Diagnosis and Initial Management of HIV/AIDS:
What the Primary Care Provider Should Know

Carolyn K. Burr, EdD, RN
Co-Clinical Director NY/NJ AETC LPS
Deputy Director François-Xavier Bagnoud Center
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Objectives

• Describe two ways HIV can be transmitted
• Identify two laboratory tests used to assess HIV disease
• Describe the clinical progression of HIV
• Discuss the purpose of antiretroviral treatment
What is HIV

- **H**uman
- **I**mmunodeficiency
- **V**irus

- HIV is a retrovirus that attacks the immune system.
- Its genetic material, RNA, must be converted into DNA during replication.
- Over time, the immune system and the body lose its ability to fight the virus.
HIV and the Immune System

- The CD4 cells coordinate a body’s immune response to an invader (bacteria, virus, etc.)

- BUT, when HIV enters CD4 cells for reproduction, it damages the CD4 cell, eventually killing it.

- The body’s immune system works hard making more CD4 cells

- Overtime, HIV destroys the CD4 cells faster than the immune system can make new ones

- So, HIV damages the very system that usually protects the body from infection.
HIV Life Cycle
Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Race/Ethnicity, Year-end 2010—United States and 6 Dependent Areas

Males
N = 665,872*

- 38% White
- 37% Black/African American
- 21% American Indian/Alaska Native
- 1% Asian
- <1% Native Hawaiian/Other Pacific Islander
- <1% Multiple races

Females
N = 223,045*

- 60% White
- 19% Hispanic/Latino
- 18% Black/African American
- 2% American Indian/Alaska Native
- <1% Asian
- <1% Native Hawaiian/Other Pacific Islander
- <1% Multiple races

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, but not for incomplete reporting.

* Includes Asian/Pacific Islander legacy cases.

† Hispanics/Latinos can be of any race.

* Total males include 582 persons and total females include 180 persons with unknown race/ethnicity.
HIV in New Jersey

- 36,648 people are living with HIV

- 78% Minorities

- 79% 40 years or older

- 34% Women (53% between 20-49)

- 159 perinatal exposures

- 3% infected
HIV Transmission

- Blood
- Semen
- Vaginal Secretions
- Breast milk

- Comes into contact with:
  - mucous membranes, damaged tissue, or is injected into the body

- Through:
  - Vaginal, anal, or oral sex
  - Contaminated needles
  - IV drug use
Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Transmission Category, 2011—United States and 6 Dependent Areas

**Males**
- Male-to-male sexual contact: 78%
- Injection drug use (IDU): 12%
- Male-to-male sexual contact and IDU: 6%
- Other: 4%
- Unknown: <1%

**Females**
- Heterosexual contact: 86%
- Other: 14%
- Unknown: <1%

*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 transmission category, but not for incomplete reporting.*

*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

- Perinatal transmission during pregnancy, labor and deliver, or breastfeeding
- Occupational exposure via needle stick or exposure to eyes, nose, or open wound
  - Since 1981 there have been 57 documented cases of occupational transmission in the US
- Blood transfusion or organ donation from an HIV infected donor (rare in US)
HIV Transmission

• HIV is NOT transmitted by casual contact
  – Working or playing with an HIV positive person
  – Closed mouth kissing
  – Shaking hands
  – Public pools
  – Hugging
  – Public toilet

• HIV is not transmitted by air, food, or mosquito and does not survive long outside the body.
HIV Testing

- CDC recommends **routine** HIV testing for ALL patients:
  - Aged 13-64
  - Initiating TB treatment
  - Seeking treatment for STI’s
  - Who are pregnant
- Repeat Screening Recommended
  - Annually people at high risk
  - Before beginning a new sexual relationship
  - When clinically indicated
  - After an occupational exposure
HIV Testing

- Benefits of routine **opt-out** HIV testing
  - Reduces the stigma of testing
  - Reduces transmission
  - Majority of people aware of their HIV status reduce behaviors that transmit infection
  - Perinatal transmission can be prevented if mother’s HIV status is known
  - Improves patient outcomes (with early diagnosis of HIV)
Sequence of HIV Assay Reactivity During Early HIV Infection relative to Western Blot*

Estimated # of days HIV assay is reactive before a positive Western blot result is obtained

*Assay sensitivity above is based on frozen plasma only. Whole-blood and oral fluid has not been characterized for early infection.

**Current data suggests that the Gen-Probe Aptima can detect HIV-1 RNA ~9-11 days after infection.

HIV Laboratory Tests – CD4 Count

- CD4 count – measures state of a person’s immune function
  - Adult values are approximately 500-1300
  - Used to determine stage of HIV progression
  - Determines risk of opportunistic infection
  - Historically guided decisions about antiretroviral therapy (ART)
HIV Laboratory Tests – Viral Load

• Detects the amount of virus present
  • High viral loads increase risk for disease progression and HIV transmission

• Monitors effectiveness of ART
  • Goal of therapy is an undetectable viral load

• Used during acute infection to detect virus

• Measured by HIV-1 RNA PCR
Clinical Progression

• Acute Retroviral Syndrome
  – Two thirds of all patients experience symptoms
  – Occurs 2-6 weeks after initial infection
  – Symptoms last 2-4 weeks
  – May be mistaken for influenza, mononucleosis, or other viral process
  – During this period HIV virus is replicating rapidly and CD4 count decreases until the body’s immune response recovers CD4 cells and decreases viral load
Clinical Progression

- **Clinical Latency**
  - Virus is replicating at low levels
  - CD4 cells are maintained at a healthy level
  - Virus is transmittable
  - This period may last for several years
Clinical Progression

• Clinical symptoms will begin to develop at the end of this period as CD4 count falls and viral load increases.

• May include
  – Bacillary angiomatosis (lesion on skin caused by infection with gram negative organism)
  – Persistent or resistant vulvovaginal candidiasis
  – PID
  – Cervical Dysplasia
  – Hairy leukoplakia
  – Herpes Zoster
  – Fever or diarrhea lasting longer than one month
AIDS

• AIDS is characterized by certain infections that take advantage of the body’s weakened immune system.
• A diagnosis of AIDS is made when an HIV positive patient has a CD4 count of less that 200 or 14% or the patient is diagnosed with an AIDS defining condition
• Progression from initial infection with HIV to advanced HIV/AIDS varies among people and can take several months to up to 10 years or more.
Opportunistic Infections

• Opportunistic infections are infections that take advantage of a weakened immune system to cause more frequent or severe illness
  • CDC identifies 29 infections
  • Prophylactic drugs may be given to prevent illness for some conditions
  • Other clinical options include
    • Effective ART
    • Vaccination
    • Avoiding exposure to certain pathogens
    • Disease treatment
    • Preventing disease recurrence (secondary prophylaxis or chronic maintenance therapy)
Clinical Progression

**Beginning:**
No symptoms, no weight loss.

**After few years:**
Mild weight loss, mouth ulcers, itching, skin disease.

**After several years:**
Important weight loss, thrush, TB, fever.

**After 10 years:**
Wasting syndrome, chronic herpes, simplex ulcerations, extrapulmonary TB

5–10 YEARS
What can we do?
Antiretroviral Therapy

- Recommended for all HIV-positive people
  - To prevent disease progression
  - To prevent transmission of infections

- Strength of recommendation based on
  - CD4 count
  - Transmission risk

- See *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents* available at [http://www.aidsinfo.nih.gov/](http://www.aidsinfo.nih.gov/) for more info
Confusing terminology?

- ART = Anti Retroviral Therapy
- ARV = Anti Retro Virals
- HAART = Highly Active Anti Retroviral Therapy
- Triple Therapy = Three Antiretrovirals
- “The Cocktail”
Basic Facts about ARVs

• ARVs are divided into classes, each of which attacks HIV in a different way.
• New classes becoming available through clinical trials.

• Always use 3 or more different ARV medications for therapy.
• Regimen should be selected by an experienced HCW.
• Other medications interact with ARVs.
HIV as a Chronic Disease

ARVs change HIV from a terminal (fatal) disease to a “chronic disease”

Examples of chronic diseases:
- Diabetes
- High blood pressure
- Asthma
- Schizophrenia
Advantages of ARV Therapy

- Improved patient health
- Reduced illness
- Reduced hospitalisations
- Fewer deaths from AIDS
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
How do ARVs control HIV?

• ARVs reduce the ability of the HIV virus to replicate

• In turn, this increases the ability of the body to fight disease

• Reduces the risk of HIV transmission
The Ideal ARV

- Good tolerability
- Complete viral suppression
- No toxicities
- No resistance
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
- Advantages and disadvantages to each type of regimen
- Individualize regimen choice
Achievable…..?

**YES**

ARVs are able to significantly reduce viral load, allowing the immune system to recover followed by an increase in quality of life and reduction in morbidity and mortality

**BUT**

they are not perfect………..
Managing Side Effects

‘Acceptable’
(transient, manageable)

Versus

‘Unacceptable’
(severe, adverse reactions)

…..but, **ALL** must be reported so that they can be managed appropriately
Basic Facts about Adherence and ARV Therapy

• ARV blood concentrations must remain constant; low concentrations allow HIV to mutate.

• HIV mutations cause drug resistance.

• ARV medications must be taken every day otherwise they will not work.

• Things that can lower drug concentrations:
  – Missing 1 or 2 ARV medication doses regularly
  – Taking ARV medication late
  – Taking ARVs with certain foods or other medications
Treatment Adherence

- A patient’s ability to follow a prescribed treatment regimen
- Major factor in success of drug regimen
- Significant determinant of survival
- Willingness to start treatment and take medications exactly as directed
- Level of adherence affects how well ART decreases the HIV viral load
- Average US ART adherence rate is about 70%
Treatment Adherence

• Factors associated with poor adherence
  – Depression
  – Active alcohol or drug use
  – Low literacy
  – Lack of social support (unstable social situation, chaotic lifestyle)
  – Lack of support from partner
  – Advance HIV infection
  – Young age
  – Disbelief in treatment efficacy
  – Unstable housing
  – Cognitive impairment
  – Competing priorities
    • Childcare, food and work
Treatment Adherence

- Complexity of medication regimen
- Adverse drug effects
- Poor patient provider relationships
- Lack of resources
- Poor literacy
- Substance abuse
- Stigma
- Travel away from home
- Sleeping through doses
- Treatment fatigue
  - Adherence should be assessed at each visit
Treatment Adherence

• Strategies to improve adherence
  – Choose once daily dosing if possible
  – Avoid complex or poorly tolerated regimes
  – Use fixed dose combinations if possible
  – Use multidisciplinary approach
  – Provide tools and support
    • Reminder alarms
    • Text message reminders
    • Education and counseling
    • Pill boxes
Resistance

- Skipping doses of medications may cause the virus to mutate leading to strains of HIV that are resistant to medications

- Drug resistant strains can be transmitted

- Viral fitness: Ability of a virus to enter and destroy CD4 cell (caused by the number resistant mutations developed)
Resistance Testing

• **Genotype**
  – Amplifies and sequences HIV to look for mutations known to correlate with drug resistance. Most successful if viral load is above 1000 copies/ml
  – Recommended as initial form of resistance testing
    • Use to select effective ART

• **Phenotype**
  – HIV reverse transcriptase and protease genes are spliced and created into a laboratory strain
  – The strain is grown in the presence of escalating concentrations of ARV drugs
    • Process takes 2-3 weeks and is costly
  – Recommended for patients with complicated multidrug resistance patterns
Take Home Messages: HIV 101

• HIV infection is a treatable, chronic illness
• Routine HIV testing is essential not only for treatment of HIV but also for prevention
• ART improves quality of life and decreases
  – Mortality
  – Morbidity
  – Risk of transmission to partners
• Adherence is key to ARV effectiveness
Resources

- AIDS Education and Training Center National Resource Center [www.aidsetc.org](http://www.aidsetc.org)
- NY/NJ AETC Trainings On-Demand Online Courses [http://www.nynjaetc.org/on-demand/index.html#CME](http://www.nynjaetc.org/on-demand/index.html#CME)
- National Clinicians Consultation Center [www.nccc.ucsf.edu](http://www.nccc.ucsf.edu)
- François-Xavier Bagnoud Center [http://fxbcenter.org/](http://fxbcenter.org/)
THANK YOU!