Human Immunodeficiency Virus Update

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Clinical Physician, Infectious Diseases and HIV, Summa Health System
Who of the following is recommended to have HIV Antibody testing?

A. 22 year old IV drug abuser admitted with an overdose
B. 19 year old college freshman with upper respiratory infection
C. 44 year old business professional for routine physical examination
D. All of the above
E. None of the above
Objectives

- Discuss the current epidemiology of HIV
- Identify patients with HIV
- Identify patients who need treatment
- Discuss Treatment options
HIV Timeline

- 1981: Acquired Immune Deficiency Syndrome
- 1983: Virus identified (HTLV III; LAV) – HIV
- 1983: Blood test
- 1986: AZT
- 1986-1996: PCP prophy, ddi, ddc, d4T
- 1996: HAART
- 2008: “Chronic Disease” in developed world
- NOW: CDC rec routine testing adults/adolescents
Present Concerns

- Adherence, Pill burden
- Drug Interactions
- Adverse effects
  - Metabolic, long term complications of HIV
- Resistance
HIV: Epidemiology

- AIDS kills more people than malaria
- Leading cause of death +/- Tb from a specific pathogen
- Central Africa:
  - Causes 40-50% of all deaths, 89% of deaths ages 25-34
  - Botswana 25% infection rate
  - Zimbabwe 30-50% pregnant women infected
- Increases in Asia, Former Soviet Republics
HIV: Epidemiology-USA

- Roughly 1/250 Americans infected
- New cases decreasing, but total number increases
  - Declining mortality rate
- Fastest rates of new infection
  - Women
  - Teenagers
  - People of color
  - Heterosexuals
HIV Epidemiology

- HIV/AIDS in the US 2008
  - Living with HIV/AIDS: 1.1 Million (0.45%) 
  - Prevalance
    - African-Americans: 1.7%
    - Hispanics 0.6%
    - White: 0.23%
    - 11% Increase since 2003

- New Infections per Year: 60000

- MMWR 57: 1073 (10/2/08)
- Hall et al, JAMA 2008; 300:520.
## Regional HIV and AIDS statistics and features, 2008

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.

<table>
<thead>
<tr>
<th>Region</th>
<th>Adults &amp; children living with HIV</th>
<th>Adults &amp; children newly infected with HIV</th>
<th>Adult prevalence (15–49) [%]</th>
<th>Adult &amp; child deaths due to AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>22.4 million [20.8 – 24.1 million]</td>
<td>1.9 million [1.6 – 2.2 million]</td>
<td>5.2 [4.9 – 5.4]</td>
<td>1.4 million [1.1 – 1.7 million]</td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td>310 000 [250 000 – 380 000]</td>
<td>35 000 [24 000 – 46 000]</td>
<td>0.2 [&lt;0.2 – 0.3]</td>
<td>20 000 [15 000 – 25 000]</td>
</tr>
<tr>
<td>South and South-East Asia</td>
<td>3.8 million [3.4 – 4.3 million]</td>
<td>280 000 [240 000 – 320 000]</td>
<td>0.3 [0.2 – 0.3]</td>
<td>270 000 [220 000 – 310 000]</td>
</tr>
<tr>
<td>East Asia</td>
<td>850 000 [700 000 – 1.0 million]</td>
<td>75 000 [58 000 – 88 000]</td>
<td>&lt;0.1 [&lt;0.1]</td>
<td>59 000 [46 000 – 71 000]</td>
</tr>
<tr>
<td>Latin America</td>
<td>2.0 million [1.8 – 2.2 million]</td>
<td>170 000 [150 000 – 200 000]</td>
<td>0.6 [0.5 – 0.6]</td>
<td>77 000 [66 000 – 89 000]</td>
</tr>
<tr>
<td>Caribbean</td>
<td>240 000 [220 000 – 260 000]</td>
<td>20 000 [16 000 – 24 000]</td>
<td>1.0 [0.9 – 1.1]</td>
<td>12 000 [9300 – 14 000]</td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Europe</td>
<td>1.5 million [1.4 – 1.7 million]</td>
<td>110 000 [100 000 – 130 000]</td>
<td>0.7 [0.6 – 0.8]</td>
<td>87 000 [72 000 – 110 000]</td>
</tr>
<tr>
<td>Western &amp; Central Europe</td>
<td>850 000 [710 000 – 970 000]</td>
<td>30 000 [23 000 – 35 000]</td>
<td>0.3 [0.2 – 0.3]</td>
<td>13 000 [10 000 – 15 000]</td>
</tr>
<tr>
<td>North America</td>
<td>1.4 million [1.2 – 1.6 million]</td>
<td>55 000 [36 000 – 61 000]</td>
<td>0.6 [0.5 – 0.7]</td>
<td>23 000 [9100 – 55 000]</td>
</tr>
<tr>
<td>Oceania</td>
<td>59 000 [51 000 – 68 000]</td>
<td>3900 [2900 – 5100]</td>
<td>0.3 [&lt;0.3 – 0.4]</td>
<td>2000 [1100 – 3100]</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>33.4 million [31.1 – 35.8 million]</strong></td>
<td><strong>2.7 million [2.4 – 3.0 million]</strong></td>
<td><strong>0.8 [&lt;0.8 – 0.8]</strong></td>
<td><strong>2.0 million [1.7 – 2.4 million]</strong></td>
</tr>
</tbody>
</table>
Global estimates 1990–2008

Number of people living with HIV

Number of people newly infected with HIV

Number of adult and child deaths due to AIDS

Source: UNAIDS/WHO

2009 AIDS epidemic update

Figure I
### Regional HIV and AIDS statistics
#### 2008 and 2001

(Next of 2 parts)

<table>
<thead>
<tr>
<th>Region</th>
<th>Adult prevalence (%)</th>
<th>Adult &amp; child deaths due to AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.2%</td>
<td>5.8%</td>
</tr>
<tr>
<td></td>
<td>[4.9% – 5.4%]</td>
<td>[5.5% – 6.0%]</td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td></td>
<td>[&lt;0.2% – 0.3%]</td>
<td>[0.1% – 0.2%]</td>
</tr>
<tr>
<td>South and South–East Asia</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td></td>
<td>[0.2% – 0.3%]</td>
<td>[&lt;0.3% – 0.4%]</td>
</tr>
<tr>
<td>East Asia</td>
<td>0.1%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td></td>
<td>[&lt;0.1%]</td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>0.6%</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>[0.5% – 0.6%]</td>
<td>[&lt;0.5% – 0.6%]</td>
</tr>
<tr>
<td>Caribbean</td>
<td>1.0%</td>
<td>1.1%</td>
</tr>
<tr>
<td></td>
<td>[0.9% – 1.1%]</td>
<td>[1.0% – 1.2%]</td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>0.7%</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>[0.6% – 0.8%]</td>
<td>[0.4% – 0.5%]</td>
</tr>
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<td>0.2%</td>
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<tr>
<td>North America</td>
<td>0.6%</td>
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</tr>
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<td></td>
<td>[0.5% – 0.7%]</td>
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<td>Oceania</td>
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<td>0.2%</td>
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<tr>
<td></td>
<td>[&lt;0.3% – 0.4%]</td>
<td>[&lt;0.2% – 0.3%]</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>0.8%</td>
<td>0.8%</td>
</tr>
<tr>
<td></td>
<td>[&lt;0.8% – 0.8%]</td>
<td>[&lt;0.8% – 0.8%]</td>
</tr>
</tbody>
</table>
Adults and children estimated to be living with HIV, 2008

Total: 33.4 million (31.1 – 35.8 million)
Estimated number of adults and children newly infected with HIV, 2008

- **Western & Central Europe**: 30,000 (23,000 – 35,000)
- **Eastern Europe & Central Asia**: 110,000 (100,000 – 130,000)
- **Middle East & North Africa**: 35,000 (24,000 – 46,000)
- **Sub-Saharan Africa**: 1.9 million (1.6 – 2.2 million)
- **Eastern Europe & Central Asia**: 110,000 (100,000 – 130,000)
- **North America**: 55,000 (36,000 – 61,000)
- **Caribbean**: 20,000 (16,000 – 24,000)
- **South & South-East Asia**: 280,000 (240,000 – 320,000)
- **Oceania**: 3,900 (2,900 – 5,100)
- **Latin America**: 170,000 (150,000 – 200,000)
- **East Asia**: 75,000 (58,000 – 88,000)
- **South & South-East Asia**: 280,000 (240,000 – 320,000)
- **Caribbean**: 20,000 (16,000 – 24,000)
- **Total**: 2.7 million (2.4 – 3.0 million)
Estimated adult and child deaths due to AIDS, 2008

- Western & Central Europe: 13,000 (10,000 – 15,000)
- Middle East & North Africa: 20,000 (15,000 – 25,000)
- Sub-Saharan Africa: 1.4 million (1.1 – 1.7 million)
- Eastern Europe & Central Asia: 87,000 (72,000 – 110,000)
- South & South-East Asia: 270,000 (220,000 – 310,000)
- East Asia: 59,000 (46,000 – 71,000)
- Latin America: 77,000 (66,000 – 89,000)
- Caribbean: 12,000 (9,300 – 14,000)
- North America: 25,000 (20,000 – 31,000)
- Oceania: 2,000 (1,100 – 3,100)

Total: 2.0 million (1.7 – 2.4 million)
Over 7400 new HIV infections a day in 2008

• More than 97% are in low- and middle-income countries

• About 1200 are in children under 15 years of age

• About 6200 are in adults aged 15 years and older, of whom:
  — almost 48% are among women
  — about 40% are among young people (15–24)
Estimated Numbers of HIV/AIDS Cases among Adults and Adolescents, by Transmission Category
1994–2007—25 States

Male-to-male sexual contact
High-risk heterosexual contact
Injection drug use
Male-to-male sexual contact and injection drug use

No. of cases

Year of diagnosis

Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status at diagnosis. Data from 25 states with confidential name-based HIV infection reporting since at least 1994. Data have been adjusted for reporting delays and missing risk-factor information.
*Data on male-to-male sexual contact exclude cases among men who reported sexual contact with other men and injection drug use.
†Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
‡Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
Percentages of HIV/AIDS Cases among Adults and Adolescents, by Sex and Transmission Category 2007—34 States

Males
- Male-to-male sexual contact: 71%
- Injection drug use (IDU): 14%
- Male-to-male sexual contact and IDU: 10%
- <1%

Females
- High-risk heterosexual contact: 16%
- Other/not identified†: 83%

Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status at diagnosis.
Data from 34 states with confidential name-based HIV infection reporting since at least 2003.
Data have been adjusted for reporting delays and missing risk-factor information.
*Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
†Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
HIV: Transmission

- **Sexual**
  - Multiple partners, anal intercourse, infected partner, genital lesions, oral contraception?
  - Semen: High level of HIV even in early asymptomatic infection
  - Reduced risks: Condoms, circumcision

- **Blood**
  - IVDU
  - Blood transfusions (extremely rare now)

- **Health Care Workers**
  - Needle Sticks (hollow bore)
  - Universal precautions

- **Perinatal** (15-20% risk without treatment, <5% with treatment)
Estimate of the annual number of infant infections averted through the provision of antiretroviral prophylaxis to HIV-positive pregnant women, globally, 1996–2008
### Risk of Heterosexual Transmission of HIV-Single encounter

<table>
<thead>
<tr>
<th>Partner</th>
<th>Condom</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ HIV</td>
<td>-</td>
<td>1:500</td>
</tr>
<tr>
<td>High Risk ? HIV</td>
<td>-</td>
<td>1:1000</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>1:10000</td>
</tr>
<tr>
<td>Low Risk ? HIV</td>
<td>-</td>
<td>1:5M</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>1:50M</td>
</tr>
<tr>
<td>Low Risk (-) HIV</td>
<td>+</td>
<td>1:5B</td>
</tr>
</tbody>
</table>
Replicative Cycle/Pathogenesis

- HIV-1, HIV-2 (Mostly W. Africa)
  - Infects and kills helper CD4 T lymphocytes
    - Loss of cell mediated immunity

- Retrovirus
  - Binding of gp120 envelope protein to CD4 protein on cell surface
  - Interaction with chemokine receptors
  - Gp41 mediates fusion of viral envelope with cell membrane
    - Virion core containing nucleocapsid, RNA genome, and reverse transcriptase enters the cytoplasm.
Pathogenesis

- Chemokine receptors CXCR4 and CCR5 required for entry
  - T cell tropic binds to CXCR4, Macrophage tropic strains bind to CCR5
    - Mutations in CCR5 confer protection from HIV
    - Homozygotes resistant, hetero, slow progressors

- Reverse transcriptase transcribes genome RNA to DS-DNA-goes to nucleus and integrates to host cell DNA (Integrase)

- Host RNA polymerase makes viral mRNA from proviral DNA

- Gag/Pol reverse transcriptase, integrase, protease

- Virion buds from cell membrane

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Natural History

- **Primary Infection**
- **Acute HIV syndrome**
  - Wide dissemination of virus
  - Seeding of lymphoid organs
- **Clinical Latency**
- **Opportunistic Diseases**
- **Constitutional Symptoms**
- **Death**

**CD4^+ T Lymphocyte Count (cells/mm^3)**

**HIV RNA Copies per ml Plasma**
Clinical Manifestations

A. Acute retroviral syndrome (I)
   - Fever, rash, adenopathy, pharyngitis, mononucleosis-like syndrome, resolves

B. Latent (II)
   - Clinically latent, but virus still replicating

C. Symptomatic (III)
   - Thrush, diarrhea, lymphadenopathy, weight loss, fever

D. AIDS (IV)
   - Opportunistic infections
     - PCP, Cryptococcosis, Toxoplasmosis, MAI
   - AIDS associated malignancies, KS, CNS lymphoma
   - CD4 <200 or CD4% <14.
Acute retroviral syndrome

- 50-60% of infected patients
- 3-7 weeks following infection
- Fever, pharyngitis, adenopathy
- HA; arthralgia/myalgia, lethargy
  - CNS – aseptic meningitis, peripheral neuropathy
  - Derm – Rash, mucocutaneous ulcers
How to identify an HIV patient?

- HIV patients don’t need to have opportunistic infections to present to the hospital

- Risk factors
  - Anyone with high risk sexual behaviors, multiple partners
  - EtOH, IVDU
  - Pregnant Patients
  - STD history

- Non-biased questions
  - How many sexual partners?
  - STDs?
  - Relations with men, women, both?
  - IVDU?
Who do you test?

- Anyone with high risk sexual behavior
  - MSM, sex for money, drugs, known contact
- Multiple sex partners
- IVDU
- STD
- Pregnant patients
- Medical conditions that raise suspicion
  - AIDS-defining illnesses, PCP, Tb, recurrent giardiasis, esophageal candidiasis
- Anyone exposed to HIV, body fluid exposure
- Anyone who asks
- Everyone!
CDC Recommendations

- Routine HIV screening of adults, adolescents
- Reduce barriers to HIV testing, consents

Rationale

- People infected
  - Not able to take advantage of therapies that can maintain health and save lives
  - Do not have knowledge to protect partners
- Several studies suggest routine testing can increase quality of life and save money

CDC Revised recommendations for HIV Testing Sept 2006
HIV Consent?

- Ohio law has changed October 2009
- It is still complex
- Bottom line…for most instances you don’t need separate consent to do an HIV test.
Informed consent for HIV testing

- 3701.242 Informed consent to HIV test required.
  - (A) An HIV test may be performed by or on the order of a health care provider who, in the exercise of the provider’s professional judgment, determines the test to be necessary for providing diagnosis and treatment to the individual to be tested, if the individual or the individual’s parent or guardian has given consent to the provider for medical or other health care treatment. The health care provider shall inform the individual of the individual’s right under division (D) of this section to an anonymous test.
  - (B) A minor may consent to be given an HIV test. The consent is not subject to disaffirmance because of minority. The parents or guardian of a minor giving consent under this division are not liable for payment and shall not be charged for an HIV test given to the minor without the consent of a parent or the guardian.
  - (C) The health care provider ordering an HIV test shall provide post-test counseling for an individual who receives an HIV-positive test result. The public health council may adopt rules, pursuant to recommendations from the director of health and in accordance with Chapter 119. of the Revised Code, specifying the information to be provided in post-test counseling.
  - (D) An individual shall have the right to an anonymous test. A health care facility or health care provider that does not provide anonymous testing shall refer an individual requesting an anonymous test to a site where it is available.
  - (E) Divisions (B) to (D) of this section do not apply to the performance of an HIV test in any of the following circumstances:
    - (1) When the test is performed in a medical emergency by a nurse or physician and the test results are medically necessary to avoid or minimize an immediate danger to the health or safety of the individual to be tested or another individual, except that post-test counseling shall be given to the individual if the individual receives an HIV-positive test result;
    - (2) When the test is performed for the purpose of research if the researcher does not know and cannot determine the identity of the individual tested;
    - (3) When the test is performed by a person who procures, processes, distributes, or uses a human body part from a deceased person donated for a purpose specified in Chapter 2108. of the Revised Code, if the test is medically necessary to ensure that the body part is acceptable for its intended purpose;
    - (4) When the test is performed on a person incarcerated in a correctional institution under the control of the department of rehabilitation and correction if the head of the institution has determined, based on good cause, that a test is necessary;
    - (5) When the test is performed in accordance with section 2907.27 of the Revised Code;
    - (6) When the test is performed on an individual after the infection control committee of a health care facility, or other body of a health care facility performing a similar function determines that a health care provider, emergency medical services worker, or peace officer, while rendering health or emergency care to an individual, has sustained a significant exposure to the body fluids of that individual, and the individual has refused to give consent for testing.

Amended by 128th General Assembly File No. 9, HB 1, § 101.01, eff. 10/16/2009.
Effective Date: 10-06-1994
Testing

- HIV ELISA (HIV Ab)
  - Confirm with Western Blot
- Rapid HIV Test
  - Confirm with Western Blot
- HIV Viral Load
  - Best for suspicion of Acute retroviral syndrome when patients may be in window period.
## OPPORTUNISTIC DISEASES

Conditions correlated with CD4

<table>
<thead>
<tr>
<th>CD4 Count</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>200-500</td>
<td>Thrush-Candida, Kaposi’s sarcoma*, reactivation TB lymphoma*</td>
</tr>
<tr>
<td></td>
<td>Pneumocystis*</td>
</tr>
<tr>
<td>100-200</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacterial sinusitis, Herpes zoster, Bacterial pneumonia</td>
</tr>
<tr>
<td>50-100</td>
<td>Systemic fungi†*</td>
</tr>
<tr>
<td></td>
<td>Primary TB</td>
</tr>
<tr>
<td></td>
<td>Cryptosporidiosis*</td>
</tr>
<tr>
<td>0-50</td>
<td>Cytomegalovirus*</td>
</tr>
<tr>
<td></td>
<td>disse MAC*</td>
</tr>
<tr>
<td></td>
<td>nonHodg</td>
</tr>
</tbody>
</table>

*Included in definition as OI
† Cryptococcal meninigitis, disseminated Histoplasmosis
When to treat - Opportunistic Infections

- Treat if there is an OI
- Use prophylaxis to prevent them—When to “Prophylax”

**CD4 < 200**
- *Pneumocystis jiroveci*
  - TMP-SMX DS daily or qM/W/F, Dapsone, atovaquone, Inh pentamidine

**CD4 < 100**
- *Toxoplasma gondii*
  - TMP-SMX DS or atovaquone

**CD4 < 50**
- *Mycobacterium avium intracellulare* complex
  - Azithromycin 1200mg qwk
When to Treat - HIV

- When to start?
- What to use?
- When to switch?
- What to use next?
- What to expect?
Goals of Therapy

- Suppression of the virus
- Restoration of immune function
- Improvement in quality of life
- Reduction in HIV-Related Morbidity and Mortality
- Decreased risk of non-HIV complications
- Decreased risk of transmission
When to treat-HIV

- **Patient must be willing to start**
  - Adequate coverage of medications ensured
  - Regular follow-up can be ensured

- **Status of disease**
- **Risks of therapy**
  - Non-adherence
  - Risks of resistance
## Recommendations for Initiating ART

<table>
<thead>
<tr>
<th>Clinical Category or CD4 Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of AIDS-defining illness</td>
<td>Initiate ART</td>
</tr>
<tr>
<td>CD4 count &lt;350 cells/µL</td>
<td></td>
</tr>
<tr>
<td>CD4 count 350-500 cells/µL</td>
<td></td>
</tr>
<tr>
<td>Pregnant women</td>
<td></td>
</tr>
<tr>
<td>HIV-associated nephropathy (HIVAN)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B (HBV) coinfection, when HBV treatment is indicated*</td>
<td></td>
</tr>
</tbody>
</table>

* Treatment with fully suppressive drugs active against both HIV and HBV is recommended.
### Recommendations for Initiating ART

<table>
<thead>
<tr>
<th>Clinical Category or CD4 Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 count &gt;500 cells/µL, asymptomatic, without conditions listed above</td>
<td>50% of the panel favor starting ART; 50% view ART as optional</td>
</tr>
</tbody>
</table>
Consider More Rapid Initiation of ART

- Pregnancy
- AIDS-defining condition
- Acute opportunistic infection
- Lower CD4 count (eg, <200 cells/µL)
- Rapid decline in CD4
- Higher viral load
- HIVAN
- HBV coinfection when HBV treatment is indicated
European Aids Clinical Society
www.europeanaidsclinicalsociety.org (11/20/2009)

- All with CD4 < 350/mm³
- CD4 350-500/mm³
  - Hep C coinfection, Hep B requiring therapy
  - HIV nephropathy or other organ damage
  - High cardiovascular risk, malignancy
  - HIV RNA > 100,000/mm³
  - CD4 decline > 50 – 100 cells per year
  - Age > 50
HAART

- Use of three active agents
  - Achieve maximal suppression
  - Reduce risk of resistance
- “Highly-Active Anti-Retroviral Therapy”
Antiretroviral Therapy Options

### Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Name</th>
<th>Abbreviation</th>
<th>Trade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>AZT/ZDV</td>
<td>Retrovir</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>3TC</td>
<td>Epivir</td>
</tr>
<tr>
<td>Emtriva</td>
<td>FTC</td>
<td>Emtricitabine</td>
</tr>
<tr>
<td>Stavudine</td>
<td>d4T</td>
<td>Zerit</td>
</tr>
<tr>
<td>Didanosine</td>
<td>ddI</td>
<td>Videx EC</td>
</tr>
<tr>
<td>Abacavir</td>
<td>ABC</td>
<td>Ziagen</td>
</tr>
<tr>
<td>Tenofovir (nucleotide)</td>
<td>TDF</td>
<td>Viread</td>
</tr>
<tr>
<td>AZT + 3TC</td>
<td>CBV</td>
<td>Combivir</td>
</tr>
<tr>
<td>AZT + 3TC + ABC</td>
<td>TZV</td>
<td>Trizivir</td>
</tr>
<tr>
<td>ABC + 3TC</td>
<td>Epzicom</td>
<td></td>
</tr>
<tr>
<td>FTC + TDF</td>
<td>Truvada</td>
<td></td>
</tr>
</tbody>
</table>
# Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Name</th>
<th>Abbreviation</th>
<th>Trade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>EFV</td>
<td>Sustiva</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>NVP</td>
<td>Viramune</td>
</tr>
<tr>
<td>Etravirine</td>
<td>ETR</td>
<td>Intelence</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>RPV</td>
<td>Edurant</td>
</tr>
<tr>
<td>TDF+FTC+EFV</td>
<td></td>
<td>Atripla</td>
</tr>
<tr>
<td>TDF+FTC+RPV</td>
<td></td>
<td>Complera</td>
</tr>
</tbody>
</table>
## Protease Inhibitors (PIs)

<table>
<thead>
<tr>
<th>Name</th>
<th>Abbreviation</th>
<th>Trade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saquinavir</td>
<td>SQV</td>
<td>Invirase, Fortobase</td>
</tr>
<tr>
<td>Indinavir</td>
<td>IND</td>
<td>Crixivan</td>
</tr>
<tr>
<td>Ritonovir</td>
<td>rit, r</td>
<td>Norvir</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>NFV</td>
<td>Viracept</td>
</tr>
<tr>
<td>fosamprenavir</td>
<td>fAMP</td>
<td>Lexiva</td>
</tr>
<tr>
<td>atazanavir</td>
<td>ATZ</td>
<td>Reyataz</td>
</tr>
<tr>
<td>Lopinovir/ritonovir</td>
<td>LPV/r</td>
<td>Kaletra</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>TIP</td>
<td>Aptivus</td>
</tr>
<tr>
<td>Darunavir</td>
<td>DRV</td>
<td>Prezista</td>
</tr>
</tbody>
</table>
Other agents

- **Fusion Inhibitor**
  - T-20, Enfurvir tide, Fuzeon

- **Integrase Inhibitor**
  - Raltegravir, Isentress
  - Integrase Combo: Elvit + Cobi + TDF/FTC (Quad-Stribild)

- **CCR5 Inhibitor**
  - Maraviroc, Selzentry
Initial ART Regimens: DHHS Categories

- **Preferred**
  - Randomized controlled trials show optimal efficacy and durability
  - Favorable tolerability and toxicity profiles

- **Alternative**
  - Effective but have potential disadvantages
  - May be the preferred regimen for individual patients

- **Acceptable**
  - Less virologic efficacy, lack of efficacy data, or greater toxicities
  - May be acceptable but should be used with caution
  - Effective in some studies but have safety, resistance, or efficacy concerns
Initial Treatment: Choosing Regimens

- 3 main categories:
  - 1 NNRTI + 2 NRTIs
  - 1 PI + 2 NRTIs
  - 1 II + 2 NRTIs
- Combination of NNRTI, PI, or II + 2 NRTIs preferred for most patients
- Fusion inhibitor, CCR5 antagonist not recommended in initial ART
- Few clinical end points to guide choices
- Advantages and disadvantages to each type of regimen
- Individualize regimen choice
## Initial Regimens: Preferred

<table>
<thead>
<tr>
<th>Type</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI based</td>
<td>EFV/TDF/FTC&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td>PI based</td>
<td>ATV/r + TDF/FTC&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>DRV/r (QD) + TDF/FTC&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>II based</td>
<td>RAL + TDF/FTC&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>LPV/r (BID) + ZDV/3TC&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

1. EFV should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.
2. 3TC can be used in place of FTC and vice versa. TDF should be used with caution in patients with renal insufficiency.
# Initial Therapy: Dual-NRTI Pairs

| Preferred: TDF/FTC | • Once-daily dosing  
|                   | • High virologic efficacy  
|                   | • Active against HBV  
|                   | • Potential for renal and bone toxicity |
| Alternative: ABC/3TC | • Once-daily dosing  
|                    | • Risk of hypersensitivity reaction if positive for HLA-B*5701  
|                    | • Possible risk of cardiovascular events; caution in patients with CV risk factors  
|                    | • Possible inferior efficacy if baseline HIV RNA >100,000 copies/mL |
| Acceptable: ZDV/3TC | • Twice-daily dosing  
|                    | • Preferred dual NRTI for pregnant women  
|                    | • More toxicities than TDF/FTC or ABC/3TC |
1. EFV should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.

2. 3TC can be used in place of FTC and vice versa. TDF should be used with caution in patients with renal insufficiency.

3. ABC should not be used in patients who test positive for HLA-B*5701; caution if HIV RNA >100,000 copies/mL, or if high risk of cardiovascular disease.

4. RPV: Use with caution if pretreatment HIV RNA >100,000 copies/mL.
## Initial Regimens: Alternative (2)

<table>
<thead>
<tr>
<th>PI based</th>
<th>IV based</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV/r + ABC/3TC&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>RAL + ABC/3TC&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td>DRV/r + ABC/3TC&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>FPV/r (QD or BID) + (ABC/3TC or TDF/FTC)&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>LPV/r (QD or BID)&lt;sup&gt;4&lt;/sup&gt; + (ABC/3TC or TDF/FTC)&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

1. 3TC can be used in place of FTC and vice versa. TDF should be used with caution in patients with renal insufficiency.
2. ABC should not be used in patients who test positive for HLA-B*5701; caution if HIV RNA >100,000 copies/mL, or if high risk of cardiovascular disease.
3. QD LPV/r is not recommended in pregnant women.
<table>
<thead>
<tr>
<th>NNRTI based</th>
<th>EFV¹ + (ZDV/3TC)²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NVP⁴ + (TDF/FTC or ZDV/3TC)²,³</td>
</tr>
<tr>
<td></td>
<td>NVP⁴ + ABC/3TC²,³</td>
</tr>
<tr>
<td></td>
<td>RPV⁵ + ZDV/3TC²</td>
</tr>
</tbody>
</table>

1. EFV should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.
2. 3TC can be used in place of FTC and vice versa. TDF should be used with caution in patients with renal insufficiency.
3. ABC should not be used in patients who test positive for HLA-B*5701; caution if HIV RNA >100,000 copies/mL, or if high risk of cardiovascular disease.
4. NVP should not be started if pre-ARV CD4 >250 in women or >400 in men.
5. RPV: Use with caution if pretreatment HIV RNA >100,000 copies/mL.
### Initial Regimens: Acceptable (2)

<table>
<thead>
<tr>
<th>PI based</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ATV⁴ + (ABC or ZDV)/3TC¹</td>
</tr>
<tr>
<td></td>
<td>ATV/r + ZDV/3TC¹</td>
</tr>
<tr>
<td></td>
<td>DRV/r + ZDV/3TC¹</td>
</tr>
<tr>
<td></td>
<td>FPV/r + ZDV/3TC¹</td>
</tr>
<tr>
<td></td>
<td>LPV/r + ZDV/3TC¹,²</td>
</tr>
</tbody>
</table>

1. 3TC can be used in place of FTC and vice versa.
2. Preferred regimen for pregnant women.
<table>
<thead>
<tr>
<th>Regimen</th>
<th>Option 1</th>
<th>Option 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>II based</td>
<td>RAL + ZDV/3TC</td>
<td>MVC$^3$ + ZDV/3TC$^2$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MVC$^3$ + TDF/FTC$^1$ or ABC/3TC$^{1,2}$</td>
</tr>
</tbody>
</table>

1. 3TC can be used in place of FTC and vice versa. TDF should be used with caution in patients with renal insufficiency.
2. ABC should not be used in patients who test positive for HLA-B*5701; caution if HIV RNA >100,000 copies/mL, or if high risk of cardiovascular disease.
3. Tropism testing required before treatment with MVC; use only if CCR5-tropic virus is present.
<table>
<thead>
<tr>
<th>Reason</th>
<th>ARVs Not Recommended in Initial Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High pill burden/ Dosing inconvenience</td>
<td>IDV (unboosted)</td>
</tr>
<tr>
<td>Lack of data in initial treatment</td>
<td>- ABC + TDF</td>
</tr>
<tr>
<td></td>
<td>- ABC + ddi</td>
</tr>
<tr>
<td></td>
<td>- DRV (unboosted)</td>
</tr>
<tr>
<td></td>
<td>- ENF (T-20)</td>
</tr>
<tr>
<td></td>
<td>- ETR</td>
</tr>
<tr>
<td>No benefit over standard regimens</td>
<td>- 3-class regimens</td>
</tr>
<tr>
<td></td>
<td>- 3 NRTIs + NNRTI</td>
</tr>
</tbody>
</table>
ARV Medications: Should Not Be Offered at Any Time

- ARV regimens not recommended:
  - Monotherapy with NRTI*
  - Dual-NRTI therapy
  - 3-NRTI regimen (except ABC + 3TC + ZDV or possibly TDF + 3TC + ZDV, when other regimens are not desirable)

* If ZDV monotherapy is being considered for prevention of mother-to-child transmission, see Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.
ARV Medications: Should Not Be Offered at Any Time

- ARV components not recommended:
  - ddI + d4T
  - FTC + 3TC
  - d4T + ZDV
  - DRV, SQV, or TPV as single PIs (unboosted)
ARV Medications: Should Not Be Offered at Any Time (3)

- ARV components not recommended:
  - EFV during pregnancy and in women with significant potential for pregnancy
  - NVP initiation in women with CD4 counts of >250 cells/µL or in men with CD4 counts of >400 cells/µL
  - ETR + unboosted PI
  - ETR + RTV-boosted ATV, FPV, or TPV
  - 2-NRTI combination
Estimated number of new child infections at current levels of antiretroviral prophylaxis and without antiretroviral prophylaxis, globally, 1996–2008

![Graph showing estimated number of new child infections from 1996 to 2008. The graph compares infections with and without antiretroviral prophylaxis.](image)
Estimated number of AIDS-related deaths with and without antiretroviral therapy, globally, 1996–2008

- No antiretroviral therapy
- At current levels of antiretroviral therapy
Estimated number of Life-years added due to antiretroviral therapy, by region, 1996–2008

- Western Europe and North America: 7.2 million
- Sub-Saharan Africa: 2.3 million
- Latin America: 1.4 million
- Asia: 590,000
- Eastern Europe and Central Asia: 73,000
- Caribbean: 40,000
- Oceania: 49,000
- Middle East and North Africa: 7,500
Lab Monitoring

- On stable regimen
  - CD4, HIV Viral load about q4 mos.
  - On new regimen, expect CD4 to start rising after 1-2 mos
  - Expect VL to show suppression after 4 wks on therapy
    - May not be fully suppressed for a 6 mos.
  - LFT, CBC may need to be monitored
  - Lipids may need to be monitored

- Yearly STD screens
  - GC/Chlamydia
  - RPR
  - Hepatitis A, B, C
Therapeutic Failure

- With adherence
  - expect maintained suppression of HIV Viral Loads (Undetectable)
  - Expect Cd4 to stabilize or rise
- Falling Cd4 or %, rising VL may suggest failure
- Failure with consistently elevated VL
  - Genotype to help identify mutations to determine new regimen
    - VL usually needs to be >1000 to genotype
What should I do for...

- Stable HIV patient who gets admitted?
- Newly diagnosed HIV patient in the office?
- Newly diagnosed HIV patient in the hospital?
- Screening for complications?
Stable HIV patient who gets admitted

- Known stable CD4, Suppressed Viral Load
  - Check CD4 and HIV Viral load if > 3 mos.
  - Acute illness CD4 may be falsely low.
Newly diagnosed patient in the office

- Best to set up with HIV provider
- Would not start HAART
- Can get screening labs
  - CD4, HIV Viral Load
  - Hep A Total, Hep Bs Ag, Bs Ab, Hep C Ab
  - Toxoplasma IgG
  - Urine for GC/Chlamydia NAAT
  - CBC, CMP
  - RPR
  - PPD/Quantiferon
- HIV Genotype
Newly diagnosed inpatient

- Same as outpatient
- In general, don’t start HAART as inpatient
  - Social factors limits this ability
What should I look for?

- HIV providers stick with HIV
- Most common complications associated with HIV therapy and HIV
  - Hypercholesterolemia
    - May have higher Cardiovascular risk
    - Treat to NCEP guidelines, check for statin interactions
  - Hyperglycemia
    - Treat to DM guidelines
  - Fat Redistribution
    - Viewed as largely cosmetic
Summary

- Test frequently
  - Separate consent not needed
- HIV is a treatable disease
- HIV population is still growing
- Patient living nearly normal life spans
- Watch for long term complications
  - Mostly cardiovascular, metabolic
- Work with your HIV provider
- HIV patients get “healthy patient diseases” too.