HIV & Hepatitis: What Every Health Provider Should Know

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The University of Kansas School of Medicine - Wichita
This May Be the Most Dangerous Time Yet!
Time Line of HIV Infection

- Acute Infection
- Asymptomatic HIV Infection: 10-15 Years
- Symptomatic HIV Infection: 3-5 Years
- AIDS: ? Years
- Positive Ab Test Result (6 months)
- DEATH?
Case Study

- 52 y.o., white male, engineer
- Ill since November 28, 2003 with cough, weight loss, oral ulcers and skin rash
- Seen by ENT
  - Oral ulcers – bx. Nonspecific
- Seen by dermatology
  - Diagnosis December – scabies
  - Diagnosis January – eczema
- Seen by pulmonology
  - 2/28 – working diagnosis – sarcoid
  - Bronch bx – negative
Case Study

Open lung bx = PCP
HIV+
CD4 - 2
VL > 750,000
About 14 000 new HIV infections a day in 2004

- More than 95% are in low and middle income countries
- Almost 2000 are in children under 15 years of age
- About 12 000 are in persons aged 15 to 49 years, of whom: almost 50% are women & about 50% are 15–24 year old

- A new infection every 6 sec,
- A death every 9 sec
- A new orphan every 14 seconds
A Global View of the AIDS Pandemic
End of 2004: 40 million infected, 25 million dead!

“A Tsunami every 3-4 weeks, a Katrina every day in Africa”
Around half of all people who become infected with HIV do so before they are 25 and are killed by AIDS before they are 35.

Source - http://www.avert.org/aidsnews.htm
Prevalence Trends: 2005

- Although increases in prevalence has gone up throughout most of Europe and Central Asia by 25% (to 1.6 million)…
  - Kenya, Zimbabwe and some countries in the Caribbean region have recently experienced declines in HIV prevalence rates…

- Downward trends are due to:
  - Increased condoms use
  - Delay of first sex
  - Reduction in the number of sexual partners

Source - http://www.avert.org/aidsnews.htm
AIDS Rates, Reported in 2004—United States

Rate (per 100,000 population)
- <5.0
- 5.0 - 15.0
- >15.0

Guam 0.6
Pacific Islands, US 0
Puerto Rico 23.4
Virgin Islands, US 18.4

CDC
Proportion of AIDS Cases among Adults and Adolescents, by Transmission Category and Year of Diagnosis, 1985–2004—United States

Note: Data adjusted for reporting delays and cases without risk factor information were proportionally redistributed. *Heterosexual contact with a person known to have or at high risk for HIV infection.
Reported AIDS Cases, by Age and Sex
Cumulative through 2004—United States

No. of cases (in thousands)

Age at diagnosis

Males N* = 742,094
Females N* = 176,190


* Excludes 2 persons of unknown sex.
Kansas HIV Disease Prevalence and Deaths Related to HIV / AIDS by Year
<table>
<thead>
<tr>
<th>Kansas AIDS Cases as of 12/31/2005</th>
<th>Newly Reported AIDS Cases</th>
<th>Prevalent AIDS Cases</th>
<th>Cumulative AIDS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>ADULT/ ADOLESCENT</td>
<td>115</td>
<td>100.0</td>
<td>1162</td>
</tr>
<tr>
<td>PEDIATRIC (&lt;13 YEARS OLD)</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>100.0</td>
<td>1168</td>
</tr>
</tbody>
</table>
## Kansas AIDS Cases as of 12/31/2005

<table>
<thead>
<tr>
<th>Gender</th>
<th>Kansas Newly Reported AIDS Cases</th>
<th>Kansas Prevalent AIDS Cases</th>
<th>Kansas Cumulative AIDS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Male</td>
<td>91</td>
<td>79.1</td>
<td>977</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>20.9</td>
<td>191</td>
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</table>
## Kansas AIDS Cases as of 12/31/2005

<table>
<thead>
<tr>
<th>Exposure Category</th>
<th>Newly Reported AIDS Cases</th>
<th>Prevalent AIDS Cases</th>
<th>Cumulative AIDS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Exposure Category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men who have sex with men (MSM)</td>
<td>48</td>
<td>41.7</td>
<td>648</td>
</tr>
<tr>
<td>Injection Drug User (IDU)</td>
<td>7</td>
<td>6.1</td>
<td>104</td>
</tr>
<tr>
<td>MSM and IDU</td>
<td>11</td>
<td>9.6</td>
<td>106</td>
</tr>
<tr>
<td>Hemophilia and/or Coagulation Disorder</td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>High Risk Heterosexual Contact</td>
<td>18</td>
<td>15.7</td>
<td>177</td>
</tr>
<tr>
<td>Transfusion/Transplant</td>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>No Identified Risk (NIR)</td>
<td>31</td>
<td>27.0</td>
<td>103</td>
</tr>
<tr>
<td>Pediatric-Hemophilia and/or Coagulation Disorder</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Pediatric-Mother with HIV</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Pediatric-Transfusion/Transplant</td>
<td></td>
<td></td>
<td>1</td>
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<tr>
<td>Pediatric-No Identified Risk (NIR)</td>
<td></td>
<td></td>
<td>1</td>
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## AIDS Cases by Age 12/31/2005

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Newly Reported AIDS Cases</th>
<th>Prevalent AIDS Cases</th>
<th>Cumulative AIDS Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>&lt;13</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>13 TO 14</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>15 TO 24</td>
<td>7</td>
<td>6.1</td>
<td>83</td>
</tr>
<tr>
<td>25 TO 34</td>
<td>33</td>
<td>28.7</td>
<td>435</td>
</tr>
<tr>
<td>35 TO 44</td>
<td>40</td>
<td>34.8</td>
<td>431</td>
</tr>
<tr>
<td>45 TO 54</td>
<td>25</td>
<td>21.7</td>
<td>169</td>
</tr>
<tr>
<td>55 TO 64</td>
<td>6</td>
<td>5.2</td>
<td>37</td>
</tr>
<tr>
<td>65 or Older</td>
<td>4</td>
<td>3.5</td>
<td>6</td>
</tr>
</tbody>
</table>
### Kansas AIDS Cases by Race/Ethnicity
**As of 12/31/05**

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Newly Reported AIDS Cases</th>
<th>Prevalent AIDS Cases</th>
<th>Cumulative AIDS Cases</th>
<th>% of Total Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>23</td>
<td>20.0</td>
<td>145</td>
<td>12.4</td>
</tr>
<tr>
<td>American-Indian</td>
<td>1</td>
<td>0.9</td>
<td>11</td>
<td>0.9</td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Black</td>
<td>42</td>
<td>36.5</td>
<td>266</td>
<td>22.8</td>
</tr>
<tr>
<td>White</td>
<td>49</td>
<td>42.6</td>
<td>723</td>
<td>61.9</td>
</tr>
<tr>
<td>Old Asian/Pacific Islander</td>
<td>3</td>
<td>0.3</td>
<td>8</td>
<td>0.3</td>
</tr>
<tr>
<td>Multi-race</td>
<td>17</td>
<td>1.5</td>
<td>22</td>
<td>0.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>0.1</td>
<td>1</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Trends in Age-Adjusted* Rates of Death due to the 7 Leading Causes and HIV Disease, USA, 1987–2002

Deaths per 100,000 Population

1987 1989 1991 1993 1995 1997 1999 2001

Heart disease
Cancer
Stroke
Chronic lung disease
Unintentional injury
Diabetes
Pneumonia
HIV disease

Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.

*Standard: age distribution of 2000 US population
Estimated Number of AIDS Cases, Deaths, and Persons Living with AIDS, 1985-2003, United States

Note. Data adjusted for reporting delays.
Factors that facilitate transmission

- High HIV titers in plasma reflected in semen, vaginal and rectal secretions-ART reduces titer
- Co-infections with malaria, tuberculosis and especially other STDs increase viral load-activate CD4
- Genital ulcers facilitate submucosal inoculation
- Lack of circumcision facilitates spread to male
- Menses, vaginal mucosal thinning (estrogen deficiency), cervical ectopy inc tx to & from woman
This Epidemic is far from over---

Counsel all patients in your practice, young and old, about HIV prevention

New CDC HIV Prevention Initiative
Strategies of the Initiative

Four priority strategies

- Make voluntary HIV testing a routine part of medical care
- Implement new models for diagnosing HIV infections outside medical settings
- Prevent new infection by working with persons diagnosed with HIV and their partners
- Further decrease perinatal HIV transmission
Strategy 1: Make Voluntary Testing a Routine Part of Medical Care

- Work with physicians to include HIV testing, when indicated, as a part of routine medical care;
- Expand routine offering of testing;
- Promote adoption of simplified voluntary testing procedures that do not require prevention counseling prior to testing;
- Fund demonstration projects of routine offering HIV testing to all patients in high HIV prevalence health care setting;
Of the approximately 1 million Americans infected with HIV, 250,000 to 300,000 are unaware of their serostatus.
Main Reason for HIV Test*, by Gender, June 1997 - December 2000
(Supplement to HIV and AIDS Surveillance Project)

* At first (+) HIV test
Infection Ignored

31% Of positive HIV test results are never picked up by the patient.

41% Of HIV-infected people are diagnosed with full-blown AIDS within one year of a positive HIV test.

42% Of those found to be HIV+ are tested because of an illness.

10% Of men found to be HIV+ were tested because the service was offered by a health care provider.

17% Of women found to be HIV+ were tested because the service was offered by a health care provider.
Who is Testing Late and Why…

- Racial/ethnic minority populations, heterosexuals, or persons who have low education are more likely to test late for HIV.

- Majority of late testers sought testing because of illness.
Rapid HIV Testing: The Waive of the Future
OraQuick

New!

- Finger stick sample
- 20 minutes to process
- Accurate results
OraQuick Advance

- Sometimes confused with OraSure, a non-rapid oral-fluid test
- Average acquisition cost for a rapid HIV test is about $17.50 (Kansas).
- The only rapid test approved for use
  - with oral fluid as well as whole blood and plasma
  - both HIV-1 and HIV-2
OraQuick: Oral fluid, serum, whole blood
FDA-approved November 7, 2002 for use with fingerstick whole blood specimens
How it Works…The Set Up

- Set up a clean, absorbant area for placement
- Blue holder must be used for each test
- Holder up cannot be moved after paddle is placed in solution
How it Works…The Specimen

- Glove
- Use lancet to obtain specimen
- Fill loop
Similar loop is used with several rapid tests
Insert loop into vial and stir
How it Works…The Test

- Stir loop in solution
- Insert paddle
- Begin timing
- Watch for control line to be sure test is functional
- Read test after 20 minutes
Test develops in 20 minutes
Read results

**Test Kit:** OraQuick

**Test Type:** HIV-1/2

**Results:**
- **Positive**: Sample 305 shows a positive result.
- **Negative**: Sample 306 shows a negative result.

**Control:** Both samples show a positive control line.
Oral fluid specimens reduce hazards, facilitate testing in field settings
When Is A Rapid Test Indicated?

- Obstetric admissions
- Healthcare worker occupational exposures
- Urgent care clinics and Emergency departments
- Public health settings
- Developing countries
- The Primary Care office
More is Better

- Earlier access to available medications – resulting in increased length of life
- Those who know they are positive tend to take more precautions to protect others
- On a population wide basis, such screening could reduce spread
  – because medications suppress viral load and reduce the chance of transmission
“There’s a significant proportion of practitioners who aren’t doing testing at all, and I’m not even clear if they have the resources to refer people to someone else”

Howard Grossman, MD, Executive Director
The American Academy of HIV Medicine
Test at Least Once…

Encourage your patients to be tested for HIV at least once---whether you work in New York City, Kansas City or Sioux City, Iowa
Future Considerations

- More patients prefer it
  - Less anxiety
  - Ability to begin appropriate care right away

- More patients learn of their HIV+ status
  - Reduction in transmission rates
  - Maintain health status longer and lengthen life
Routine Testing

Routine one-time testing of everyone would cut new infections each year by just over 20%.

Every HIV-infected patient identified would gain an average of $1\frac{1}{2}$ years of life.

Source: study by researchers at Duke and Stanford Universities and the Veterans Affairs Palo Alto Health Care System
Three FDA Rapid HIV Tests Approved

- **OraQuick Advance**
  - OraSure Inc.
  - [http://www.orasure.com](http://www.orasure.com)
  - CLIA waived

- **Uni-Gold Recombigen**
  - Trinity Biotech PLC
  - [http://trinitybiotech.com](http://trinitybiotech.com)
  - CLIA waived

- **Reveal G2**
  - MedMira Inc.
  - [http://medmira.com](http://medmira.com)
  - Not CLIA waived
  - (multi-step process)
Strategy 3: Prevent New Infections by Working with Persons Diagnosed with HIV

In 2004…

- Prevention for Positives initiative
  - PCM (prevention case management) for people with HIV who have ongoing high-risk behavior
  - New models of PCRS (partner counseling and referral services).
Sexual Transmission of HIV Directly Related to Plasma HIV RNA Level

Strategy 4: Further Decrease Perinatal HIV Transmission

- Work with physicians to promote routine, voluntary prenatal testing, with right of refusal;
- Develop guidance for using rapid tests during labor and delivery or post partum;
- Provide training in conducting prenatal testing;
- Monitor integration of routine prenatal testing into medical practice.
Aggressive HIV Testing Initiative Unveiled by CDC

- Opt – Out HIV testing of all pregnant women
- HIV testing recommended in routine care of all patients at doctor’s offices and clinics
- Urges widespread use of OraQuick rapid HIV test
- Encourages greater integration of HIV prevention education into the medical care of HIV patients.

www.thebodypro.com, 4/23/03, Bi-weekly Professionals Update newsletter
Prenatal HIV Screening

Based on information presented in the MMWR – Both “opt-out” and prenatal maternal screening and mandatory newborn screening achieve higher maternal screening rates than “opt-in” prenatal screening

CDC recommends that clinicians routinely screen all pregnant women for HIV infection using an “opt-out” approach
Estimated Number of Perinatally Acquired AIDS Cases, 1985-2003, United States

Note: Data adjusted for reporting delays and for estimated proportional redistribution of cases in persons initially reported without an identified risk factor.
Perinatal Testing Project: Wichita, Kansas

Deliveries
Known HIV Status
Unknown HIV Status
Screen Refused
Rapid HIV Screen
The CDC Recommends that...

“hospitals adopt a policy of routine rapid HIV testing by using an opt-out approach for women whose HIV status is unknown when presenting for labor and delivery”
Public Health Settings

- 30-40% of patients do not return for their test result
- Groups least likely to return:
  - Adolescents
  - African Americans
  - Persons tested at an STD clinic

Source: www.cdc.gov/hiv/pubs/cts98.pdf
Public Health Settings

- Tracking data shows that 6,000 to 8,000 patients per year have an HIV test that is positive, but never return for the results
  - HIV testing resources are squandered
  - Opportunities for timely treatment and prevention counseling are lost

Source: www.cdc.gov/hiv/pubs/cts98.pdf
Developing Countries

- Already in use
  - Technically simple
  - Accurate
  - Cost-effective

- A definitive diagnosis of HIV infection can be achieved by using two or three different rapid HIV tests in combination

- These protocols yield sensitivity and specificity equal to those of standard EIA and Western blot methodologies

- This is recommended by the World Health Organization
Test at Least Once…

Encourage your patients to be tested for HIV at least once---whether you work in New York City, Kansas City or Sioux City, Iowa
HIV Replication Cycle and Sites of Drug Activity

- **Attachment Inhibitors**
  - HIV Virions
  - CD4 Receptor
  - CCR5 or CXCR4 co-receptor
- **NRTIs**
  - Reverse Transcriptase
  - Viral RNA
- **NNRTIs**
  - Uncoating
- **Protease Inhibitors**
  - Protease
  - Protease Inhibitors
  - New HIV particles
- **Reverse Transcriptase**
  - Unintegrated double stranded Viral DNA
- **Integrase**
  - Nucleus
  - Cellular DNA
  - Integrated viral DNA
  - Viral mRNA
- **Protease**
  - gag-pol polyprotein
- **Assembly and Release**
  - Capsid proteins and viral RNA

Number of Approved Antiretroviral Agents by Year

Note: These were fixed dose combinations of existing drugs
### Licensure of Antiretroviral Agents by Year

- **1987:** zidovudine (Retrovir)
- **1989:** didanosine (Videx)
- **1990:** zalcitabine (Hivid)
- **1991:** stavudine (Zerit)
- **1992:** lamivudine (Epivir)
- **1993:** saquinavir (Inverase)
- **1994:** ritonavir (Norivir)
- **1995:** nelfinavir (Viracept)
- **1996:** indinavir (Crixivan)
- **1997:** delavirdine (Rescriptor)
- **1998:** efavirenz (Sustiva)
- **1999:** amprenavir (Agenerase)
- **2000:** lopinavir/ritonavir (Kaletra)
- **2001:** tenofovir (Viread)
- **2003:** enfuvirtide (Fuzeon)
- **2004:** enfuvirtide (Fuzeon)
- **2005:** Tipranavir (Aptivus)
- **2006:** atazanavir (Reyataz)
- **2007:** nelfinavir (Viracept)
- **2008:** indinavir (Crixivan)
- **2009:** lopinavir/ritonavir (Kaletra)
- **2010:** tenofovir (Viread)
- **2011:** enfuvirtide (Fuzeon)
- **2012:** tipranavir (Aptivus)
- **2013:** enfuvirtide (Fuzeon)
- **2014:** lopinavir/ritonavir (Kaletra)
- **2015:** tenofovir (Viread)
- **2016:** enfuvirtide (Fuzeon)
- **2017:** tipranavir (Aptivus)

* Fixed dose combinations of existing drugs
### When to Start Treatment

<table>
<thead>
<tr>
<th>Clinical Category</th>
<th>CD4+ Cell Count</th>
<th>Plasma HIV-1 RNA</th>
<th>General Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-defining illness or severe symptoms*</td>
<td>Any value</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&lt; 200</td>
<td>Any value</td>
<td>Treat</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>200-350</td>
<td>Any value</td>
<td>Treatment should be offered following full discussion of pros and cons of treatment.</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&gt; 350</td>
<td>≥ 100,000</td>
<td>Most clinicians recommend deferring therapy, but some clinicians will treat.</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>&gt; 350</td>
<td>&lt; 100,000</td>
<td>Defer therapy</td>
</tr>
</tbody>
</table>

DHHS Guidelines: 4/7/2005
No Antiretroviral Drug is Ideal

- Too toxic
- Too many pills
- Suboptimal activity
- Low threshold for development of resistance
Lipodystrophy and Metabolic Toxicity

- **Hyperlipidemia, insulin resistance**
  - Modify external factors (eg: diet, exercise)
  - Switch therapy
    - PI to NVP
    - PI to ABC
  - Add other therapy (eg: statins/fibrates, insulin sensitizing agents)

- **Visceral fat accumulation**
  - Modify external factors (eg: diet, exercise)

- **Subcutaneous fat wasting**
  - Switch therapy
    - d4T to ZDV or ABC
  - Collagen fillers – Sculptra
Lipodystrophy Syndrome: NRTIs vs PIs

NRTIs vs PIs

NRTIs: d4T > ZDV

- ↑ Lactic acid
- ↑ SC fat wasting
- ↑ TG

PIs:

- ↑ Intra-abdominal fat
- ↑ Cholesterol
- ↑ TG
- ↑ Insulin resistance

Encourage Healthy Lifestyle Choices

- Quit smoking
- Regular exercise
- Balanced diet with lots of nuts, fruits, and vegetables
- Stress reduction
- Quit / avoid all drug use - especially crystal methamphetamine
- Eliminate / avoid excess alcohol use
Co-Existing Problems to Consider

- Pregnancy (+/or potential)
- Lipid status
- Diabetic
- Hepatitis B / C
- Drug and Alcohol Use
18-yo HIV+ Caucasian man screened at health clinic with fatigue and headaches. Likely acquired HIV through unprotected sex with internet contacts.

Medical History
- Depression diagnosed at age 16
- Allergic to penicillin
Clinical Scenario #1

History, cont’d.

- Family History
  - Father had 1st MI at age 45

- Social History
  - Going to Junior College and working at the mall
  - Eating habits are chaotic
  - Concerned about complicated dosing schedules
  - Afraid of severe side effects
  - Concerned about confidentiality
Clinical Scenario #1

**Labs**

- **HIV**
  - HIV RNA = 275,000 c/mL
  - CD4 = 260 cells/mm³
  - Genotype = K103N

- **Hematology**
  - H/H = 14.3 g/dL / 42.9%

- **Lipids**
  - TC = 173 mg/dL

- **Kidney/metabolic**
  - Fasting glucose = 69 U/L
  - Urinalysis negative for protein, glucose
  - Serum creatinine = 0.9 mg/dL
  - GFR = 117 mL/min/1.7m² estimated by MDRD

- **Hepatitis**
  - HBV S Ab+, S Ag-, C Ab-
Discussion

- What are some of the considerations in diagnosing and treating HIV disease in people 18-25?
- Do the patient’s chaotic eating habits bring up specific tolerability issues?
- Does the dosing schedule of ART affect your choice of initial regimen?
- Is sequencing important in the long term management of this patient?
The Tip Of The Iceberg---

Just as photographic technology has increased to allow us to see the entire iceberg, the same is true with HIV---we know more --- but the hazard remains