Global summary of the AIDS epidemic

Number of people living with HIV in 2008

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Adults</th>
<th>&lt;15yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33.4 million</td>
<td>31.3 million</td>
<td>2.1 million</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td>31.3 million</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td>15.7 million</td>
</tr>
</tbody>
</table>

People newly infected with HIV in 2008

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Adults</th>
<th>Children under 15 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.7 million</td>
<td>2.3 million</td>
<td>430 000</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td>2.3 million</td>
<td></td>
</tr>
<tr>
<td>Children under 15 yrs</td>
<td></td>
<td></td>
<td>430 000</td>
</tr>
</tbody>
</table>

AIDS-related deaths in 2008

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Adults</th>
<th>Children under 15 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.0 million</td>
<td>1.7 million</td>
<td>280 000</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td>1.7 million</td>
<td></td>
</tr>
<tr>
<td>Children under 15 yrs</td>
<td></td>
<td></td>
<td>280 000</td>
</tr>
</tbody>
</table>

About 7400 new HIV infections a day in 2008

- More than 97% are in low & middle income countries.
  - Most unaware of infection
- About 6,200 are in persons aged 15 to 49 years, of whom:
  - 50% are in women
  - about 40% are 15–24 years old
  - in sub-Saharan Africa women 61%
- Almost 1200 are in children under 15 yrs of age

Adults and children estimated to be living with HIV/AIDS Dec 2008

UNAIDS 8/2008
Overview of the AIDS Epidemic in the US Surveillance Through 2007

- Total AIDS cases in US approaching 1 million, with deaths exceeding one-half million
- More than 400,000 persons are living with AIDS
- 34 states mandate reporting of HIV+ persons, in the other 16 only AIDS is reportable

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults/Adolescents</td>
<td>1,021,042</td>
<td>562,637</td>
</tr>
<tr>
<td>Children &lt;13 y</td>
<td>9590</td>
<td>5625</td>
</tr>
<tr>
<td>Total</td>
<td>1,030,832</td>
<td>550,394</td>
</tr>
</tbody>
</table>

Percentage of HIV/AIDS Cases among Adults and Adolescents, by Race/Ethnicity, 2004-2007-34 States

African-American women have a 23 times higher incidence of HIV infection than white women in the US
HIV Treatment

HIV-1 Lifecycle

Antiretroviral Medications - 2010

<table>
<thead>
<tr>
<th>Nucleoside Rev. Transcriptase Inhibitor</th>
<th>Protease Inhibitor</th>
<th>Fusion Inhibitor</th>
<th>Integrase Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Atazanavir</td>
<td>Enfuvirtide</td>
<td>Raltegravir</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Darunavir</td>
<td>CCR5 Antagonist</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>Fosamprenavir</td>
<td>Maraviroc</td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Indinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine</td>
<td>Lopinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Nelfinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Saquinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NonNRTI</td>
<td>Tipranavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Atripla</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etravirine</td>
<td>Trizivir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Truvada</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epzicom</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Effect of Treatment on HIV Viral Load

- **Baseline**
- **ZDV max fall 0.7 log**
- **ZDV+3TC max fall 1.8 log**
- **ZDV+3TC+ PI or nNRTI or NRTI max fall >3 log**

*Lower limit of measurement* "undetectable"
**Estimated Numbers of AIDS Cases and Deaths among Adults and Adolescents with AIDS 1985-2007**

*United States and Dependent Areas*

![Graph showing estimated numbers of AIDS cases and deaths](image1)

**“Typical” Course of Untreated HIV**

![Graph showing typical course of untreated HIV](image2)

**Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents**

http://www.aidsinfo.nih.gov

*December 1, 2009*

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

**Goals of Treatment**

- Improve quality of life
- Reduce HIV-related morbidity and mortality
- Restore and/or preserve immunologic function
- Maximally and durably suppress HIV viral load
- Prevent HIV transmission
Characterization of HIV disease status

Baseline Diagnostic Studies

- HIV serology – if needed confirm diagnosis
- CD4 cell count, CD4% - extent of immune injury
  - Key factor in decision to start ART or OI prophylaxis
- Plasma HIV RNA – severity of infection
  - Critical in determining response to ART, goal < 50
- Antiviral drug resistance test (genotype)

When to Start Anti-Retroviral Therapy (ART)

- Exact CD4 count at which to initiate therapy not known, but evidence points to starting at higher count
- ART may improve/preserve immune function in most patients with virologic suppression, regardless of baseline CD4 count
  - Earlier ART may result in better immunologic responses, outcomes
  - Reduction in AIDS & non-AIDS-associated morbidity and mortality
  - Reduction in HIV-associated inflammation and associated complications
  - Reduction in HIV transmission
- Current recommendation: ART for all with CD4 <500 cells/µL

SMART trial of HIV treatment strategies (drug sparing vs continuous therapy with viral suppression)

- Development of treatment-related short term side effects, and long term toxicities
- Another $15,000-$20,000/yr of cost
- Premature use of therapy before the development of more effective, less toxic, and/or better studied combinations of antiretroviral drugs
- Development of drug resistance from incomplete viral suppression, resulting in loss of future treatment options
- Transmission of drug-resistant virus in patients who do not maintain full virologic suppression

Limitations of Early Therapy (CD4 count >500 cells/µL)
What HIV medications to start?
Initial Treatment: Preferred Regimens

| NNRTI based | EFV/TDF/FTC (one pill - Atripla) |
| Protease Inhibitor based | ATV/rtv + TDF/FTC (3 pills once daily)  
                         | DRV/rtv (OD) + TDF/FTC |
| Integrase based | RAL + TDF/FTC |
| Pregnant Women | LPV/rtv (BID) + ZDV/3TC |

EFV/TDF/FTC = efavirenz + tenofovir + emtricitabine (Atripla - 1 pill daily)  
TDF/FTC = tenofovir + emtricitabine (Truvada)

Considerations in Choosing ART
(Leave to HIV consultant)

- Results of drug resistance testing
- Co-morbidities (e.g., liver, psychiatric, CVD, TB)
- Pregnancy potential (efavirenz)
- Potential adverse effects
- Potential drug interactions (especially protease inhibitors)
- Adherence potential
- Specific ART issues
  - Gender and CD4 count, if considering nevirapine
  - HLA B*5701 testing, if considering abacavir
  - Co-receptor tropism assay

Adverse Effects: NRTIs

- All NRTIs:
  - Lactic acidosis and hepatic steatosis
  - Higher incidence with d4T  
    (d4T > ddi = ZDV > TDF = ABC = 3TC = FTC)
  - Lipodystrophy
- ZDV (AZT; Retrovir) – Bone marrow suppression
- TDF (Vired) Renal impairment
- d4T (Zerit) - Peripheral neuropathy
- Abacavir (Ziagen) – severe hypersensitivity reaction
- ddi (Videx) - GI intolerance, Pancreatitis

HIV-Associated Lipodystrophy

**Adverse Effects: Protease Inhibitors**

- All PIs:
  - Hyperlipidemia
  - Insulin resistance and diabetes
  - Lipodystrophy
  - Elevated LFTs
  - Significant drug-drug interactions
- Always check for drug interactions in patients receiving HIV medications

**Metabolic Changes Associated With ART and HIV Infection**

Unclear etiology

- Lipid abnormalities
- Dysregulation of glucose metabolism
- Fat accumulation
- Fat atrophy

**HIV Transmission**

- Virus found in blood, CSF, breast milk, semen, vaginal fluids
- Plasma viral level correlates infectivity via all modes
- Minimal virus in sweat, saliva, feces, urine & not considered infectious
  1. Sexual contact: M to F more likely than F to M, ? 1 in 1000
  - STDs especially genital ulcers predispose to transmission
  2. Inoculation of contaminated blood or blood products (needlestick exposure) e.g. IVDU, occupational exposure
    - Occupational exposure of HCW (rare; < 60 cases reported)
      - Risk from needlestick overall 1 in 300
    - Only one documented instance of HCW to patient spread,
  3. Perinatal spread: 30% without intervention
    - Intrauterine, peripartum, postpartum (breast milk)
HIV Prevention Efforts: New Hope

- HIV testing – results do alter behavior
- Male Circumcision – clearly decreases acquisition
- Microbicides – like spermacides, recent +/- study
- HIV vaccines – recent study showing effectiveness
  ✓ Some data suggest broader use would limit epidemic
- Pre-exposure prophylaxis with ART for HIV negative
- Maternal to Child Transmission

Issues in HIV testing – "Opt-out" testing

- CDC strategy: normalize HIV testing by making it a routine, voluntary part of care for everyone aged 13–64
  ✓ Overall consent for medical care should include HIV test
  ✓ Individual can decline test (opt-out)
- ACP
  ✓ Recommends that clinicians adopt routine screening for HIV and encourage patients to be tested
  ✓ Recommends that clinicians determine the need for repeat screening on an individual basis.
- Goals:
  ✓ Identify ~252–312K HIV+ persons – including pregnant women – who are unaware of serostatus
  ✓ Refer for care, preserve immune function, reduce transmission and stem US epidemic

South African Circumcision Trial
New HIV Infections

<table>
<thead>
<tr>
<th>Arm</th>
<th>Month 0-3</th>
<th>Month 4-12</th>
<th>Month 12-21</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circ (n=1538)</td>
<td>2</td>
<td>7</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Control (n=1590)</td>
<td>9</td>
<td>15</td>
<td>25</td>
<td>49</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>22</td>
<td>36</td>
<td>69</td>
</tr>
</tbody>
</table>

Incidence
- Circumcision arm: 0.85 / 100 person years
- Control arm: 2.10 / 100 person years
- Risk ratio = 0.40
- Protection = 60% trial stopped early!!
**Prevention - Vaccine**

- The Sanofi – Pasteur / Vaxgen Trial with CDC and DOD
- This trial primed individuals with a sub-unit vaccine of recombinant gp120 (VaxGen) and then boosted the immune response with a recombinant canarypox vector expressing same gp120 (Clades B and E)

**First Partially Effective HIV Vaccine Trial**

**Cumulative Rates of Infection**

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Years</th>
<th>Placbo</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>81/94</td>
<td>77/75</td>
<td>74/74</td>
</tr>
<tr>
<td>Vaccine</td>
<td>81/97</td>
<td>77/97</td>
<td>74/97</td>
</tr>
</tbody>
</table>

Cumulative No. of Infections:
- Placebo: 30, 50, 65, 74
- Vaccine: 12, 32, 45, 51

**Antiviral Treatment as Prevention**

**ART-Induced Reduction in Plasma HIV RNA Associated with Decreased Levels in Semen**

- Controls (drug naive) n=55
- Potent ART n=114

**Impact of Antiretroviral (ART) on HIV Transmission Among HIV Serodiscordant Couples**

- ART offered in Kigali, Rwanda since 2003
- 1034 serodiscordant couples followed
- 248 “index cases” receiving ART (CD4<200)
- In spite of counseling, 42 seroconversions
- Only 2/42 seroconversions with partner on ART
- Persons on antiretroviral therapy had 80% less HIV infections than those on no therapy (OR=0.19 (95% CI 0.05-0.80)
- There are models suggesting this could work to decrease HIV spread within treated community
<table>
<thead>
<tr>
<th>New Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Find better ways to achieve behavior modification to reduce transmission</td>
</tr>
<tr>
<td>2. Provide better access to care and make therapy available to the peoples of the developing world.</td>
</tr>
<tr>
<td>3. Find methods to get better drug adherence</td>
</tr>
<tr>
<td>4. Develop new antiretroviral agents that are better tolerated, more convenient, less toxic and active against resistant virus.</td>
</tr>
<tr>
<td>5. Develop vaccine, and vaccinate world</td>
</tr>
</tbody>
</table>

Pennsylvania/MidAtlantic AIDS Education and Training Center
www.pamaaetc.org

National Resource Center www.aidsetc.org