What Every Healthcare Provider Should Know About HIV

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Howard University School of Medicine
Overview

- HIV Testing Missed Opportunities
- Acute Retroviral Syndrome
- Opportunistic Infections
- Treatment
- Reminders
TESTING
Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings
Missed opportunities for HIV Diagnosis
Case 1, Mr. Smith

- 73 y/o male
- PMH- DM II, HTN, recurrent dysuria
- PCP- “one of those clinics”
- HIV+, diagnosed June ‘09
  - Urology pre-op
CD4 =173, CD4%= 11

“How did I get HIV?”

“I have been seeing the doctor for years and I get tested for everything. Nobody ever told me I had HIV”.
<table>
<thead>
<tr>
<th>Age/Gender</th>
<th>Co-morbid conditions</th>
<th>CD4 count at diagnosis</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>38 Male</td>
<td>HTN</td>
<td>4</td>
<td>Gay</td>
</tr>
<tr>
<td>66 Female</td>
<td>HTN, Diabetes</td>
<td>166</td>
<td>Widow</td>
</tr>
<tr>
<td>62 Female</td>
<td>HTN, Renal insufficiency</td>
<td>76</td>
<td>Heterosexual</td>
</tr>
<tr>
<td>42 male</td>
<td>Asthma, heart disease, Chronic cough</td>
<td>11</td>
<td>Heterosexual</td>
</tr>
<tr>
<td>26 Male</td>
<td>h/o syphilis and gonorrhea</td>
<td>116</td>
<td>Gay</td>
</tr>
<tr>
<td>33 Male</td>
<td></td>
<td>2</td>
<td>Gay</td>
</tr>
</tbody>
</table>
Other Examples, Missed Ops

- 66 y/o Ethiopian woman in US and celibate for 10+ years
- 73 y/o woman nursing home resident
- 59 y/o married woman with pneumonia
Missed Opportunities, Routine Screening 2007

- 71.4% of new positives who had a healthcare visit in last 12 months
- 50.6% of new positives offered an HIV test at last visit healthcare visit

Courtesy: DC Department of Health, 2009
37 year male executive
1 week fever, headache, rash malaise
No travel, sick contacts or pets
Cervical and axillary lymphadenopathy
  5-8cm
Generalized erythematous rash
  Trunk worse than extremities
WBC 2.1, Hb 9.3, Plt 53K

CSF Normal glc, pro, few lymphs

HIV rapid test negative

Serology RMSF, Lyme negative

Dx = Viral meningitis

Rx = Ceftriaxone, supportive care
Day 4, continued fever

Antibiotics spectrum broadened
  - Zosyn, Vanc

Surgery consulted for biopsy

Pathology reactive nodal swelling

ID consulted
Differential Diagnosis

- Syphilis
- Bacterial infection
  - Pneumococcal disease
- Viral exanthem
  - Epstein-Barr virus
    - Mononucleosis
  - Cytomegalovirus
  - Influenza
  - West Nile
  - Enterovirus
- Rickettsial disease
- Lyme disease
- Leptospirosis
- Rheumatologic diseases
  - Still’s
  - Kawasaki’s
  - Systemic Lupus
- HIV
EJ, cont’d

- Additional History
  - Bisexual
  - Last unprotected sexual encounter two months prior

- Viral load (VL) ordered

- Two weeks later
  - Patient evaluated for fever, malaise at outside hospital
  - Monospot positive

- VL from Howard >500,000 copies/mL

- 1 week later ELISA and Western blot positive
Acute Retroviral Syndrome (ARS)

- Mononucleosis-like illness
  - Non-specific signs and symptoms
- 40-90% of patients symptomatic
- Typically presents 1-4 weeks post-exposure
- High index of suspicion is critical
Acute Retroviral Syndrome (ARS) – a Great Mimiker!

- Rash
- Fever
- Headache +/- nuchal rigidity
- Malaise and fatigue
- Lymphadenopathy
- Neutropenia, anemia, thrombocytopenia
Main symptoms of Acute HIV infection

Systemic:
- Fever
- Weight loss

Central:
- Malaise
- Headache
- Neuropathy

Pharyngitis

Mouth:
- Sores
- Thrush

Esophagus:
- Sores

Muscles:
- Myalgia

Liver and spleen:
- Enlargement

Skin:
- Rash

Lymph nodes:
- Lymphadenopathy

Gastric:
- Nausea
- Vomiting
Table 3. Commonly Reported Signs, Symptoms, and Laboratory Findings in Patients with Acute HIV-1 Infection.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Pharyngitis\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Lymphadenopathy\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Rash\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Diaphoresis or night sweats\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Headache\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Anorexia\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Nausea or vomiting\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Myalgia and arthralgia\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Oral or genital ulcers</td>
</tr>
<tr>
<td>Nuchal rigidity, photophobia, or both (in patients with aseptic meningitis)\textsuperscript{\dagger}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Leukopenia</td>
</tr>
<tr>
<td>Lymphopenia\textsuperscript{\dagger}</td>
</tr>
<tr>
<td>Elevated aminotransferase levels</td>
</tr>
</tbody>
</table>

\textsuperscript{a} HIV-1 denotes human immunodeficiency virus type 1.  
\textsuperscript{\dagger} This finding appeared in the patient.
More sensitive than HIV antibody or p24 Ag test

Positive one to three weeks before antibody test

General high volume viremia
  - 500,000-1,000,000 copies/mL

False positives can occur
  - Most false positives are low level (<10,000 copies/mL)
  - HIV VL <10,000 copies/mL should probably be considered “indeterminate”
Diagnostic Testing for ARS

![Graph showing the progression of HIV RNA and HIV-1 Antibodies over days post-exposure.](image)

- **HIV RNA**
  - Peaks around 30 days post-exposure.
  - Decreases sharply after 40 days.

- **HIV-1 Antibodies**
  - Increases gradually from day 20 onwards.
  - Peaks around 50 days post-exposure.

- **P24 +**
  - Detected from day 20 onwards.

- **Symptoms**
  - Detected from day 20 onwards.
  - Increase in symptoms coincides with the rise in P24 +.

- **Exposure**
  - Occurs at day 0.
Public health importance of diagnosis

- Patients are highly infectious
  - Warrants urgent identification

- Viral load and transmission directly correlated
  - Probability of HIV transmission increases as viral load increases

- Frontline providers must recognize and consider ARS
  - Flu-like symptoms may be your only clue
  - Suspicious cases?
    - HIV and viral load testing
HIV Management and Treatment
Management of Newly Diagnosed HIV Infection

Scott M. Hammer, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

As part of a routine examination for insurance coverage, a 25-year-old previously healthy woman is found to have a positive test for human immunodeficiency virus type 1 (HIV-1) antibody. Heterosexual contact is her only risk factor for HIV acquisition. She is asymptomatic and has a normal physical examination. The results of hematologic and other routine laboratory tests are normal. Her CD4 cell count is 325 cells per cubic millimeter, and her plasma HIV-1 RNA level is 60,000 copies per milliliter (both confirmed on repeated testing). How should her case be managed?

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In the United States, it is estimated that 900,000 to 1 million persons are infected with HIV-1. One quarter to one third of these persons do not know their infection status, thus jeopardizing their own care and putting others at risk through transmission that might be prevented with counseling, behavior modification, and potentially, antiretroviral therapy. The number of new cases of acquired immunodeficiency syndrome (AIDS) reported each year in the United States has been stable, at approximately 40,000, but the incidence of HIV-1 infection and other sexually transmitted infections has increased in certain at-risk populations, such as men who have sex with men. Blacks, Hispanics, and women are disproportionally represented among persons with HIV-1 infection, AIDS, or both.
Baseline Evaluation

- **Complete H&P**
- **Laboratory testing:**
  - HIV antibody
  - CD4 cell count
  - Genotype
  - Plasma HIV RNA
  - CBC, chemistry profile
  - BUN, Cr
  - Transaminases
  - Fasting glucose and lipids
  - RPR or VDRL
  - Hepatitis A, B, C serology
  - Toxoplasma IgG

- Tuberculin skin test (TST) or IFN-γ release assay
- Chest X ray (if symptoms, or positive TST or IFN-γ release assay)
- Gynecologic exam with Pap smear
- Testing for chlamydia and gonorrhea
- Ophthalmology exam (CD4 count <100 cells/µL)
Opportunistic Infections (OI)

- OIs still prevalent
  - Pneumocystis jiroveci pneumonia (PCP)
    - Formerly *pneumocystis carinii* pneumonia
  - CMV
    - Eye, GI, pulmonary
  - Cryptococcocal disease
  - Toxoplasmosis
  - Lymphoma
HIV and TB: Double Trouble!
An HIV-infected, TB-exposed person’s lifetime risk of developing active TB is 100%!

.....if untreated
HIV and TB: Considerations

- Test for latent TB
  - TST vs. Interferon Gamma Release Assays
    - Neither is perfect

- Annual CXRs not necessary
  - Clinical picture should guide you

- Prophylaxis important!
  - 9 months INH/B6

- Disease can occur at any CD4 count
# Primary Prophylaxis Against OIs

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>CD4 Count (cells/mm³)</th>
<th>Agent</th>
<th>Major Side Effects</th>
<th>Alternative Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis jirovei</em></td>
<td>&lt;200</td>
<td>Trimethoprim–sulfamethoxazole, 160 mg and 800 mg, once daily</td>
<td>Rash, fever, abnormal liver-enzyme levels, hematologic toxicity, pancreatitis</td>
<td>Dapsone, 100 mg once daily (if G6PD level is normal)</td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em></td>
<td>&lt;100</td>
<td>Trimethoprim–sulfamethoxazole, 160 mg and 800 mg, once daily</td>
<td>Rash, fever, abnormal liver-enzyme levels, hematologic toxicity, pancreatitis</td>
<td>Dapsone, 200 mg, plus pyrimethamine, 75 mg, plus leucovorin, 25 mg, once weekly</td>
</tr>
<tr>
<td><em>Mycobacterium avium complex</em></td>
<td>&lt;50</td>
<td>Azithromycin, 1200 mg, once weekly</td>
<td>Gastrointestinal symptoms</td>
<td>Clarithromycin, 500 mg, twice daily</td>
</tr>
<tr>
<td><em>M. tuberculosis</em></td>
<td>Any (tuberculin skin test, positive at induration of ≥5 mm, or history of significant exposure)</td>
<td>Isoniazid, 300 mg, once daily (with pyridoxine, 50 mg, once daily) for 9 months; Active tuberculosis should be ruled out before initiating treatment with isoniazid</td>
<td>Abnormal liver-enzyme levels, peripheral neuropathy</td>
<td>Risks and benefits of alternative prophylactic regimens should be carefully evaluated on an individual basis</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Any, but response to vaccine is better in persons with &gt;200</td>
<td>23-valent pneumococcal polysaccharide vaccine; need for revaccination after 5 years has not been established</td>
<td>Local reaction at site of injection; transient systemic symptoms</td>
<td></td>
</tr>
<tr>
<td><em>Influenza virus</em></td>
<td>Any</td>
<td>Inactivated influenza vaccine once yearly</td>
<td>Local reaction at site of injection; transient systemic symptoms</td>
<td>Oseltamivir, 75 mg, once daily during outbreak if not protected by vaccination</td>
</tr>
<tr>
<td><em>Hepatitis A virus</em></td>
<td>Any</td>
<td>Hepatitis A vaccine</td>
<td>Local reaction at site of injection</td>
<td>Combined hepatitis A and B vaccine now available</td>
</tr>
<tr>
<td><em>Hepatitis B virus</em></td>
<td>Any</td>
<td>Hepatitis B vaccine</td>
<td>Local reaction at site of injection; transient systemic symptoms</td>
<td>Combined hepatitis A and B vaccine now available</td>
</tr>
</tbody>
</table>

* G6PD denotes glucose-6-phosphate dehydrogenase. Data are from the CDC²⁴ and the U.S. Public Health Service."³⁵

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Treatment is available now

- 30 HIV meds available
- Less pills to take
- HIV-infected people live active, healthy lives
HIV Pill Burden can be low
# Current ART Options

## The POZ and AIDSmeds Drug Chart

A comprehensive drug chart for individuals on ART. This chart offers guidance on medication options, dosages, and potential side effects. It is designed to help individuals and healthcare providers make informed decisions about treatment regimens. The chart also includes sections on non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs), along with other important information related to ART options.

### Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combivir (abacavir + lamivudine)</td>
<td>Combination tablet once a day, Combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Etravirine (etravirine)</td>
<td>800 mg two times a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Emtricitabine (emtricitabine)</td>
<td>200 mg two times a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Epivir (lamivudine)</td>
<td>300 mg once a day, 20 mg once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Optionar (abacavir + lamivudine)</td>
<td>Combination tablet once a day, Combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Retrovir (zidovudine)</td>
<td>300 mg once a day, Combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Trizivir (abacavir + lamivudine + zidovudine)</td>
<td>Combination tablet once a day, Combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Truvada (emtricitabine + lamivudine)</td>
<td>20 mg once a day, Combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Videx EC (dideoxycytidine)</td>
<td>Available generically in the U.S.</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Viracept (tenofovir)</td>
<td>100 mg three times a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Zentinel (stavudine)</td>
<td>300 mg once a day, combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Zidovine (zidovudine)</td>
<td>300 mg once a day, combination NRTI twice a day</td>
<td>Nausea with or without food</td>
</tr>
</tbody>
</table>

### Protease Inhibitors (PIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atripla (emtricitabine + tenofovir + efavirenz)</td>
<td>One tablet once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Crisona (rilpivirine + etravirine)</td>
<td>Combination tablet once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Invirex (saquinavir)</td>
<td>100 mg once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Kaletra (lopinavir + ritonavir)</td>
<td>Combination tablet once a day</td>
<td>Nausea with or without food</td>
</tr>
</tbody>
</table>

### Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone (methadone + atazanavir)</td>
<td>Combination tablet once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Etravirine (etravirine)</td>
<td>Combination tablet once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Nevirapine (nevirapine)</td>
<td>300 mg once a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Ritonavir (ritonavir)</td>
<td>100 mg three times a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Stavudine (stavudine)</td>
<td>600 mg once a day</td>
<td>Nausea with or without food</td>
</tr>
</tbody>
</table>

### Integrase Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instent (raltegravir)</td>
<td>One 400 mg tablet twice a day</td>
<td>Nausea with or without food</td>
</tr>
</tbody>
</table>

### Fusion and Entry Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuzeta (enfuvirtide)</td>
<td>One 50 mg injection three times a day</td>
<td>Nausea with or without food</td>
</tr>
<tr>
<td>Solazym (monotherapy)</td>
<td>One 50 mg injection three times a day</td>
<td>Nausea with or without food</td>
</tr>
</tbody>
</table>

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*Drugs not shown in chart. Please refer to the complete prescribing information for each medication for details.*
Initial Treatment: Choosing Regimens

- 4 categories:
  - 1 NNRTI + 2 NRTIs
  - 1 PI + 2 NRTIs
  - 1 Integrase Inhibitor + 2 NRTIs
  - 3 NRTIs

- NNRTI, Integrase Inhibitor or PI + 2 NRTIs preferred

- Fusion inhibitor, CCR5 antagonist not recommended in initial ART
Case 3- Sarah

- 25 y/o
- CD4 absolute 420
- CD4% = 15
- Viral load = 65,000
- No co-morbidities
- Sexually active
Gray Area

- Should you offer Sarah treatment?
Early Treatment Initiation

- HIV-1 RNA > 100,000 copies/mL
- CD4+ cell count decline > 100 cells/mm³/year
- Older age
- HBV or HCV coinfection
- Presence of risk factors for non-AIDS diseases
  - Cancer, cardiovascular disease
- HIV-associated nephropathy

PREVENTION?
### NA-ACCORD: Survival Benefit With Earlier vs Deferred HAART

Increased relative hazard of death with deferral of HAART remained unchanged when adjusted for IDU or for HCV coinfection, which were both independent predictors of mortality.


<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; 350 cells/mm³ (vs starting at 350-500 cells/mm³)</td>
<td>1.7 (1.0-2.5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.1 (1.0-2.6)</td>
<td>.290</td>
</tr>
<tr>
<td>Older age (per 10 yrs)</td>
<td>1.6 (1.1-2.6)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>BL CD4+ cell count (per 100 cells/mm³ increase)</td>
<td>0.9 (0.6-1.3)</td>
<td>.083</td>
</tr>
</tbody>
</table>
Providers
- Primary care providers are a critical public health partner
  - Identify cases
  - Don’t forget about ARS
  - Refer HIV-positive persons for care immediately

Prevention counseling

Patients/clients
- Treatment is no picnic!
  - Lifelong commitment to pills
  - Time schedules
  - Side effects
  - Drug interactions
- Engage in care with an HIV specialist
GOAL = End AIDS
Updated HIV Clinical Guidelines, 2008-2009

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

November 3, 2008

Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

February 23, 2009

Public Health Service Task Force

Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

July 9, 2008

How to Cite the Adult and Adolescent Guidelines:

ARVs - Adults and Adolescents

Ols - Adults and Adolescents

ARVs - Pediatric

Ols - Pediatric

ARVs - Perinatal

www.aidsinfo.nih.gov
Web-based Guidelines

- www.aidsetc.org
- www.Clinicaloptions.com
REFERENCES

1. DHHS guidelines. Available at: http://www.aidsinfo.nih.gov


Questions?

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Thank you!