Evolving Advances in HIV Care

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Disclosures

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- Thanks to Drs Monica Parker (NYS Wadsworth Laboratory), Doug Fish (Albany Medical Center) and Lou Smith (NYS BHAЕ) for the use of their slides

Objectives

- 1) Understand recent epidemiologic trends in HIV disease
- 2) Know what is new in HIV testing
- 3) Know when to treat HIV infection
- 4) List the preferred regimens for HIV therapy
- 5) How are we doing - the HIV Care Cascade
Epidemiologic Trends in HIV Infection

Number and Percent HIV Positive Women Giving Birth in New York State by Year of Delivery, 1990 - 2012
Percent of Women Aware of HIV Status Prior to Delivery in New York State
By Year of Delivery, 1997 - 2012

From 1997 to 2003, the percentage of women aware of their HIV status before delivery increased from 64% to 95% and has remained at 95%–96% since then.

Trends in Antiretroviral (ARV) Use* by HIV-Positive Pregnant Women and Their Infants in New York State, 1997-2010

*Data presented for cases where some level of prenatal care was received and medical record abstraction contained data on all arms of ARV
Number Infected Infants and Perinatal HIV Transmission Rate in New York State by Year of Delivery, 1990* - 2012

Number of HIV Infected Infants

Year of Delivery


Transmission Rate (per 100 HIV-exposed infants)

*1990 – estimated based on 1,998 exposures and an estimated 25% transmission rate
** Comprehensive testing of newborns began February 1, 1997. Data from 1997 through 2012 are actual numbers and rates.

Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2010—46 States and 5 U.S. Dependent Areas

N=48,079

<1%

18%

10%

3%

5%

61%

Male-to-male sexual contact
Injection drug use (IDU) – Males
Injection drug use (IDU) – Females
Male-to-male sexual contact and IDU
Heterosexual contact* – Males
Heterosexual contact* – Females
Other*

Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk factor information. Data not for incomplete reporting.

*Heterosexual contact includes sex between persons having had sexual contact at any time during HIV infection.

** Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Transmission Category, 2010—46 States and 5 U.S. Dependent Areas

**Males**
- N=37,910
- Male-to-male sexual contact: 12%
- Injection drug use (IDU): <1%
- Male-to-male sexual contact and IDU: <1%
- Heterosexual contact: 7%
- Other*: 4%

**Females**
- N=10,168
- Male-to-male sexual contact: <1%
- Injection drug use (IDU): 14%
- Male-to-male sexual contact and IDU: <1%
- Heterosexual contact: 86%
- Other*: 7%

*Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk factor information, but not for incomplete reporting. *Includes hemophilia, blood transfusion, perinatal exposure, and risk factors not reported or not identified.

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Diagnosed HIV Infections Attributed to Male-to-Male Sexual Contact, by Race/Ethnicity, 2010—46 States and 5 U.S. Dependent Areas

<table>
<thead>
<tr>
<th>Race/ethnicity</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian/Alaska Native</td>
<td>119</td>
<td>0.4</td>
</tr>
<tr>
<td>Asian</td>
<td>584</td>
<td>2.0</td>
</tr>
<tr>
<td>Black/African American</td>
<td>10,842</td>
<td>37.1</td>
</tr>
<tr>
<td>Hispanic/Latino*</td>
<td>6,803</td>
<td>23.3</td>
</tr>
<tr>
<td>Native Hawaiian/other Pacific Islander</td>
<td>53</td>
<td>0.2</td>
</tr>
<tr>
<td>White</td>
<td>10,396</td>
<td>35.6</td>
</tr>
<tr>
<td>Multiple races</td>
<td>396</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29,194</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

*Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk factor information, but not for incomplete reporting. *Hispanic/Latino can be of any race.
Other Trends in the Epidemic

- In 2009, African Americans comprised 14% of the US population but accounted for 44% of all new HIV infections.
  - In 2009, black men accounted for 70% of the estimated new HIV infections among all blacks.
  - 25% (22,000) of all those living with HIV in New York City are over the age of 50. *
  - 82.6 million adults age 18-64 reported they had been tested for HIV in the US. This is an increase of more than 11 million since 2006, when CDC issued its recommendations for expanded testing in health care settings.

Newly Diagnosed HIV Cases by Region
New York State, 2002-2012

DEC2013 NYSDOH/AI/BHAE
Awareness of Serostatus Among People with HIV and Estimates of Transmission

- ~25% Unaware of Infection
  - Revised 10/3/08
  - 21% (233,000)
- ~75% Aware of Infection

People Living with HIV/AIDS: 1,039,000 - 1,185,000

New Sexual Infections Each Year: ~32,000

accounting for:

- ~54% of New Infections
- ~46% of New Infections

Marks, et al
AIDS 2006;20:1447-50
MMWR October 3, 2008
57(39):1073-1076

CDC

Late HIV Testing is Common

- In the US in 2007, within one year of HIV diagnosis, 32.3% of patients had received an AIDS diagnosis (“late testers”)¹
  - In New Jersey- 37.8% were diagnosed ‘late’
  - In New York- 33.6% were diagnosed ‘late’

- Late testing has been shown to be greater among: ²
  - Older populations
  - Minorities
  - Men

1. MMWR December, 2010; 59(47):1550-1555
2. MMWR June, 2009; 58(24):661-665
Exposure to HIV at mucosal surface (sex)

Virus collected by dendritic cells, carried to lymph node

HIV replicates in CD4 cells, released into blood

Virus spreads to other organs
New Model of Pathogenesis of Acute HIV-1 Infection

Detection of HIV by Diagnostic Tests

After Fiebig et al., AIDS 2003; 17(13):1871-9
Offer of HIV Testing ...

- currently mandated by NYS law

- to **ALL** individuals between the ages of **13** and **64** years of age; (and younger or older if there is evidence or indication of risk activity)

- offer must be **documented**.
**HIV Testing Remains Voluntary**

- The law mandates **the offer** of HIV testing only.
- HIV testing is voluntary and requires the consent of the person being tested, or someone authorized to consent for the individual (minors with capacity are allowed to consent for HIV testing).
- No change in exceptions.

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**Recommended Frequency of HIV Testing**

- **At least once** to every person between the ages of 13 and 64 (or younger or older, if indicated).
- Additional offers of testing are required for those whose risk behaviors indicate need for testing.
- Testing should be offered to persons of risk even if they have previously declined.
Providers Required to Make the Offer *Regardless* of Setting

<table>
<thead>
<tr>
<th>Primary Care Providers</th>
<th>Primary Care Fields of Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse Midwives</td>
<td>OB/GYN primary care</td>
</tr>
<tr>
<td>Nurse Practitioners</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>Physician Assistants</td>
<td>Family Medicine</td>
</tr>
<tr>
<td>Physicians</td>
<td>General Pediatrics</td>
</tr>
<tr>
<td></td>
<td>General Practice</td>
</tr>
</tbody>
</table>

Settings Impacted by the Law

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HOSPITALS</strong></td>
</tr>
<tr>
<td>Outpatient Primary Care</td>
</tr>
<tr>
<td>Emergency Department</td>
</tr>
<tr>
<td>In-patient</td>
</tr>
<tr>
<td><strong>DIAGNOSTIC AND TREATMENT CENTERS</strong></td>
</tr>
<tr>
<td><strong>PRIVATE PHYSICIAN OFFICES</strong></td>
</tr>
<tr>
<td>Outpatient Primary Care</td>
</tr>
</tbody>
</table>
HIV Confidentiality Law...

- Article 27-F NYS Public Health Law ~ *Protects the confidentiality of HIV-related information about people who receive services from most health care or social services in NYS*

New York State Law

Article 27-F governs...

- HIV testing
- HIV confidentiality
- HIV case reporting & partner notification*
  *(NYS HIV Case Reporting and Partner Notification Law is in Public Health Law Article 21, Title III)*
Changes in Testing Law

May 2, 2014

Elimination of the requirement for written consent for an HIV test, outside of Corrections. Verbal consent is necessary.

7 points must be given to the patient. You may use posters, fliers or handouts to notify patients of the 7 points.

7 Key Facts to Know Before Getting an HIV Test

- HIV is the virus that causes AIDS. It can be spread through unprotected sex (vaginal, anal, or oral sex) with someone who has HIV, contact with HIV-infected blood by sharing needles (piercing, tattooing, drug equipment, including needles); by HIV-infected pregnant women to their infants during pregnancy or delivery, or by breast feeding.

- There are treatments for HIV/AIDS that can help a person stay healthy.

- People with HIV/AIDS can use safe practices to protect others from becoming infected. Safe practices also protect people with HIV/AIDS from being infected with different strains of HIV.

- Testing is voluntary and can be done without giving your name at a public testing center (anonymous testing).

- By law, HIV test results and other related information are kept confidential (private).

- Discrimination based on a person’s HIV status is illegal. People who are discriminated against can get help.

- Consent for HIV-related testing remains in effect until it is withdrawn verbally or in writing. If the consent was given for a specific period of time, the consent applies to that time period only. Persons may withdraw their consent at any time.
HIV-related Information Includes ...

- an HIV-related test or lab test (CD-4 count, viral load, etc), regardless of result
- presence of HIV infection, HIV related illness or AIDS
- current or past treatment for HIV
- HIV-specific medications
- a “contact” of someone with HIV (spouse, sexual or needle-sharing partner)
- exposure to HIV
New HIV Testing Algorithm - 2013

- HIV EIA/ELISA with HIV-1/2 serology
  - If positive, discriminatory HIV-1 vs HIV-2 test, then appropriate RNA testing
  - If negative, nucleic acid RNA test, which detects to 30 copies/mL
    - To screen for acute HIV
    - Narrows window for acute HIV to 7-10 days

www.health.ny.gov/diseases/aids/testing/

Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection; Approved Guideline (M53-A); CLSI July 18, 2011.

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New HIV Diagnostic Testing Algorithm

1. HIV-1/2 Ag/Ab combo immunoassay (4th generation)
   - (+) Negative for HIV-1 and HIV-2 antibodies and p24 Ag
   - (−)

2. HIV-1/HIV-2 antibody differentiation immunoassay
   - HIV-1 (+) or indeterminate HIV-2 (−)
     - HIV-1 RNA assay
       - RNA (−) Negative for HIV-1
         - Initiate care
       - RNA (+)
         - Positive for HIV-1
         - Initiate care
     - HIV-1 (−)
     - Initiate care
     - HIV-2 (+)
     - Initiate care
   - HIV-1 (−)
   - Positive for HIV-2 antibodies
   - Initiate care
   - HIV-1 (+)
   - Positive for HIV-1 antibodies
   - Initiate care

Slide courtesy of Monica Parker, PhD, Wadsworth Laboratory
When to Treat?

NA-ACCORD: Earlier vs Deferred HAART

- NA-ACCORD, established in 2006, includes 22 HIV research cohorts
  - Current analysis includes 9174 patients with CD4+ cell count ≥ 500 cells/mm$^3$ at study visit between 1996-2006
- Compared outcomes based on treatment according to following definitions
  - Immediate treatment: initiated HAART within 1.5 years of first CD4+ cell count of ≥ 500 cells/mm$^3$
  - Deferred treatment: did not initiate HAART within 1.5 years of first CD4+ cell count of ≥ 500 cells/mm$^3$ but did initiate HAART within 1.5 years of first CD4+ cell count of < 500 cells/mm$^3$
- Primary outcome: death from any cause

NA-ACCORD: Survival Benefit of Earlier HAART by Baseline Factor

<table>
<thead>
<tr>
<th>Parameter Associated With Risk of Death*</th>
<th>Relative Hazard† (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deferral of HAART until &lt; 500 cells/mm³ (vs starting at ≥ 500 cells)</td>
<td>1.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.2</td>
<td>.117</td>
</tr>
<tr>
<td>Older age (per 10 yrs)</td>
<td>1.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Baseline CD4+ cell count (per 100 cells/mm³ increase)</td>
<td>1.0</td>
<td>.696</td>
</tr>
</tbody>
</table>

*All causes of death unspecified. †Stratified by cohort and calendar year.


NA-ACCORD: Increasing Life Expectancy in North American HIV+ Pts on HAART

- Analysis of 23,730 HIV+ pts in NA-ACCORD, on ART, with recent active data available
- Estimated life expectancy at age 20 yrs increased in later periods

<table>
<thead>
<tr>
<th>Life Expectancy at 20 Yrs of Age, 1996-2007, Yrs</th>
<th>NA-ACCORD</th>
<th>US Life Expectancy Data After Age 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41.3</td>
<td>55.3</td>
</tr>
<tr>
<td>Female</td>
<td>42.7</td>
<td>60.4</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>41.0</td>
<td>54.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>52.6</td>
<td>61.4</td>
</tr>
<tr>
<td>White</td>
<td>50.0</td>
<td>59.0</td>
</tr>
<tr>
<td>Transmission category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterosexual</td>
<td>47.7</td>
<td>NR</td>
</tr>
<tr>
<td>IDU</td>
<td>28.1</td>
<td>NR</td>
</tr>
<tr>
<td>MSM</td>
<td>51.6</td>
<td>NR</td>
</tr>
</tbody>
</table>

CASCADE: Risk of AIDS and Death by CD4+ Cell Count Strata at Start of ART

- CASCADE collaboration: observational cohort of HIV seroconverters from 23 clinical cohorts in Europe, Australia, Canada similar to NA-ACCORD and ART-CC
  - Current analysis included 9455 patients ≥ 6 mos after estimated seroconversion in CD4+ cell count strata up to 799 cells/mm³
  - Study period: January 1, 1996 - May 31, 2009
- Endpoints
  - AIDS or death
  - Death
  - Non-AIDS outcomes not included

Effect of Tx Initiation on AIDS and Death

<table>
<thead>
<tr>
<th>CD4+ Cell Count, cells /mm³</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-49</td>
<td>0.32 (0.17-0.59)</td>
</tr>
<tr>
<td>50-199</td>
<td>0.48 (0.31-0.74)</td>
</tr>
<tr>
<td>200-349</td>
<td>0.59 (0.43-0.81)</td>
</tr>
<tr>
<td>350-499</td>
<td>0.75 (0.49-1.14)</td>
</tr>
<tr>
<td>500-799</td>
<td>1.10 (0.67-1.79)</td>
</tr>
</tbody>
</table>

Effect of Tx Initiation on Death

<table>
<thead>
<tr>
<th>CD4+ Cell Count, cells /mm³</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-49</td>
<td>0.37 (0.14-0.95)</td>
</tr>
<tr>
<td>50-199</td>
<td>0.55 (0.28-1.07)</td>
</tr>
<tr>
<td>200-349</td>
<td>0.71 (0.44-1.15)</td>
</tr>
<tr>
<td>350-499</td>
<td>0.51 (0.33-0.80)</td>
</tr>
<tr>
<td>500-799</td>
<td>1.02 (0.49-2.12)</td>
</tr>
</tbody>
</table>


When to Start ART: IAS-USA Recommendations 2014

ART is recommended for treatment of HIV infection and prevention of transmission of HIV regardless of CD4 cell count (A1a-BIII)
- Lack of demonstrated harm with early initiation, cost effective, clinically beneficial
- ART is cost-effective in resource-rich and -poor countries
- In next 4 years, more than 20 drugs are expected to become available as generics

When to Start ART:
IAS-USA Recommendations 2014

Offer ART to all patients with acute or early infection; start as soon as possible to maximize benefit
- Reduced proviral DNA and plasma viral load, lower viral set point, robust immune reconstitution, and CD4 cell counts greater than 900/µL
- Planned discontinuation after specific duration is not recommended except in research settings


When to Start ART:
IAS-USA Recommendations 2014

- ART is recommended regardless of CD4 cell count
- The patient must be willing and ready to initiate therapy; patients not ready to start ART should remain in clinical care, with regular monitoring and ongoing discussion about need for ART
- The strength of recommendations and evidence increase as CD4 cell counts decrease and in the presence of certain conditions

New York City Department of Health

**Antiretroviral Therapy - 2011**

The Health Department now recommends offering antiretroviral treatment (ART) to any person living with HIV, regardless of the person’s CD4 cell count. The recommendation is based on evidence that ART can improve the health of people living with HIV and that ART can prevent transmission of HIV from an HIV-infected person to an uninfected sexual partner.

San Francisco Department of Health issued similar guidance in 2010

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When to Start ART: IAS-USA Recommendations 2014

Strength of recommendation and quality of evidence varies

- According to CD4 cell count:
  - CD4 cell counts ≤500 µL (AIIa)
  - CD4 cell counts of >500 µL (BIII)

- According to clinical condition with CD4 cell counts of >500 µL:
  - Pregnancy (AIIa)
  - Chronic HBV co-infection (AIIa)
  - HIV-associated nephropathy (AIIa)

Recommendations for Initiating ART: CD4 Count or Clinical Category

- Recommended for all CD4 cell counts
  - CD4 cell counts <350 cells/μL (AI)
  - CD4 cell counts 350-500 cells/μL (AII)
  - CD4 cell counts > 500 cells/μL (BIII)
- Recommended regardless of CD4 cell count
  - Pregnancy (AI)
  - History of AIDS-defining illness (AI)
  - HIV-associated nephropathy - HIVAN (AII)
  - Chronic hepatitis B coinfection (AII)
  - Age > 50 years (BIII)


When to Start ART: IAS-USA Recommendations 2014

- According to clinical condition (cont’d):
  - Acute phase of primary HIV infection, regardless of symptoms (BIII)
  - Preferably within first 2 weeks of diagnosis of opportunistic infections (Ala)
  - Early in treatment for cryptococcal meningitis, when expert management of both HIV and cryptococcal infection is available (BIII)

**START (Strategic Timing of ART)**

- **INSIGHT Network:** Multinational
- **Study population:** Adults with CD4 >500 cells/cmm
- **Study treatment:**
  - Immediate ART
  - CD4 <350 cells/cmm
- **Study endpoints:**
  - Serious AIDS-defining illness, non-AIDS illness, death
- **Sample size:**
  - N=900 (pilot for feasibility; enrollment completed)
  - N=3100 (definitive)
- **Duration:** ~6 yrs.

http://insight.ccbr.umn.edu- START Protocol Synopsis

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**HIV Therapy**
What Treatment to Start: IAS-USA Recommendations 2014

- ART is considered lifelong; sustained viral suppression is foundation for immune recovery, optimal health, and prevention of resistance and transmission.
- Maximize adherence and minimize toxicity: Goal is to treat with effective, well-tolerated therapy, with limited drug interactions and effects on comorbid conditions.
- Base selection on baseline resistance testing and patient characteristics and preferences.

Five Classes of Antiretroviral Medications

1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
   - Nucleotide RTIs (tenofovir)
2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI's)
3. Protease Inhibitors (PIs)
4. Fusion Inhibitors: enfuvirtide, CCR5 antagonists
5. Integrase Inhibitors
Current ARV Medications

NRTIs
- Abacavir (ABC)
- Didanosine (ddI)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine (d4T)
- Tenofovir (TDF)
- Zidovudine (AZT)

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

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

Integrase Inhibitors
- Raltegravir (RAL)
- Elvitegravir (EVG)
- Dolutegravir

Fusion Inhibitor
- Enfuvirtide (ENF, T-20)

CCR5 Antagonist
- Maraviroc (MVC)

Single Tablet Regimens
- Atripla
- Complera
- Stribild
- Triumeq

Initial Regimens: Preferred

NNRTI based
- Tenofovir/emtricitabine/efavirenz\(^1,2\)

PI based
- Atazanavir + Ritonavir + Truvada\(^2\)
- Darunavir + Ritonavir + Truvada\(^2\)

II based
- Raltegravir + Truvada\(^2\)
- Dolutegravir + Epzicom or Truvada
- Truvada/cobicistat/elvitegravir

Pregnant women
- Lopinavir/ritonavir (BID) + Combivir\(^2\)

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.

www.aidsetc.org
DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. 2013.
Available at: http://www.aidsinfo.nih.gov.
Recommendations for Initial Treatment in the Settings of Specific Conditions

- Pregnancy: ART should be initiated in all HIV-infected women who become pregnant; ZDV/3TC plus either RTV-boosted LPV or RTV-boosted ATV are preferred.
- Comorbid diseases: Choice of regimen is influenced by chronic and acute comorbidities; assess for exacerbation of comorbid conditions, negative clinical outcomes, increased ARV toxicity, drug interactions with ARV agents.


Recommendations for Initial Treatment in the Settings of Specific Conditions, cont’d.

- The ART regimen for HIV- and HBV–coinfected persons should include TDF and FTC or 3TC as the NRTI background.
- DTG- or RAL-based regimens are recommended for patients receiving anticancer or immunosuppressive drugs.
- In the setting of HCV and HIV co-infection, consult guidance from the AASLD, IDSA, or IAS-USA.

Summary of Selected New Recommendations
and Those for Which the Strength or Quality of Evidence Has Changed Substantially, cont’d.

Changes in Recommendations for What Treatment to Start:
- DTG-based regimens and co-formulated EVG/cobi/TDF/FTC have been added to the list of recommended initial regimens (Ala).
- Co-formulated RPV/TDF/FTC has been added as an initial recommended regimen in patients with HIV-1 RNA levels <100,000 copies/mL (Ala).
- RAL plus ABC/3TC has been added as an alternative initial regimen (Bla).
- ATV/cobi plus 2 NRTIs was added as an alternative initial regimen (Bla).


How do you decide?
- Considerations in choosing a regimen
  - Side effects (matched with patient co-morbidities)
  - Adherence potential (pill burden/frequency)
    - 3 single tablet regimens now available
  - Drug interaction potential
  - Resistance pattern
  - Efficacy
Atazanavir/Ritonavir (Reyataz/Norvir)

Tenofovir/Emtricitabine/Efavirenz (Atripla)

Darunavir/Ritonavir (Prezista/Norvir)

Tenofovir/Emtricitabine (Truvada)

Raltegravir (Isentress)

IAS-USA RECOMMENDATIONS 2014

Monitoring

Recommendations for Monitoring Upon Initiation of or Change in ART

**HIV-1 RNA levels:**
- Monitor at approximately 4 weeks after treatment initiation or change;
- Monitor every 3 months to confirm suppression of viremia to below the limitation of quantification of sensitive commercial assays (AIIa).

**CD4 cell count:**
- Monitor every 3 months after initiation of ART, especially for patients with cell counts of <200 µL;
- results will determine need to initiate or discontinue primary opportunistic infection prophylaxis (BIII).


Recommendations for Ongoing Monitoring

- Monitor at intervals of ≤6 months if viral load is suppressed for 1 year, CD4 cell count is stable at ≥350 µL, and patient’s adherence is dependable (CIII).
- Monitoring is optional if viral load is suppressed consistently for more than 2 years, CD4 cell counts are persistently >500/µL, except in setting of virologic failure or immunosuppressive treatments or conditions (CIII).
- If HIV-1 RNA level is detectable (>50 copies/mL) during therapy, confirm within 4 weeks before making changes (BIII).
- If HIV-1 RNA level is greater than 200 copies/mL during therapy, evaluate factors leading to failure and consider switch in ART (AIIa).

Resistance Testing

- Recommended when patients enter into care, regardless of whether therapy will be initiated immediately or deferred
  - If therapy is deferred, repeat testing at the time of ART initiation should be considered
- Testing should be performed when managing sub-optimal viral load reduction and in the setting of virologic failure
  - Testing should be performed while patients still on meds or at least within 4 weeks of therapy discontinuation


Genotype example

Phenotype example

<table>
<thead>
<tr>
<th>Drug</th>
<th>Genotype</th>
<th>Drug Resistance Associated Mutations Detected</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>M41L, D67N, K70R, M264V, T215F, K219E</td>
<td>ABC</td>
<td>Reduced Susceptible</td>
</tr>
<tr>
<td>Didanosine</td>
<td>M41L, D67N, Y115F, T215F, K219E</td>
<td>3TC</td>
<td>Reduced Susceptible</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>M41L, D67N, K70R, M264V, T215F, K219E</td>
<td>FTC</td>
<td>Reduced Susceptible</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>M100V, K219E</td>
<td>RTV</td>
<td>Reduced Susceptible</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>M41L, D67N, K70R, T215F, K219E</td>
<td>ZDV</td>
<td>Reduced Susceptible</td>
</tr>
</tbody>
</table>

Recommendations for Changing the ART Regimen in Treatment-Experienced Patients

- Design of a new regimen should consider previous ART exposure, previous resistance profile, and history of intolerance or toxic effects (AIIa).
- Depending on the resistance profile, viral tropism, and options available for patients with multidrug resistance, inclusion of a boosted PI and agents from newer drug classes (eg, an INSTI or maraviroc) should be considered (AIIa).
- Monotherapy with a boosted PI is not recommended when other options are available (AIIa).
HIV Care Cascade and Treatment as Prevention

HIV Care Cascade

Out of the more than one million Americans with HIV:

- 942,000 know they are infected
- 726,000 were linked to HIV care
- 480,000 have stayed in HIV care
- 437,000 are receiving treatment
- 328,000 have a very low amount of virus in their bodies

MMWR #60; 1618-1623; 2011.
Cascade Results Comparison
New York State (2011) and the US (CDC, July 2012)

Percent of Persons Living with Diagnosed HIV Infection

- Retained in Care*
  - NYS: 57%
  - US: 46%
- Virally Suppressed
  - NYS: 45%
  - US: 30%

* CDC and NY methods for retention differ.

NY State’s Strategy to End AIDS

- Reduce transmissions to below 700 per year, from current level of over 3,000 per year.
- Early diagnosis, linkage and retention to care
- Pre-exposure prophylaxis as primary prevention
In+ Care Campaign

HPTN 052: Treatment as Prevention

- 1763 serodiscordant couples
- CD4 350 – 550 cells/cmm
  - Immediate vs. delayed therapy arms
- 39 transmissions
- 28 virologically linked to infected partner
  - 27 infections occurred in the delayed therapy arm and 1 in the early therapy arm
  - 23 of 28 infections occurred in African sites
- Adjusted hazards ratio for linked transmission in the early-therapy 0.04; p<0.001 (96% protection)
- Self-reported condom use at baseline was associated with reduced risk of HIV transmission

CDC Interim Guidance on PrEP for Heterosexual Adults

- PrEP = Pre-Exposure Prophylaxis

- PrEP should be targeted to persons at very high risk for HIV acquisition, especially uninfected persons whose regular sexual partners are known to have HIV infection

- PrEP is accompanied by monitoring of HIV status, pregnancy status, side effects, adherence, and risk behaviors at each quarterly follow-up visit.

Pre-exposure Prophylaxis

- PrEP is delivered as part of a comprehensive set of prevention services, including risk-reduction, PrEP medication adherence counseling, and ready access to condoms

- Sexually transmitted infection treatment is provided when indicated by laboratory screening tests conducted at least every 6 months, and

- PrEP is accompanied by monitoring of HIV status, pregnancy status, side effects, adherence, and risk behaviors at each quarterly follow-up visit.
CDC Interim Guidance on PreP for Heterosexual Adults

- PrEP should be targeted to persons at very high risk for HIV acquisition, especially uninfected persons whose regular sexual partners are known to have HIV infection
- Adherence is critical to daily medication and its influence on efficacy is clearly discussed with provider prescribing
- Couples understand that although no adverse effects have been found among infants exposed to TDF/FTC during pregnancy and breastfeeding, these data are incomplete for women in HIV-discordant couples using TDF/FTC to prevent acquisition of HIV

August 10, 2012 MMWR

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Take-Home Points

**RECOMMEND TESTING FOR ALL BETWEEN AGES 13 AND 64.**

TREATMENT OF HIV IS NOW RECOMMENDED, REGARDLESS OF CD4 CELL COUNT

Long-term non-progressors and elite controllers are possible exceptions

**PLAN FOR NORMAL LIFE EXPECTANCY FOR HIV-POSITIVE INDIVIDUALS**

**TREATMENT IS PREVENTION – EPIDEMIC COULD END**
Thank You!

- Office 518-262-4043
- Clinical consult line 518-262-6864

References

- IAS-USA Guidelines 2014
- DHHS Guidelines: [www.aidsinfo.org](http://www.aidsinfo.org)