Managing TB-HIV Co-infection

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TB-HIV Co-infection

- Epidemiology
- Diagnosis: pulmonary
- Diagnosis: extra-pulmonary
- Treatment

Adults and children with HIV, 2007

Total: 33.2 (30.6 – 36.1) million
**HIV in New TB Cases**

www.who.int/tb

**Estimated HIV Coinfection in Persons Reported with TB, United States, 1993–2008***

![Graph showing the estimated HIV coinfection rate in the United States from 1993 to 2008.](http://wonder.cdc.gov/tb-v2006.html)

*Updated as of May 20, 2009.*

Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group.

**HIV-TB Co-Infection per Year, U.S. 2002-2006**

![Map showing the distribution of HIV-TB co-infection by state in the United States from 2002 to 2006.](http://wonder.cdc.gov/tb-v2006.html)
Effects of TB on HIV Progression

- TB increases HIV progression
- Individuals with active TB often have very high HIV viral loads
- Immunosuppression progresses more quickly, and survival may be shorter despite successful treatment of TB
- Individuals with TB/HIV have a shorter life expectancy than persons with HIV who never had TB

Effects of HIV on TB Progression

- More likely to progress rapidly to active TB disease following infection
- Greater risk of reactivation of latent TB infection
- Higher risk of becoming re-infected with M.tb (even after prior treatment)
- With LTBI: 5–10% annual risk of developing active TB (versus 10% lifetime risk among HIV-negative individuals)


Effect of HIV on Incidence of TB

[Nunn P, JID 2007 196(s1):S5–S14]
Features Suggestive of HIV

• History
  – Sexually transmitted infections
  – Herpes zoster (shingles)
  – Recent or recurrent pneumonia
  – Severe bacterial infections
  – Recent tuberculosis

• Symptoms
  – Weight loss >10kg (or >20% of body weight)
  – Diarrhea >1 month
  – Pain on swallowing (odynophagia)
  – Burning sensation in feet (neuropathy)
Features Suggestive of HIV

- Scar of previous shingles (herpes zoster)
- Itchy, papular skin rash
- Dark or dark-red skin or mucous membrane lesions (Kaposi’s sarcoma)
- Generalized lymphadenopathy

Features Suggestive of HIV

- Oral candidiasis (thrush)
- Oral hairy leukoplakia
- Necrotizing gingivitis
- Aphthous ulcers (severe or recurrent)
- Persistent painful genital ulceration

Whom to Test for HIV

- Ideally, all patients with TB should have HIV testing performed
- In a high-HIV prevalence setting:
  - Test all patients with suspected TB
- In a low HIV-prevalence setting (if all patients cannot be tested):
  - Test if HIV signs, symptoms, and/or risk factors are present.
Reporting of HIV Test Results in Persons with TB by Age Group United States, 1993–2008*

*Updated as of May 20, 2009.

Note: Includes TB patients with positive, negative, or indeterminate HIV test results. Persons from California reported with AIDS only through 2004. (HIV test results are not reported from California)

Reporting of HIV Test Results

PULMONARY TB

Diagnosis of LTBI in HIV

- Anergy likely with low CD4 counts
- Repeat testing after CD4 > 350
- Annual re-testing for persons at increased risk for exposure
- IGRAs have increased sensitivity
  - QuantiFERON
  - T-SPOT.TB
Diagnosis of Active TB in HIV

• Cannot rely on “typical” indicators of TB
• Fever and weight loss are important symptoms
• Cough is less common
• Chest radiographic pattern more variable
• More extrapulmonary and disseminated TB
• Differential diagnosis is broader

TB and Stage of HIV

<table>
<thead>
<tr>
<th>Features of PTB</th>
<th>Stage of HIV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td>Clinical picture</td>
<td>Often resembles post-primary PTB</td>
</tr>
<tr>
<td>Sputum smear result</td>
<td>Often positive</td>
</tr>
<tr>
<td>CXR appearance</td>
<td>Often cavities</td>
</tr>
</tbody>
</table>

CXR Patterns

<table>
<thead>
<tr>
<th>CLASSICAL PATTERN</th>
<th>ATYPICAL PATTERN</th>
</tr>
</thead>
<tbody>
<tr>
<td>upper lobe infiltrates</td>
<td>interstitial infiltrates (especially lower zones)</td>
</tr>
<tr>
<td>bilateral infiltrates</td>
<td></td>
</tr>
<tr>
<td>cavitation</td>
<td>intrathoracic lymphadenopathy</td>
</tr>
<tr>
<td>pulmonary fibrosis and shrinkage</td>
<td>no abnormalities</td>
</tr>
</tbody>
</table>
TB or PCP?

<table>
<thead>
<tr>
<th>Typical of PCP</th>
<th>Typical of TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>symptoms</td>
<td></td>
</tr>
<tr>
<td>dry cough</td>
<td>productive cough</td>
</tr>
<tr>
<td>purulent sputum</td>
<td></td>
</tr>
<tr>
<td>hemoptysis</td>
<td></td>
</tr>
<tr>
<td>dyspnoea</td>
<td></td>
</tr>
<tr>
<td>sputum mucoid (if any)</td>
<td>pleuritic chest pain</td>
</tr>
<tr>
<td>signs</td>
<td></td>
</tr>
<tr>
<td>may be normal</td>
<td>signs of consolidation</td>
</tr>
<tr>
<td>fine inspiratory crackles</td>
<td>of plural effusion</td>
</tr>
<tr>
<td>CXR</td>
<td></td>
</tr>
<tr>
<td>bilateral diffuse</td>
<td>pleural effusion</td>
</tr>
<tr>
<td>interstitial shadowing</td>
<td>pleural effusion</td>
</tr>
<tr>
<td>may be normal</td>
<td>pleural effusion</td>
</tr>
</tbody>
</table>

Is this TB?

53 y.o. male with HIV, CD4 375 on ART and 4 weeks of cough, 10 lbs. weight loss and night sweats

- Classic TB symptoms
- “Typical” CXR Pattern:
  (Reactivation / Post-primary TB pattern)

Is this TB?

22 y.o. male with HIV, CD4 50 presenting with malaise for 2 weeks, mild dyspnea with fever (no cough)

- Both symptoms and CXR may be atypical
- “Atypical” (primary-TB) CXR pattern more common with lower CD4
Atypical CXR Patterns

“Atypical” pattern (Primary TB pattern)

- Distribution: Any lobe involved (slight lower lobe predominance)
- Air-space consolidation
- Cavitation is uncommon (< 10%)
- Adenopathy is common (esp. in children and HIV)

[Image credit: Francis J. Curry National Tuberculosis Center, University of California, San Francisco]

Miliary TB

[Image credit: Francis J. Curry National Tuberculosis Center, University of California, San Francisco]

Is this TB?

30 y.o. female with HIV, CD4 112, close contact to smear+ case, cough for 3 weeks with weight loss and fever

- CXR may be normal in 10-20% of pts with HIV

[Image credit: Francis J. Curry National Tuberculosis Center, University of California, San Francisco]
CXR Pattern: Early vs. Advanced HIV

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Early HIV (CD4 &gt;200)</th>
<th>Advanced HIV (CD4 &lt;200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infiltrate</td>
<td>“Typical” (Reactivation)</td>
<td>“Atypical” (Primary)</td>
</tr>
<tr>
<td>Cavitation</td>
<td>Upper lobes</td>
<td>Lower lobes, multiple sites, or miliary</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Effusion</td>
<td>Uncommon</td>
<td>More common</td>
</tr>
</tbody>
</table>

Sputum Microscopy

- All patients suspected of having pulmonary TB should have at least two sputum specimens obtained for microscopic examination.
- When possible, at least one early morning specimen should be obtained.

Smear-negative pulmonary TB

- If CD4 <200, higher incidence of smear-negative sputum
- If smear-negative sputum, obtain culture (if available)
- Chest X-ray more critical in evaluation
  - May shorten delays in diagnosis
  - Should be done early in the work-up
- Difficult to distinguish smear-negative pulmonary TB from other HIV-related pulmonary diseases
EXTRA-PULMONARY TB

Extrapulmonary TB (EPTB)

• In HIV-positive pts:
  – Higher incidence of EPTB (increased with advanced immunosuppression)
  – Greater risk for disseminated disease and rapid clinical deterioration
• Presentation: Constitutional symptoms (fever, night sweats, weight loss), with signs and symptoms specific to the extrapulmonary site

TB/HIV: Common EPTB sites

• Lymph Nodes: Cervical > axillary > inguinal
• Serosal disease: pleural, pericardial
• Genitourinary tract
• Central nervous system: meningitis, tuberculoma
• Bone and joint
• Soft tissue abscesses
• Disseminated disease
Extrapulmonary Tuberculosis

Extrapulmonary TB: Diagnosis

- Diagnostic tools: X-rays, fine needle aspirates, ultrasound, biopsy
- Diagnosis may be presumptive, provided other conditions are excluded
- If EPTB: look for pulmonary TB with sputum smears and chest X-Ray
- In HIV, EPTB is a sign of more advanced disease

TREATMENT
## Treatment: Interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td>NNRTI</td>
<td>Dec NNRTI</td>
</tr>
<tr>
<td>Rifampin</td>
<td>PI</td>
<td>Dec PI</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Maraviroc</td>
<td>Dec Mar</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>NNRTI</td>
<td>Dec Rif</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>PI</td>
<td>Inc Rif</td>
</tr>
<tr>
<td>INH</td>
<td>NRTI</td>
<td>Neuropathy</td>
</tr>
</tbody>
</table>

## Rifampin Recommendations

- Efavirenz: No dose adjustments
- Nevirapine: No dose adjustments
- Etravirine: Avoid combo
- Atazanavir: Avoid combo
- Lopinavir/R: Inc Lop/R dose
- Maraviroc: Inc Mar dose
- Raltegravir: No dose adjustments

## Rifabutin Recommendations

- Efavirenz: Inc Rif dose
- Nevirapine: No dose adjustments
- Etravirine: No dose adjustments
- Atazanavir: Dec Rif dose
- Lopinavir/R: Dec Rif dose
- Maraviroc: No dose adjustments
- Raltegravir: No dose adjustments
### Adverse Events

- **Rash**
  - Manage based on likely cause
- **Elevation of LFTs**
  - $>3x$ ULN with symptoms
  - $>5x$ ULN without symptoms
- **IRIS**

### Immune Reconstitution Syndrome

- Seen after initiation of ART (< 30d)
- Attributed to recovering immune function
- Associated with initial CD4 count < 100
- Seen when ART started within 2 months of TB diagnosis
- Signs include fever, worsening resp status, enlarging lymph nodes

### ART recommendations for TB, WHO

<table>
<thead>
<tr>
<th>CD4 Count</th>
<th>Recommendation</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt; 200/\text{mm}^3$</td>
<td>Start TB treatment. Start ART between 2-8 wks (EFZ containing regimens)</td>
<td>Start</td>
</tr>
<tr>
<td>200-350/\text{mm}^3</td>
<td>Start TB treatment. Start ARV after initiation phase (unless severely compromised)</td>
<td>Consider</td>
</tr>
<tr>
<td>$350+/\text{mm}^3$</td>
<td>Start TB treatment</td>
<td>Defer</td>
</tr>
</tbody>
</table>
Management of IRIS

- Exclude other causes
- NSAID
- Prednisone
- Hold ART
- Excision of lymph nodes

Summary

- Multiple challenges for each infection
- Increase risk for TB in individuals with HIV
- Unusual presentations
- IRIS
- Drug interactions