HIV/AIDS

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HIV through the Decades

Recognition of Syndrome
Opportunistic Infections
Complications of Therapy
Co-Morbidities


Identifying Virus
Focus on CD4

Measuring Viral Load
Once daily Fixed Dose Combinations

"Typical" Course of Untreated HIV Infection

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Recognition of Syndrome
Opportunistic Infections
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Identifying Virus
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Measuring Viral Load
Once daily Fixed Dose Combinations
90% of new infections in males ages 13-24 were attributable to male-to-male sexual contact.
Cumulative Viral Load Predicts Mortality in ART-Treated Patients

- Estimated cumulative VL (viremia copy-yrs) assessed in 33,563 pts at 17 sites of ART Cohort Collaboration
- After adjusting for age, sex, risk group, BL and time-related VL and cohort, viremia copy-yrs stratum predicted
  - All-cause mortality
  - AIDS-related mortality


Normalization of CD4/CD8 Ratio and Non-AIDS Events

- 3,236 pts on ART with virologic suppression
  - 7,305 PYFU
  - 458 pts reached CD4/CD8 ≥ 1
  - Median time to normalization: 10.1 yrs
- Younger pts, those starting ART in recent yrs, and those with higher CD4+ counts more likely to normalize
- Current CD4/CD8 ratio predicted incidence of clinical progression
- Remained predictive after adjusting for current CD4+ cell count


Common Co-morbid Conditions in HIV-infected Persons

- Cardiovascular diseases
- Metabolic complications
  - lipids/diabetes
- Bone disorders
- Renal
- Liver
- Malignancies
Projecting CVD Risk in HIV:
Cumulative Risk by Age and Over a Lifetime


Competing mortality due to HIV-related causes and other non-HIV causes within the HIV-infected population results in lower overall CVD lifetime risk for HIV-infected persons.

Incidence of MI in HIV+ vs HIV-

• Retrospective analysis of Kaiser cohort EMRs during 1996-2011 for inpatient MI diagnosis
• HIV-/HIV+ pts matched 10:1
• MI rates in HIV+ and HIV- converged over time
  – 40% increased risk of MI in HIV+ pts overall, but difference no longer observed in most recent yrs


Framingham Risk Score Components, 2010-11

HIV+ HIV P value
Mean Framingham score, 10-yr risk of MI, % 9.2 9.6 < .001
Male sex, % 90.7 90.4 .42
Mean age, yrs 47.9 48.5 < .001
TC > 200 mg/dL, % 30.0 39.6 < .001
HDL-C < 40 mg/dL, % 39.4 26.2 < .001
Hx of hypertension, % 28.5 26.2 < .001
Hx of smoking, % 48.7 34.9 < .001

### Incidence of MI in HIV+ vs HIV- Subjects in Kaiser Cohort

<table>
<thead>
<tr>
<th>Framingham Risk Score Components, 2010-11</th>
<th>HIV+</th>
<th>HIV-</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Framingham score, 10-yr risk of MI, %</td>
<td>9.2</td>
<td>9.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Male, %</td>
<td>90.7</td>
<td>90.4</td>
<td>.42</td>
</tr>
<tr>
<td>Mean age, yrs</td>
<td>47.9</td>
<td>48.5</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>TC &gt; 200 mg/dL, %</td>
<td>30.0</td>
<td>39.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>HDL-C &lt; 40 mg/dL, %</td>
<td>39.4</td>
<td>26.2</td>
<td>&lt; .001</td>
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<td>&lt; .001</td>
</tr>
</tbody>
</table>


### Excess Burden of Cancer Among HIV-Infected Persons

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Expected # of Cancers</th>
<th>Excess or Deficit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHL (1645)</td>
<td>203</td>
<td>87.7</td>
</tr>
<tr>
<td>KS (912)</td>
<td>2</td>
<td>99.8</td>
</tr>
<tr>
<td>Lung (837)</td>
<td>401</td>
<td>52.0</td>
</tr>
<tr>
<td>Anus (764)</td>
<td>20</td>
<td>97.4</td>
</tr>
<tr>
<td>Prostate (574)</td>
<td>969</td>
<td>-40.7</td>
</tr>
<tr>
<td>Liver (389)</td>
<td>106</td>
<td>72.7</td>
</tr>
<tr>
<td>Colorectal (357)</td>
<td>379</td>
<td>-5.8</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma (317)</td>
<td>29</td>
<td>90.0</td>
</tr>
<tr>
<td>Breast (177)</td>
<td>303</td>
<td>-41.6</td>
</tr>
</tbody>
</table>

Robbins et al. 12st CROI Boston 2014 #707

### HIV and Cancer-Specific Mortality in the U.S. (1996-2010)

- Retrospective analysis from 5 US Cancer registries (HIV/AIDS Cancer Match Study)
- Cancer specific mortality by HIV status
- HIV-infected cancer patients experienced higher cancer-specific mortality

| Adjusted Hazard Ratios for Cancer-Specific Mortality (HIV Infected vs Uninfected) |
|---------------------------------|----------------------------------|
| Oral cavity/pharynx             | 1.50 (1.07-2.99)                 |
| Larynx                          | 1.92 (1.23-2.98)                 |
| Pancreas                        | 1.63 (1.29-2.10)                 |
| Colon and rectum                | 1.69 (1.35-2.11)                 |
| Lung                            | 1.28 (1.17-1.40)                 |
| Melanoma                        | 1.76 (1.16-2.79)                 |
| Breast                          | 2.71 (2.10-3.50)                 |
| Prostate                        | 1.83 (1.16-2.87)                 |

Liver, anal, cervical cancers had suggested elevations
Coghill et al 21st CROI, Boston 2014 #99

### HIV and the Older Patient

- In the U.S., approximately 30% of HIV-infected persons are ≥50 years of age
- Aging-related comorbidities may complicate management of HIV
- HIV may increase risk of comorbidities and may accelerate the aging process
- Limited data on effects of ARVs in older persons (eg, adverse effects, drug-drug interactions)
HIV and the Older Patient: HIV Risk, Diagnosis, and Prevention

- Reduced mucosal and immunologic defenses and changes in risk behaviors may lead to increased risk of HIV acquisition and transmission
- HIV screening rates in older persons are low
- Older persons may have more advanced HIV at presentation and ART initiation
  - Screen for HIV per CDC recommendations
  - Sexual history, risk-reduction counseling, screening for STIs (as indicated) are important to general health care for HIV-infected and HIV-uninfected older persons

Recommendations for HIV Testing

- HIV screening is recommended for patients in all health-care settings
  - Patient should be notified that testing will take place unless patient declines (opt-out testing)
- Persons at high risk for HIV should be screened at least annually
- HIV screening should be included in the routine panel of prenatal screening for pregnant women
- Neither separate written consent nor prevention counseling should be required

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### 2014 DHHS Guidelines: When to Start ART

<table>
<thead>
<tr>
<th>Clinical Category</th>
<th>CD4 Cell Count (cells/mm³)</th>
<th>2014 DHHS Guidelines</th>
<th>Strength-Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-defining illness</td>
<td>Any value</td>
<td>Treat</td>
<td>A-I</td>
</tr>
<tr>
<td></td>
<td>&lt;350</td>
<td>Treat</td>
<td>(A-I, A-III)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>350 to 500</td>
<td>Treat</td>
<td>A-II</td>
</tr>
<tr>
<td></td>
<td>&gt;500</td>
<td>Treat</td>
<td>B-III</td>
</tr>
<tr>
<td>Transmission prev:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Any value</td>
<td>Treat</td>
<td>A-I</td>
</tr>
<tr>
<td>Sexual (heterosexual, other)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

http://aidsinfo.nih.gov  27 May 2014

### Goals of Treatment

- Decrease in morbidity/mortality
  - Improvement in quality of life
- Virologic suppression
  - VL<400 at 24wks
  - VL<50 (ND) at 48wks
  - Anything else = virologic failure
- Immunologic recovery (reconstitution)
  - Increase in CD4+ number and/or percentage
  - Anything else = immunologic failure
  - Especially decline in CD4+ to <200
- Surveillance for side effects

http://aidsinfo.nih.gov/

### Current ARV Medications

**NRTI**
- Abacavir (ABC)
- Didanosine (ddI)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine (d4T)
- Tenofovir (TDF)
- Zidovudine (AZT, ZDV)

**NNRTI**
- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)

**Protease Inhibitor (PI)**
- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Indinavir (IDV)
- Lopinavir (LPV)
- Nelfinavir (NFV)
- Ritonavir (RTV)
- Saquinavir (SQV)
- Tipranavir (TPV)

* EVG currently available only in coformulation with cobicistat (COBI)/TDF/FTC

**Integrase Inhibitor (II)**
- Dolutegravir (DTG)
- Elvitegravir* (EVG)
- Raltegravir (RAL)

**Fusion Inhibitor**
- Enfuvirtide (ENF, T-20)

**CCR5 Antagonist**
- Maraviroc (MVC)

* EVG currently available only in coformulation with cobicistat (COBI)/TDF/FTC

www.aidsetc.org  May 2014
2014 DHHS Guidelines: Regimens for Treatment-Naïve Patients

**Recommended**
- EFV
- ATV/r, DRV/r (QD)
- DTG, RAL, EVG/cobi
- DTG + ABC/3TC (1)

*Recommendations for pregnant women differ; see (a)*

For patients with VL<100,000
- EFV + ABC/3TC (1)
- RPV + TDF/FTC (for patients with CD4 > 200)
- ATV/r + ABC/3TC (1)

**Alternative Regimens**
- DRV/r + ABC/3TC (1)
- LPV/r + (ABC/3TC or TDF/FTC) (1)
- RAL + ABC/3TC (1)

**Notes**
- 1 – only in patients who are HLA-B*5701 negative
- 2 – 3TC and FTC may be used interchangeably throughout

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**Advances**

- Comparative effectiveness (1)
  - ATV/r vs DRV/r vs RAL (with TDF/FTC)
  - RAL superior, mostly d/t tolerability
- New agents (2)
  - Long-acting, injectable agents
  - Phase IIb, equivalent to TDF/FTC/EFV

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**Prevention**

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>ART for prevention; HPTN 052, Africa, Asia, Americas</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td>PrEP for discordant couples; Partners PrEP, Uganda, Kenya</td>
<td>73 (49-95)</td>
</tr>
<tr>
<td>PrEP for heterosexual men and women; TDF2, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>54 (38-66)</td>
</tr>
<tr>
<td>PrEP for MSMs; iPrEx, Americas, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment; Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td>Microbicide; CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td>HIV vaccine; RV144, Thailand</td>
<td>31 (1-51)</td>
</tr>
</tbody>
</table>

CDC PrEP Recommendations

Promising Studies

- Adults “cured” of HIV
  - Patient with AML, s/p BMT
    - Remains ND off ART (1)
  - Others s/p BMT → relapse of HIV (2)
- Infants “cured” of HIV
  - One in Mississippi, ND off ART (3)
  - One new infant, ND on ART (4)

2. CROI 2014. Abstract 144LB
3. CROI 2013. Abstract 48LB
4. CROI 2014. Abstract 75LB

Cure Research

Promising Studies

- Failure of PrEP
  - Possibility of reduced seeding of reservoir (1)
- Gene “editing”
  - Removal of co-receptor from CD4 cells by use of a Zn-finger endonuclease (2)

1. CROI 2014, Abstract 397LB