TB Nurse Case Management
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TB/HIV Co-Infection

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Tuberculosis and HIV Co-Infection

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Case Scenario #1

• A 35 year old HIV+ male (A.G.) is referred to you for a TST measuring 12 mm.

• On questioning, the patient states he was skin tested because one of his roommates was diagnosed with pulmonary cavitary TB.
  – How should you approach this patient?

Classifying the Tuberculin Reaction

5 mm is classified as positive in

• HIV-positive persons
• Recent contacts of TB case
• Persons with fibrotic changes on chest radiograph consistent with old healed TB
• Patients with organ transplants and other immunosuppressed patients
Case Scenario # 1 (cont)

• A.G. reveals his TST 3 years ago was ‘negative’.

• He currently takes Atripla, his CD4 count is 453 and his viral load is <40.

• He has HCV and htn managed with HCTZ.

Testing for TB Infection - Principles

• Individuals who have a
  – + TST result,
  – a + IGRA result or
  – symptoms suggestive of TB (regardless of TST/IGRA results)
    should be evaluated with an chest x-ray

• Patients with HIV who may not react to testing by TST or IGRA
  should have a chest x-ray if TB is suspected or if exposed to an
  active TB case

• If abnormalities are noted, or the client has symptoms
  suggestive of extrapulmonary TB, additional diagnostic tests
  should be conducted
CXR – HIV infected persons

- May cause infiltrates without cavities in any lung zone
- May cause mediastinal or hilar lymphadenopathy with or without infiltrates or cavities

In HIV-infected persons almost any abnormality on CXR may indicate TB

Case Scenario #1 (cont)

- He has 2 other roommates who will see you later this week. They are also HIV+ but were TST-negative.
  - How would you evaluate these individuals?
Case Scenario #1 (cont)

- **Roommate #1** only recently moved into the home. He has a CD4 count of 638, takes no meds, has no significant health issues and denies any current symptoms.

- **Roommate #2** was recently diagnosed with HIV and is not currently on medications. His CD4 count is 45 and he has a cough he attributes to post-nasal drip. He feels well, denies weight loss or other suggestive symptoms.

Case Scenario #1 (cont)

- Assuming a negative CXR in all three, how would you approach each patient?
  - A.G. (TST 12 mm, CD4 453, HCV, denies symptoms)
  - Roommate #1 (TST 0 mm, CD4 638, no symptoms)
  - Roommate #2 (TST 0 mm, CD4 45, cough, no symptoms)
Risk reduction by treatment of Latent TB Infection (LTBI) in HIV-infected patients

Before initiating treatment for LTBI
- Rule out TB disease
  - i.e. wait for culture results if specimen obtained
- Determine prior history of treatment for LTBI or TB disease
- Assess risks and benefits of treatment
- Determine current and previous drug therapy
Clinical Presentation
HIV-positive vs. HIV-negative patients

- Driven mostly by degree of immunity

- HIV-positive patients are more likely to have:
  - Isolated extrapulmonary localization (53-63% in some studies)
  - Primary infection
  - Pulmonary basilar involvement
  - Tuberculous pneumonia
  - Hilar or mediastinal lymphadenopathies
  - Miliary or disseminated TB
  - Normal CXR (8-20% in some studies)
Primary Tuberculosis
Diagnosis

Table 1. Bacteriological and histological results observed during HIV-associated TB as a function of immune status

<table>
<thead>
<tr>
<th></th>
<th>CD4 &lt; 200/mm³</th>
<th>CD4 &gt; 200/mm³</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive tuberculin</td>
<td>30%</td>
<td>50%</td>
<td>[23]</td>
</tr>
<tr>
<td>skin test reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt; 5 mm without BCG)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acid-fast bacilli on</td>
<td>56–60%</td>
<td>50–58%</td>
<td>[22,23,25]</td>
</tr>
<tr>
<td>smear</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acid-fast bacilli on</td>
<td>60–65%</td>
<td>*</td>
<td>[22]</td>
</tr>
<tr>
<td>biopsy</td>
<td></td>
<td>50–56%</td>
<td></td>
</tr>
<tr>
<td>Granuloma in biopsy</td>
<td>60–75%</td>
<td>*</td>
<td>[23,31,32]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67–100%</td>
<td></td>
</tr>
<tr>
<td>Mycobacteraemia</td>
<td>20–49%</td>
<td>*</td>
<td>[22,30]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0–7%</td>
<td></td>
</tr>
</tbody>
</table>

Isoniazid Regimens for LTBI

- 9-month regimen of isoniazid (INH) is the preferred regimen

- 6-month regimen is less effective but may be used if unable to complete 9 months

- May be given daily or intermittently (twice weekly)
  - Use directly observed therapy (DOT) for intermittent regimen
Persons with the following conditions need special precautions while on isoniazid

- **a.** Age 35 years and over
- **b.** Taking other medications on a long term basis
- **c.** Alcohol abusers
- **d.** History of previous discontinuation of isoniazid because of toxicity/adverse reactions
- **e.** Chronic liver disease
- **f.** Peripheral neuropathy
- **g.** Pregnancy

### Rifampin Regimens for LTBI

- Rifampin (RIF) given daily for 4 months is an acceptable alternative when treatment with INH is not feasible.

- In situations where RIF cannot be used (e.g., HIV-infected persons receiving protease inhibitors), rifabutin may be substituted.

- RIF and PZA for 2 months should generally not be offered due to risk of severe adverse events.

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6 MMWR August 8, 2003; 52 (31): 736-739
LTBI treatment

TABLE. Revised drug regimens for treatment of latent tuberculosis infection (LTBI) in adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interval and duration</th>
<th>Comments</th>
<th>Rating [Evidence]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Daily for 9 months†††</td>
<td>In HIV-infected persons, isoniazid may be administered concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs).</td>
<td>A (II) A (II)</td>
</tr>
<tr>
<td></td>
<td>Twice weekly for 5 months†††</td>
<td>Directly observed therapy (DOT) must be used with twice-weekly dosing.</td>
<td>B (II) B (II)</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Daily for 6 months††</td>
<td>Not indicated for HIV-infected persons, those with fibrocicatricial lesions on chest radiographs, or children.</td>
<td>B (II) C (I)</td>
</tr>
<tr>
<td></td>
<td>Twice weekly for 6 months††</td>
<td>DOT must be used with twice-weekly dosing.</td>
<td>B (II) C (I)</td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>Daily for 4 months</td>
<td>Used for persons who are contacts of patients with isoniazid-resistant, rifampin-susceptible TB.</td>
<td>B (II) B (II)</td>
</tr>
<tr>
<td><strong>Rifampin plus</strong></td>
<td>Daily for 2 months</td>
<td>In HIV-infected persons, most protease inhibitors or de-novo protease inhibitors should not be administered concurrently with rifampin. Rifampin with appropriate dose adjustments can be used with protease inhibitors (rampage should be augmented with ritonavir and NRTIs except stavudine). Consultation should consult web-based updates for the latest specific recommendations.</td>
<td>D (II) D (II)</td>
</tr>
<tr>
<td><strong>pyridoxine (PZC)</strong></td>
<td>Twice weekly for 2–3 months</td>
<td>PZC generally should not be offered for treatment of LTBI for HIV-infected or HIV-viremic persons.</td>
<td>D (II) D (II)</td>
</tr>
</tbody>
</table>

Case Scenario #2

- A 28 year old Latino male with HIV presents with a 2 ½ month history of productive cough, night sweats, fevers, fatigue and 30 lb weight loss.

- The patient has been under the care of an ID physician for his HIV and has been stable on a PI-containing regimen. The patient has been working construction out of state and has not been able to visit his doctor until now. He has been compliant with his HIV meds and his current laboratory studies show a CD4 count of 281 and viral load <50.

- Two of 3 sputums collected on consecutive days are positive for AFB
  - Which anti-TB regimen do you start him on?
  - What do you do with his HIV meds?
Anti-tuberculosis Drugs
(ATS/CDC/IDSA)

• First-Line drugs
  – Isoniazid
  – Rifampin
  – Rifapentine
  – Rifabutin*
  – Ethambutol
  – Pyrazinamide

• Second-Line Drugs
  – Cylcoserine
  – Ethionamide
  – Levofloxacin*
  – Moxifloxacin*
  – PAS
  – Streptomycin
  – Amikacin/Kanamycin
  – Capreomycin

*Not FDA approved for TB

Anti-tuberculosis Drugs

• INH (Isoniazid)
  – Accounts for the majority of early bactericidal activity of multi-drug TB regimens
  – Excellent absorption and tissue penetration

• Rifampin
  – Bactericidal (highest sterilizing activity).
  – Activity against rapidly dividing and against semi-dormant bacterial populations.
  – Cornerstone of short course therapy
  – Well absorbed, good tissue levels
  – Longer-acting Rifapentine being investigated
Anti-tuberculosis Drugs

• Ethambutol
  – Included in first-line treatment regimens to prevent the emergence of Rifampin resistance when INH resistance may be present.

• PZA (pyrazinamide)
  – Bacteriostatic/sterilizing agent: Greatest activity against dormant or semi-dormant (slowly growing) organisms within macrophages or caseous foci (acidic environment).
  – Necessary for 6 months treatment regimen

Anti-tuberculosis Drugs

• Fluoroquinolones
  – Preferred oral agents for treating drug resistant TB that is susceptible to this class of drugs or for patients intolerant of first-line drugs
  – Activity against MTB: Moxifloxacin > levofloxacin > ofloxacin/ciprofloxacin
  – Cross resistance
Updates and Changes in TB Therapy

- Obtain a sputum smear and culture at the end of the initial phase of treatment (2 months) to identify patients at increased risk of relapse.

- Extended therapy is recommended for patients with drug-susceptible pulmonary TB who have cavitation on the initial CXR and who have a positive sputum culture at the time 2 months of therapy is completed.

- Counting Doses – treatment completion is defined by number of doses taken as well as duration of treatment.
Updates and Changes in Therapy

• Changes in dosing schedules:
  
  – HIV + individuals with low CD4 counts should NOT be given twice weekly therapy
  
  – Daily therapy can be 7 days per week OR can be 5 days per week IF given by DOT and the Mtb is drug susceptible

Role of New Agents

• Rifabutin (RBT): May be used as a primary drug for patients (especially HIV+) receiving medications having unacceptable interactions with rifampin (e.g. Protease Inhibitors, methadone)

• Fluoroquinolones: May be used when first line drugs are not tolerated or the organism is resistant
  – Moxifloxin rapidly becoming agent of choice
Treatment of Culture-Positive Drug Susceptible Pulmonary TB

• General conclusions from the literature:
  – 6 mo (26 wk) is the MINIMUM duration of Rx
  – 6 mo regimens require rifampin throughout and PZA for the first 2 months
  – 6 mo regimens are effective without INH
  – Intermittent regimens (2-3x/wk):
    • GIVEN by DOT ONLY
    • Drug susceptible isolate
    • Regimen contains INH and rifampin

• General conclusions from the literature:
  – Without PZA - minimum duration is 9 months
  – Without rifampin - minimum duration is 12 months (up to 18 months)
  – Streptomycin and ethambutol (EMB) are approximately equivalent in effect (BUT concern about increasing Streptomycin resistance among foreign born leads to preference of EMB for initial therapy)
Treatment of Patients with TB Disease

- **Initiation phase** of therapy
  - 8 weeks; INH, Rifampin and PZA +/-EMB

- **Continuation phase** of therapy
  - 16 weeks; INH and Rifampin

- **Prolongation of continuation phase**
  - Positive 2 month culture with cavitary disease
  - Extrapulmonary disease
    - Meningitis
    - Disseminated disease in children
  - HIV TB in children and adolescents

- **Consider Prolongation of continuation phase when patient:**
  - Slow to clinically or radiographically respond
  - Positive 2 month culture OR cavitary disease?
  - End of therapy (EOT) cavity present
  - <10% ideal body weight?

Management of Treatment Interruptions

- **Initial phase** of therapy
  - <14 days – complete standard # of doses
  - >14 days – restart from the beginning

- **Continuation phase**
  - >80% doses by DOT – if initial smear negative, may stop
  - Repeat culture
    - >3 month interruption restart from beginning
    - <3 month interruption, culture positive, restart
    - <3 month interruption, culture negative, give an additional 4 months
ATS recommendations for treatment of tuberculosis

Rifamycins

- Have significant interaction with all ARVs except nucleoside analogues (other than AZT) and enfuvirtide

- Once or twice weekly regimens show high rate of rifampin resistance in HIV patients with CD4 cell count <100

- Most common locus of interaction is the cytochrome P450 system
  - As inducers, rifampin > rifapentine > rifabutin
Effect of Efavirenz Dosing with rifampin on treatment outcomes

![Graph showing probability of virological success over 24 weeks with Efavirenz dosage of 600 mg or 800 mg.]

**Manosuthi et al. AIDS 2005, 19:1481–1486**

**Fig. 1.** Immunological outcomes at 48 weeks of antiretroviral therapy between the two treatment groups. --- Efavirenz 600 mg/day; —— efavirenz 800 mg/day.

**Manosuthi et al. AIDS 2006, Vol 20 No 1**

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**Rifampin and PIs**

**Table 3.** Pharmacokinetic interactions between rifampicin or rifabutin

<table>
<thead>
<tr>
<th>Rifampicin</th>
<th>PI</th>
<th>R's effect on PI</th>
<th>PI's effect on R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saquinavir</td>
<td>80% decrease saquinavir level</td>
<td>Data not reported</td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td>92% decrease indinavir level</td>
<td>Unchanged R level</td>
<td></td>
</tr>
<tr>
<td>Indinavir</td>
<td>92% decrease indinavir level</td>
<td>Data not reported</td>
<td></td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>82% decrease nelfinavir level</td>
<td>Data not reported</td>
<td></td>
</tr>
<tr>
<td>Lopinavir + ritonavir</td>
<td>75% decrease lopinavir level</td>
<td>Unchanged R level</td>
<td></td>
</tr>
<tr>
<td>Amprenavir</td>
<td>82% decrease amprenavir level</td>
<td>Unchanged R level</td>
<td></td>
</tr>
</tbody>
</table>

R, rifampicin; RFB, rifabutin; PI, protease inhibitor.

Note: Decrease in serum rifampin is NOT overcome by low dose ritonavir

<table>
<thead>
<tr>
<th>Rifabutin</th>
<th>RFB's effect on PI</th>
<th>PI's effect on RFB</th>
</tr>
</thead>
<tbody>
<tr>
<td>45% decrease saquinavir level</td>
<td>20% increase RFB level</td>
<td></td>
</tr>
<tr>
<td>Data not reported</td>
<td>17% increase RFB level</td>
<td></td>
</tr>
<tr>
<td>32% decrease indinavir level</td>
<td>20% increase RFB level</td>
<td></td>
</tr>
<tr>
<td>Data not reported</td>
<td>30% increase RFB level</td>
<td></td>
</tr>
<tr>
<td>14% decrease amprenavir level</td>
<td>20% increase RFB level</td>
<td></td>
</tr>
</tbody>
</table>

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Newer drugs and rifampin

- **Maraviroc** has a substantial reaction with rifampin
  - An increased dose of maraviroc is recommended when co-administered with rifampin but no clinical studies have been done

- Trough concentrations of **raltegravir** are decreased by ~ 60% when co-administered with rifampin

- Rifampin is PREDICTED to substantially decrease concentrations of **etravirine**, but this has not been proven

Rifabutin

- Has much less effect than rifampin on drugs metabolized by CYP3A

- Requires dosage adjustment due to effects by many other drugs (such as ritonavir). **Concerns regarding adequate dosing if patient is not compliant with PI medication**

- PIs (especially if boosted with ritonavir) cause a marked increase in serum rifabutin serum concentrations and toxicity

- Rifabutin dose should be decreased when using PI-based regimens
Rifabutin

• Good virological and immunological outcomes when administered with PI-based HAART

• Treatment of choice when pt cannot tolerate NNRTI-based treatment (though no head-to-head studies)

• Expensive
### Table 1. Recommendations for regimens for the concomitant treatment of tuberculosis and HIV infection

<table>
<thead>
<tr>
<th>Combined regimen for treatment of HIV and tuberculosis</th>
<th>PK effect of rifampicin</th>
<th>Tolerability/safety</th>
<th>Antiviral activity when used with rifampicin</th>
<th>Recommendation (comments)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAART-based ART with rifampicin-based TB treatment</td>
<td>Well-characterized, moderate effect</td>
<td>Low rate of discontinuation</td>
<td>Excellent</td>
<td>Preferred (rifampicin should not be used during the first trimester of pregnancy)</td>
</tr>
<tr>
<td>PI-based ART with rifampicin-based TB treatment</td>
<td>Little effect of rifampicin on PI concentrations, high steady-state levels</td>
<td>Low rate of discontinuation (if rifampicin is appropriately dose-reduced)</td>
<td>Feasible, though published clinical experience is not extensive</td>
<td>Preferred for patients unable to take alternative</td>
</tr>
<tr>
<td>Non-nucleoside ART with rifampicin-based TB treatment</td>
<td>Moderate effect</td>
<td>Concern about hepatotoxicity when used with stavudine, lamivudine and nevirapine</td>
<td>Feasible</td>
<td>Alternative for patients who cannot tolerate stavudine and if rifampicin not available</td>
</tr>
</tbody>
</table>

### Table 2. Recommendations for concomitantly administering antiretroviral drugs with RIFAMPIN – 2007

<table>
<thead>
<tr>
<th>Non-nucleoside reverse transcriptase inhibitors</th>
<th>Recommended change in dose of antiretroviral drug</th>
<th>Recommended change in dose of rifampicin</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>Decrease (400 mg to 200 mg for patients &lt; 65 kg)</td>
<td>No change (300 mg/kg)</td>
<td>Efavirenz AUC should be 25% to 50% lower than in patients without rifampicin, Efavirenz should not be used during the 1st trimester of pregnancy</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>No change</td>
<td>No change (300 mg/kg)</td>
<td>Nevirapine AUC should be 50% to 75% lower than with 300 mg 2/3-day dose</td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Rilpamip and delavirdine should not be used together</td>
<td>Delavirdine AUC should be 50% lower</td>
<td></td>
</tr>
<tr>
<td>Etravirine</td>
<td>Etravirine and rifampicin should not be used together</td>
<td>Etravirine AUC should be 50% lower based on data in the literature with etravirine</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Recommendations for coadministering antiretroviral drugs with RIFAMPIN – 2007

<table>
<thead>
<tr>
<th>CCR-5 receptor antagonists</th>
<th>Recommended change in dose of antiretroviral drug</th>
<th>Recommended change in dose of rifampin</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maraviroc</td>
<td>Increase maraviroc to 600 mg twice daily</td>
<td>No change (600 mg/d)</td>
<td>Maraviroc Cmax ↓ by 25%, No reported clinical experience with increased dose of maraviroc with rifampin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Integrase inhibitors</th>
<th>Recommended change in dose of antiretroviral drug</th>
<th>Recommended change in dose of rifampin</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>No change</td>
<td>No change (400 mg/day)</td>
<td>No clinical experience, raltegravir concentrations ↓ by 41-61%</td>
</tr>
</tbody>
</table>

Table 2. Recommendations for coadministering antiretroviral drugs with RIFAMPIN – 2007

<table>
<thead>
<tr>
<th>Single protease inhibitors</th>
<th>Recommended change in dose of antiretroviral drug</th>
<th>Recommended change in dose of rifampin</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>No change</td>
<td>No change (600 mg/day)</td>
<td>Use with caution, Atazanavir AUC ↓ by 50%, no change in rifampin concentrations,注意对逆转录酶活性的影响</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Efavirenz and rifampin should not be used together</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alocitavir</td>
<td>Tlordatavir and rifampin should not be used together</td>
<td>Alocitavir AUC ↓ by 50%</td>
<td></td>
</tr>
<tr>
<td>Indinavir</td>
<td>Indinavir and rifampin should not be used together</td>
<td>Indinavir AUC ↓ by 50%</td>
<td></td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Nelfinavir and rifampin should not be used together</td>
<td>Nelfinavir AUC ↓ by 60%</td>
<td></td>
</tr>
<tr>
<td>Saquinavir</td>
<td>Saquinavir and rifampin should not be used together</td>
<td>Saquinavir AUC ↓ by 60%</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Recommendations for coadministering antiretroviral drugs with RIFABUTIN – 2007

<table>
<thead>
<tr>
<th>Non-nucleoside reverse-transcriptase inhibitors</th>
<th>Antiretroviral dose change</th>
<th>Rifabutin dose change</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eflornithine</td>
<td>No change</td>
<td>4 to 400 mg (daily)</td>
<td>Rifabutin AUC 4 by 20%. Effect of eflornithine on rifabutin concentration has not been studied. Eflornithine should not be used during the 3rd trimester of pregnancy.</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>No change</td>
<td>No change (100 mg daily or thrice weekly)</td>
<td>Rifabutin and nevirapine AUC not significantly changed.</td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Patients and delavirdine should not be used together</td>
<td>Delavirdine AUC 4 by 100%, rifabutin AUC 4 by 100%.</td>
<td></td>
</tr>
<tr>
<td>Efavirenan</td>
<td>No change</td>
<td>No change (200 mg daily or thrice weekly)</td>
<td>No clinical experience; rifabutin AUC 4 by 15%, but does not warrant a change in dose.</td>
</tr>
</tbody>
</table>

Table 3. Recommendations for coadministering antiretroviral drugs with RIFABUTIN – 2007

<table>
<thead>
<tr>
<th>Single protease inhibitors</th>
<th>Antiretroviral dose change</th>
<th>Rifabutin dose change</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>No change</td>
<td>4 to 150 mg/day or 300 mg/3x weekly</td>
<td>No published clinical experience.</td>
</tr>
<tr>
<td>Indinavir</td>
<td>1000 mg every 4 hours</td>
<td>4 to 150 mg/day or 300 mg/3x weekly</td>
<td>Rifabutin AUC 4 by 100%, indinavir concentrations 4 by 14%.</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>No change</td>
<td>4 to 150 mg/day or 300 mg/3x weekly</td>
<td>Rifabutin AUC 4 by 200%, no significant change in indinavir concentrations.</td>
</tr>
</tbody>
</table>
Remember

- Rifamycins can be safely added to almost any regimen.

- Every effort should be made to treat within the CDC guidelines to
  - increase the chances of treatment success,
  - decrease the chances of relapse and
  - minimize the length of time with toxicities.
When should HAART be started when being treated for TB?

- **Considerations**
  - Treatment of HIV improves outcomes in patients with TB
    - Decreased death or relapse
  - Multiple medications with multiple potential toxicities that are overlapping

- If the CD4 count is < 200, generally most ID physicians would treat for HIV with treatment for TB

- If the CD4 count is > 200…
  - Arguments to start both treatments concurrently
  - Arguments to delay the start of HAART
Case Scenario #3

- A 30 year old black woman presents with fever, chills, night sweats and a 20 lb weight loss over the past month. She has large anterior cervical lymph nodes and a left lower lobe infiltrate.

- Biopsy of one of the lymph nodes reveals granulomas and AFB which are probe positive for Mtb. After further testing, the patient is found to be HIV positive with a CD4 count of 80.

- The patient is started on 4 drug therapy and, once stable on anti-TB drugs, is started on HAART with efavirenz.

- Two months into treatment, the patient has worsening cough, a return of fevers, night sweats and worsening LAD.
  - How do you proceed with this patient?

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**Immune Reconstitution Inflammatory Syndrome (IRIS)**

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Yes (n = 21)</th>
<th>No (n = 114)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>34.2 ± 6.9</td>
<td>34.5 ± 7.2</td>
<td>0.896</td>
</tr>
<tr>
<td>Body weight at diagnosis</td>
<td>153.1 ± 6.8</td>
<td>150.2 ± 8.7</td>
<td>0.153</td>
</tr>
<tr>
<td>GRANAT score</td>
<td>2 (14.3%)</td>
<td>2 (9.5%)</td>
<td>0.533</td>
</tr>
<tr>
<td>Size of TB</td>
<td>2 (9.5%)</td>
<td>2 (9.5%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Extrapulmonary TB</td>
<td>1 (4.8%)</td>
<td>1 (0.7%)</td>
<td>0.494</td>
</tr>
<tr>
<td>HIV-based ART</td>
<td>12 (57.1%)</td>
<td>7 (63.8%)</td>
<td>0.361</td>
</tr>
<tr>
<td>Baseline CD4 cell count,</td>
<td>44 (19-84)</td>
<td>34 (12-67)</td>
<td>0.082</td>
</tr>
<tr>
<td>ART regimens</td>
<td>4 (3-7)</td>
<td>4 (1-6)</td>
<td>0.878</td>
</tr>
<tr>
<td>Baseline plasma HIV RNA,</td>
<td>570,000 (333,500—750,000)</td>
<td>423,000 (148,000—750,000)</td>
<td>0.071</td>
</tr>
<tr>
<td>Positive culture of M. tuberculosis</td>
<td>5 (23.8%)</td>
<td>4 (32.7%)</td>
<td>0.623</td>
</tr>
<tr>
<td>Increment of CD4 cell count at 3 months, cells/mm³</td>
<td>32 (17-150)</td>
<td>63 (36-126)</td>
<td>0.979</td>
</tr>
<tr>
<td>Increment of SCr at 3 months, mg/dL</td>
<td>5 (3-11)</td>
<td>4 (2-6)</td>
<td>0.022</td>
</tr>
<tr>
<td>Drop in log HIV RNA at 3 months, log 10 copies/mL</td>
<td>3.9 (3.5–4.2)</td>
<td>3.8 (3.4–4.1)</td>
<td>0.499</td>
</tr>
</tbody>
</table>

**Manosuthi et al. 2006. Journal of Infection, p. 1-7**
### Table 3  Logistic regression of possible risk factors for TB IRIS

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Extrapulmonary TB</td>
<td>9.764</td>
<td>2.195 - 43.441</td>
</tr>
<tr>
<td>Abdominal tuberculous lymphadenitis</td>
<td>4.059</td>
<td>1.104 - 14.918</td>
</tr>
<tr>
<td>% CD4 change from baseline &gt; 4%</td>
<td>2.213</td>
<td>0.871 - 5.625</td>
</tr>
<tr>
<td>Baseline HIV RNA &gt; 5.0 log</td>
<td>3.306</td>
<td>0.420 - 26.024</td>
</tr>
<tr>
<td>Drop in HIV RNA &gt; 3.5 log</td>
<td>1.458</td>
<td>0.500 - 4.250</td>
</tr>
</tbody>
</table>

OR, odds ratio; 95% CI, 95% confidence interval.

One more thing......

Co-trimoxazole prophylaxis

![Graph showing the proportion of deaths over time for Co-trimoxazole and Placebo groups.]

<table>
<thead>
<tr>
<th>At risk</th>
<th>Time (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Co-trimoxazole</td>
</tr>
<tr>
<td>416</td>
<td>219</td>
</tr>
<tr>
<td>219</td>
<td>108</td>
</tr>
<tr>
<td>108</td>
<td>33</td>
</tr>
<tr>
<td>419</td>
<td>33</td>
</tr>
</tbody>
</table>

Fig 2  Time to death according to trial drug (based on 835 HIV positive patients newly diagnosed as having, and being treated for, tuberculosis)
THEY ALWAYS COME BACK

Do It Right The First Time!

Barbara Seaworth

Thanks!!

Questions?

1-800-TEX-LUNG