs $25 rapid)
- Lack of resources (linkage-to-care)
Testing at CHRCO: 2005-8/31/10

![Graph showing % of Teens Tested for HIV](image)

HIV Testing at CHRCO: 2006-11

<table>
<thead>
<tr>
<th>YEAR</th>
<th># TESTS</th>
<th>UDC</th>
<th># HIV infected</th>
<th>% Tests +</th>
<th>+ RATE</th>
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<td>246</td>
<td>9675</td>
<td>0</td>
<td>0</td>
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<tr>
<td>2007</td>
<td>2253</td>
<td>12002</td>
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<td>1.440</td>
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<tr>
<td>2009</td>
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<td>13471</td>
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<td>1.233</td>
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<tr>
<td>2010</td>
<td>2621</td>
<td>11107</td>
<td>5</td>
<td>0.19%</td>
<td>1.524</td>
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<tr>
<td>7 months of 2011</td>
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<td>7699</td>
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<td>0.33%</td>
<td>1.391</td>
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Recent HIV+ Teens CHRCO 2008 – July 2011

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<tr>
<th>YR</th>
<th>PT #</th>
<th>Age/R/G</th>
<th>EIA</th>
<th>WB</th>
<th>PCR</th>
<th>CD4</th>
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<td>17 O M</td>
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<td>+</td>
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<td>20</td>
<td>160000</td>
<td>ANH</td>
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<td>2</td>
<td>16 B M</td>
<td>+</td>
<td>+</td>
<td>683</td>
<td>22</td>
<td>4000</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>3</td>
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<td>+</td>
<td>479</td>
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<tr>
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<td>3700</td>
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<td>-</td>
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<td></td>
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<td>+</td>
<td>+</td>
<td>524</td>
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<td>2675</td>
<td>New inf</td>
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</tr>
<tr>
<td></td>
<td>5</td>
<td>21 B M</td>
<td>+</td>
<td>+</td>
<td>463</td>
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<td>137000</td>
<td>RPR+</td>
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<tr>
<td></td>
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<td>18 B F</td>
<td>+</td>
<td>+</td>
<td>974</td>
<td>32</td>
<td>457</td>
<td>RPR+</td>
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</table>

Caveats re: Testing

- Legal requirements vary in US*
- Many high-risk pts don’t access care so won’t be found in clinics
- Thus, community-based, non-clinical sites are critical:
  - 2001 CDC guidelines apply there
  - Different issues:
    - Confidentiality; specimen transport; reporting of results, staff safety

* Compendium of State HIV Testing Laws, 2010 at NCCC Website
Success of Testing (1)

- High acceptance in high-risk popul's
- **2006**, US: 65% adults surveyed support testing in similar manner to other dx *
- Many sites consider HIV testing to be a high priority
- Expanded testing reduced undiagnosed HIV from 25% to 21% in US

* Kaiser Family Fdtn 2009; CDC 2009; Campsmith 2010

Success of HIV Testing (2)

- Typically 10 ys from HIV infxn to AIDS dx
- Early dx ➔ early Rx ➔ lower mortality
- Late dx still problematic:
  - 38%: “AIDS” dx within 1st year after HIV dx (vs)
  - 7%: “AIDS” dx 1-3 years after HIV dx
  - Associated with lack of primary care
- Wash, DC: **2004 ➔ 2008**: 3.7 x more tests done
  - 17% more cases found; less time to get into care
  - Higher CD4 count (216 vs 343) at time of dx

CDC 2009  Castel 2010

Social Network Testing

A Community-Based Strategy for Identifying Persons with Undiagnosed HIV

Interim Guide for HIV Counseling, Testing, and Referral Programs

- Recruitment strategy
- Pub health svcs (HIV CTRs) dissem thru the community
- Uses social networks of members of the community.
- Individuals link together to form large social networks
- Infectious dis often spread through these networks.
- Social network approach:
  - broader understanding of HIV transmission
  - understand the role of all members of the network, whether infected or not, in transmission and its prevention

www.cdc.gov/hiv/resources/guidelines/snt/pdf/SocialNetworks.pdf

CDC’s Social Networks Demonstration Program (2003 – 2005):
Across nine funded sites, approx 6% of people tested were newly diagnosed with HIV.

This prevalence rate is six times higher than the average of most HIV CTR programs.
Social network diagram (15 recruiters)

- Large circles/squares — Recruiters
- Small circles/squares — Network associates
- Diamonds — Indirect network associates
- Black nodes — HIV-positive
- White nodes — HIV-negative
- Gray nodes — HIV status unknown

Diagnostic Tests for HIV
- Antibodies: HIV1, HIV2
- Antigens
- HIV RNA PCR (quant = viral load)
- HIV DNA PCR (qualitative)
- Ab / Ag (sandwich)
- 3rd and 4th gen. immunoassays

HIV Antibody Testing
- Gold standard since 1985
- 3rd gen. enzyme immunoassays (EIAs) now detect both HIV1 & HIV2 (standard)
  - >99.7% sensitivity
  - >98.5% specificity
- Positive EIA: Sample is automatically sent for a confirmatory study
  - Western Blot or IFA
  - Usually takes 4-6 days (or more)
How would you interpret + EIA?

Should 1 EIA+ be considered adequate for dx in a population with:
- 1% (1/100) infected?
  - Many would argue: ‘yes’
- 0.1% (1/1000) infected?
  - With known risk behaviors, likely real
- << 0.1% infected?
  - More likely to see false positives

Rapid HIV tests: Pros/Cons

- Why? 30% of HIV+ patients don’t return for results
- 7 rapid tests are FDA-approved in US
- 99.3-100% sensitivity; 99.5-100% specificity
  - 60 sec to 20 min to process
  - Some CLIA waived; others moderately complex
  - Sample needed varies: Oral swab, finger-stick, whole blood, serum or plasma
  - $8.50-25 vs $3-4 per test, plus tech or RN time
- Negative rapid test = high NPV
  - Thus, no confirmatory test is needed for neg Ab!

CDC 2003, CDC 2008, FDA 2010

Early HIV Infection Timeline

RNA rises first, then P24 EIA, then other EIA, eventually WB

McMichael Nature Immuno 2010

Acute HIV Infection (AHI)

- Concern: High RNA + high-risk activ → more transmission
- May acct for 14-50% of all transmission
- RNA is present first, before Ab forms
  - Caveat: 5% have negative HIV RNA
- Consider HIV RNA if EIA + or –
- Consider HIV RNA if WB indeter / neg

Ann Petru, MD

HIV Challenges in 2011

Early HIV Infection timeline

Summary of marker detection in AHI

Acute HIV Infection

• Fever
• Headache
• Sore throat
• Lymphadenopathy
• Myositis
• Dermatitis
• Hepatitis
• Gastritis, nausea

Acute HIV Infection: Clinical

• 40 - 90% develop symptoms with viremia
  – Nonspecific, hard to recognize
  – Fever, LAD, rash, pharyngitis, N/V/D
  – Among MSM with sx/sx of AHI, only 1/2 were suspected by their providers to have HIV
• 2011: 1 RNA PCR test is FDA-approved to diagnose HIV infection
  – Qualitative result; follow with Ab, VL
  – Most clinicians would send viral load regardless
So....Pop Quiz!

If you suspect AHI and HIV antibody is negative, what should you send?
- a. Western Blot test
- b. HIV DNA PCR
- c. HIV RNA PCR
- d. CBC/diff and T&B cell typing

Answers

You suspect AHI, Ab is negative, what should you do?
- a. Western Blot test? Too soon!
- b. HIV DNA PCR? Costly and ↑ time
- c. Order HIV RNA PCR: ✪
- d. T&B cell typing? Often still normal

4th generation immunoassay

Another new choice; not used much yet
- 2010: Approved by FDA
- Combined Ab/Ag (IgG, IgM, HIV p24)
- Can detect AHI if RNA ≥ 30K copies/mL
  - Detects 80-90% of AHI
  - Misses the 20-25% with RNA < 30K
- Automated, less process time, lower cost
- Doesn’t distinguish new vs prevalent HIV

Linkage-to-Care

- Enables timely treatment for HIV
- Manage co-morbid conditions
  - Essential to optimize adherence to Rx
- Address socioeconomic factors that may hinder access to care
- Case managers, peer advocates critical
Summary of Testing Issues

- Normalization of screening is essential
- Recommend screening once for all S.A. adults
- Repeat screening in high-risk populations
  - Frequency not yet clear
- Beware of sx/sx of AHF
- Goals:
  - Decrease HIV morbid/mortality
  - Increase QOL
  - Reduce new infections

2 little boys who changed my life:
Friends we are and friends we’ll be, and one of us has...H I V

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