HIV 101: Overview of HIV Epidemiology, Treatment and Outcome

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Learning Objectives:

1. Identify the virus that causes HIV
2. Explain the natural course of HIV infection
3. Understand the treatments associated with HIV
4. Discuss trends in epidemiology associated with HIV

No disclosures
HIV: what is it?

Human immunodeficiency virus
**Human immunodeficiency virus**

- Infests only humans
  - Research Studies Limited
  - Exposure Risks
The body fluids that transmit HIV
- Blood
- Semen
- Vaginal Fluids
- Breast Milk

High Risk Behaviors
- Unprotected sex
- Injection Drug use

Mother to child during pregnancy, delivery, and breast feeding
HIV: what it is

- Human immunodeficiency virus
- Disease is caused by weakened immune system
- Immune system protects from infections
  → Increased risk of infections
HIV: what it is

- Human immunodeficiency virus
- Like all viruses, it needs living cells to make copies of itself and spread
  → Not hardy outside the body

- The type of virus called a retrovirus
  - Viral RNA works with cells DNA to make more Viral RNA, and packages it as new HIV viruses
  → Long latent phase
  → Potential for increased risk cancers
Life Cycle of HIV-1

- Attachment to CD4 and CCR
- Entry of viral genomic RNA into cytoplasm
- Reverse transcription of viral RNA into DNA
- Integration of viral DNA into host chromosome
- Production of viral RNA and protein
- Assembly, release and maturation of virus particles

Figure courtesy of R. Silicano
Natural History of HIV Infection

- **Primary Infection**
  - + Acute HIV syndrome
  - Wide dissemination of virus
  - Seeding of lymphoid organs

- **Clinical latency**

- **Constitutional Symptoms**

- **Opportunistic Diseases**

- **Death**

- **CD4+ T Lymphocyte Count (cells/mmm³)**
  - 1200
  - 1100
  - 1000
  - 900
  - 800
  - 700
  - 600
  - 500
  - 400
  - 300
  - 200
  - 100

- **HIV/RNA Copies per ml Plasma**
  - $10^2$
  - $10^3$
  - $10^4$
  - $10^5$
  - $10^6$
  - $10^7$
What is the difference between HIV and AIDS?

- **Human Immunodeficiency Virus**

- **AIDS: Acquired Immunodeficiency Disease Syndrome**, the disease caused by the virus
  - *Acquired* = from another human
  - *Immunodeficiency* = weakened immune system
  - CD4 Cell count is 200 or less
  - *Syndrome*: meeting the CDC Criteria for an “AIDS-defining illness”
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal
- Cytomegalovirus disease
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcers, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal
- Kaposi sarcoma
- Lymphoid interstitial pneumonia
- Lymphoma, Burkitt or immunoblastic
- Lymphoma, primary, of brain
- Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis, of any site
- Pneumocystis jirovecii pneumonia (PCP)
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV
Historic Milestones in Treatment of HIV

1983  Isolation of the virus
1985  AZT and nucleoside RT inhibitors
1990  Non-nucleoside RT inhibitors
1990’s Combination NRTI therapy
1993  Protease inhibitors
1995  Combination of 2+ drug classes, aka:
      HAART- Highly Active Antiretroviral therapy
      cART- Combination Antiretroviral therapy
      “the cocktail”
Increase or Maintain:
- Viral suppression
- CD4 cell count
- Good Health
- Quality of life

Decrease:
- Toxicity
- Drug resistance
- Overall cost of care
Life Cycle of HIV-1 and Mechanisms of Action of Antiretroviral Drugs

1. Penetration
2. Reverse Transcription
3. Integration
4. Transcription
5. Translation
6. Assembly and Release

Reverse Transcripase Inhibitors: non-nucleoside and nucleoside
Protease Inhibitors
Reverse Transcriptase Inhibitors

<table>
<thead>
<tr>
<th>Year approved*</th>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>Zidovudine</td>
<td>Retrovir</td>
</tr>
<tr>
<td>1991</td>
<td>Didanosine</td>
<td>Videx</td>
</tr>
<tr>
<td>1992</td>
<td>Zalcitabine, Hivid (ddC, dideoxycytidine) by Roche: Mann</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>Stavudine</td>
<td>Zerit</td>
</tr>
<tr>
<td>1995</td>
<td>Lamivudine</td>
<td>Epivir</td>
</tr>
<tr>
<td>1997</td>
<td>Zidovudine/Lamivudine</td>
<td>Combivir</td>
</tr>
<tr>
<td>1998</td>
<td>Abacavir</td>
<td>Ziagen</td>
</tr>
<tr>
<td>2000</td>
<td>Zidovudine/Lamivudine/Abacavir</td>
<td>Trizivir</td>
</tr>
<tr>
<td>2001</td>
<td>Tenofovir</td>
<td>Viread</td>
</tr>
<tr>
<td>2003</td>
<td>Emtricitabine</td>
<td>Emtriva</td>
</tr>
<tr>
<td>2004</td>
<td>Abacavir/Lamivudine</td>
<td>Epzicom</td>
</tr>
<tr>
<td>2004</td>
<td>Emtricitabine/Tenofovir</td>
<td>Truvada</td>
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<table>
<thead>
<tr>
<th>Year</th>
<th>Generic Name</th>
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<tbody>
<tr>
<td>1996</td>
<td>Nevirapine</td>
<td>Viramune</td>
</tr>
<tr>
<td>1997</td>
<td>Delavirdine</td>
<td>Rescriptor</td>
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<tr>
<td>1998</td>
<td>Efavirenz</td>
<td>Sustiva</td>
</tr>
<tr>
<td>2008</td>
<td>Etravirine</td>
<td>Intelence</td>
</tr>
<tr>
<td>2011</td>
<td>Rilpivirine</td>
<td>Eduvant</td>
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### Protease Inhibitors

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug Name</th>
<th>Neighboring Drug</th>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>1995</td>
<td>Saquinavir</td>
<td>Invirase</td>
<td>SQV</td>
</tr>
<tr>
<td>1996</td>
<td>Ritonavir</td>
<td>Norvir</td>
<td>RTV</td>
</tr>
<tr>
<td>1996</td>
<td>Indinavir</td>
<td>Crixivan</td>
<td>IDV</td>
</tr>
<tr>
<td>1997</td>
<td>Nelfinavir</td>
<td>Viracept</td>
<td>NFV</td>
</tr>
<tr>
<td>1997</td>
<td>Saquinavir</td>
<td>Fortovase Manufacture discontinued in 2006; Roche Manufacture discontinued in 2007</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>Amprenavir</td>
<td>Agenerase Manufacture discontinued in 2007</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Lopinavir/ritonavir</td>
<td>Kaletra, Aluvia</td>
<td>LPV</td>
</tr>
<tr>
<td>2003</td>
<td>Atazanavir</td>
<td>Reyataz</td>
<td>ATV</td>
</tr>
<tr>
<td>2003</td>
<td>Fosamprenavir</td>
<td>Lexiva</td>
<td>FPV</td>
</tr>
<tr>
<td>2005</td>
<td>Tipranavir</td>
<td>Aptivus</td>
<td>TPV</td>
</tr>
<tr>
<td>2006</td>
<td>Darunavir</td>
<td>Prezista</td>
<td>DRV</td>
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### Integrase Inhibitors

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug Name</th>
<th>Neighboring Drug</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Raltegravir</td>
<td>Isentress</td>
<td>RGV</td>
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</tbody>
</table>

### Fusion Inhibitors & Chemokine Coreceptor Antagonists

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug Name</th>
<th>Neighboring Drug</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Enfuvirtide</td>
<td>Fuzeon</td>
<td>T-20</td>
</tr>
<tr>
<td>2007</td>
<td>Maraviroc</td>
<td>Selzentry, Celsentri</td>
<td>MVC</td>
</tr>
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### Metabolic and Morphologic

**Complications of HIV and HAART**

<table>
<thead>
<tr>
<th>Morphologic</th>
<th>Metabolic</th>
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<tbody>
<tr>
<td>• Fat accumulation</td>
<td>• Dyslipidemias</td>
</tr>
<tr>
<td>• Fat loss</td>
<td>- hypercholesteremina</td>
</tr>
<tr>
<td>Others</td>
<td>- hypertriglyceridemia</td>
</tr>
<tr>
<td>• Osteoporosis</td>
<td>• Impaired glucose</td>
</tr>
<tr>
<td>• Osteopenia</td>
<td>tolerance/ Diabetes</td>
</tr>
<tr>
<td>• Osteonecrosis</td>
<td>• Lactic acidosis</td>
</tr>
</tbody>
</table>
Viral Suppression and Adherence

Patients with HIV RNA <400 copies/mL, %

Paterson, et al. 2000
Reasons for Non-Adherence: Clinician vs Patient Views

Chesney M. Adherence to antiretroviral therapy. 12th World AIDS Conference, 1998; Geneva. Lecture 281
# Probability of ADI without ART by Baseline CD4 and Viral Load

<table>
<thead>
<tr>
<th>CD4</th>
<th>HIV RNA</th>
<th>3 years</th>
<th>9 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;350</td>
<td>&lt;20,000</td>
<td>8%</td>
<td>66%</td>
</tr>
<tr>
<td>&lt;350</td>
<td>&gt;55,000</td>
<td>73%</td>
<td>96%</td>
</tr>
<tr>
<td>350-500</td>
<td>&lt;20,000</td>
<td>6%</td>
<td>61%</td>
</tr>
<tr>
<td>350-500</td>
<td>&gt;55,000</td>
<td>48%</td>
<td>94%</td>
</tr>
<tr>
<td>&gt;500</td>
<td>&lt;20,000</td>
<td>7%</td>
<td>50%</td>
</tr>
<tr>
<td>&gt;500</td>
<td>&gt;55,000</td>
<td>33%</td>
<td>76%</td>
</tr>
</tbody>
</table>

The Balance of Antiretroviral Therapy

- Reduce Viral Load
- Increase CD4 cells
- Prevent AIDS
- Prolong life
- Reduce transmission

- Not cure HIV infection
- Drug resistance
- Toxicities / side-effects
- Access to medication & care
- Monitoring
- Cost

Amoroso, 2002
<table>
<thead>
<tr>
<th>At HAART Initiation</th>
<th>CD4 Cell Count (mm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;100</td>
</tr>
<tr>
<td>A 20 yr old will live to (years)</td>
<td>52</td>
</tr>
<tr>
<td>A 35 yr old will live to (years)</td>
<td>62</td>
</tr>
<tr>
<td>% Remaining Life Lost (all ages)</td>
<td>46%</td>
</tr>
</tbody>
</table>

By 2015, half the U.S. population living with human immunodeficiency virus (HIV) infection will be older than 50 years of age. As antiretroviral therapy (ART) coverage continues to expand worldwide, this aging of the HIV epidemic will be mirrored in developing countries. In sub-Saharan Africa, ART has already reduced mortality rates, with 320,000 (or 20%) fewer people dying of HIV-related causes in 2009 than in 2004. Currently, HIV-infected Ugandans in their 40s who are receiving ART can expect to live well into their 60s. The increased life expectancy of HIV-infected persons will lead to increases in HIV prevalence among older adults. Approximately 1 in 8 HIV-infected adults and 1 in 10 patients receiving ART in sub-Saharan Africa are older than 50 years of age, and these ratios are likely to increase manifold in the coming decades.
Proportion Patients With HIV 50+ Years of Age in United States 2001-2017

<table>
<thead>
<tr>
<th>Year</th>
<th>VA Past This Point in 2003</th>
<th>Projected*</th>
</tr>
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<tbody>
<tr>
<td>2001</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>2002</td>
<td>19%</td>
<td>33%</td>
</tr>
<tr>
<td>2003</td>
<td>21%</td>
<td>35%</td>
</tr>
<tr>
<td>2004</td>
<td>22%</td>
<td>37%</td>
</tr>
<tr>
<td>2005</td>
<td>25%</td>
<td>39%</td>
</tr>
<tr>
<td>2006</td>
<td>27%</td>
<td>41%</td>
</tr>
<tr>
<td>2007</td>
<td>27%</td>
<td>44%</td>
</tr>
<tr>
<td>2008</td>
<td>29%</td>
<td>45%</td>
</tr>
<tr>
<td>2009</td>
<td>33%</td>
<td>47%</td>
</tr>
<tr>
<td>2010</td>
<td>35%</td>
<td>50%</td>
</tr>
<tr>
<td>2011</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5. HIV Infected Veterans in VHA Care 2008 - Age by Decade of Life
Figure 4a/b. Comparison of Race/Ethnicity for New AIDS Cases Reported to the CDC in 2007 and All Veterans with HIV/AIDS in Care in 2008.

4a. Race/Ethnicity
CDC New AIDS Cases 2007
- Black: 51%
- White: 29%
- Hispanic: 18%
- Other: 2%

4b. Reported Race/Ethnicity for HIV Infected Veterans in Care - 2008
- Black: 50%
- White: 42%
- Hispanic: 7%
- Other: 1%
>50% of Deaths Attributed to Non-AIDS Events

Incident Non AIDS Events by HIV Group

Events Per 1000 Person Years

- Coronary Vascular Disease
- End Stage Liver Disease
- Bacterial Pneumonia
- COPD
- Non AIDS Cancers
- End Stage Renal Failure
- Stroke
- Fragility Fracture

HIV+  
HIV-
1995: 46 year old man diagnosed HIV
6 more years injection drug use
2001: Depression and SA treatment
2003: 54 yo after 2 yrs HAART
2004: 55 yo with DM, obesity

CD4 Cell Count (mm3)

HIV +

HAART

Lipodystrophy Syndrome

1995 2001 2003 2004 2005
2005: healthy and fit 56 year old

CD4 Cell Count (mm3)

HIV +
HAART
Exercis & diet
Healthy Aging with HIV
Take Home Points

1. Identify the virus that causes HIV
2. Explain the natural course of HIV infection
3. Understand the treatments associated with HIV
4. Discuss trends in epidemiology associated with HIV
1. Identify the virus that causes HIV
   - Requires body fluid for transmission
   - Infection and destruction of CD4 cells
   - HIV vs. AIDS: infection vs disease
2. Explain the natural course of HIV infection
   → Long latency period
   → CD4 Cells below - loss of viral control
   → AIDS Defining Illness
3. Understand the treatments associated with HIV
   → Multiple drug classes in effective combination
   → Side effects and metabolic toxicity
   → Adherence is key to prevent drug resistance
   → Individualized balancing Act
4. Discuss trends in epidemiology associated with HIV
   → Increased Life Expectancy
   → Age as the new wrinkle in the epidemic
   → Non-HIV related morbidity and mortality
www.HIV.va.gov
Additional Web resources

- Patient education material
  - aidsinfonet.org
  - aidsmeds.com

- aidsinfo.nih.gov
  See education/materials/glossary

- aids-ed.org
- hivinsite.org
- hivandhepatitis.com