TB Nurse Case Management
Norman, Oklahoma
October 8-10, 2008

Diagnosis and Treatment of Tuberculosis
David E. Griffith, MD
October 8, 2008

Diagnosis and Treatment of Tuberculosis

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Increasing Complexity of TB Control Efforts

- Foreign born
- Drug Resistant
- TB in recipients of TNF alpha blockers
- TB in transplants
- TB in dialysis and chronic renal failure
- HIV TB
- MDR TB

- Decreasing clinical experience
- Loss of traditional experienced workers
- TB care is more specialized
- Shift of services to private sector
  - Providers may see only one case in a lifetime of practice

Good Outcomes Depend on Complete Evaluation and a Correct Diagnosis

- Medical Evaluation
  - Signs and symptoms
  - History of risk factors and/or exposures
  - Physical exam
- Chest X-ray
- Bacteriology
  - Cultures of suspected site
  - Susceptibility testing of positive isolate
  - Rapid diagnostic tests (HPLC, NAA)
Where Are Patients Diagnosed With TB?

• California, 18 counties with highest TB morbidity
  – Hospital inpatient evaluation 45%
  – Outpatient clinic evaluation 32%
  – TB clinic 12%

• Seattle, Washington
  – Outpatient evaluation 48%
  – Hospital evaluation 32%
  – TB clinic 2%

Diagnosis of Tuberculosis

• Clinical suspicion is the single most important factor in the timely diagnosis of tuberculosis.

• The greatest risk for nosocomial transmission of tuberculosis is exposure to an undiagnosed case of TB.

• There is no diagnostic substitute for thinking about the diagnosis.
Reasons a Diagnosis of TB is Missed or Delayed

• Patient is diagnosed as a community acquired pneumonia and responds to a fluroquinolone
• Atypical clinical and radiographic picture
• Extrapulmonary disease
• Clinician does not consider TB a diagnosis

TB in a Recent Refugee
Classic Presentation of TB

• **Risk factors**: immigration from high incident area, homelessness, incarceration, IVDU, exposure to TB

• **Classic symptoms**: prolonged cough, sputum, fever, weight loss, night sweats

• Positive tuberculin skin test (TST)

• Positive QuantiFeron TB Gold Test

• CXR with upper lobe cavitary infiltrates

Atypical Presentation of TB

• HIV infection, chronic renal disease, diabetes, immunosuppression may alter presentation
  – CXR may be atypical; lower lobe infiltrate, adenopathy or completely normal
  – Negative TST or QTF Gold
  – Negative smear in up to 50%
  – Atypical clinical presentation
Diagnosis May Be Missed by Negative Evaluations

- CXR normal in 10% HIV +, atypical in others
- Smear neg ≥ 40%
- AFB smear
- TST
- TST neg ≥ 40%
- Symptoms may be absent or atypical

Consideration of Risk Important Especially with Negative Tests

THINK TB!

Case Study-Late Diagnosis

- 25 yr old male with 9 month history of cough and weight loss
- ER visit 6 months earlier for “bronchitis”
- Incarcerated along border x 2 yrs
- Large # family contacts and small children
- Worked as a caterer
- Picked up from mall by EMS due to severe coughing spell
Delay in Diagnosis of TB With Empiric Antibiotic Use

- Prospective study to assess delay in dx
  - June 2000 – Dec 2001 of patients who received antibiotics for non-Tb dx before Tb dx
  - 85/158 Tb patients received antibiotics first
    - 30 patients received more than one course
    - 52 courses FQN to 45 patients (38%)
    - 33 courses macrolides to 29 patients (24%)
    - 11 courses amoxicillin
    - 11 courses cephalosporins
    - 10 courses trimethoprin-sulfamethoxazole
    - 2 courses of clindamycin, 1 of vancomycin
    - 17 courses unknown

» Int J Tuberc Lung Dis 2005;9:392-397
Delay in Diagnosis of TB With Empiric Antibiotic Use

- Median delay 39 days compared to 15 controls who did not receive antibiotics
- Delay similar with all antibiotic classes
- 41/54 (79%) patients who did not get CXR at first visit received antibiotics
- 41/105 (42%) with CXR at 1st visit received antibiotics
  – 31/54 (57%) dx with CAP received CXR
- More widespread use of CXR may help

Int J Tuberc Lung Dis 2005;9:392-397

Guidelines for Evaluation of Pulmonary TB in Adults

- Any cough ≥ 2-3 wks plus at least one additional symptom: fever, night sweats, weight loss or hemoptysis
- Any high risk for TB; unexplained illness including respiratory symptoms ≥ 2-3 wks
- CXR: if suggestive of TB collect 3 sputum specimens for AFB and culture
- CXR: if suggestive of TB collect 3 sputum specimens for AFB and culture

Controlling TB in U.S. MMWR: Nov 2005
**Guidelines for Evaluation of Pulmonary TB in Adults**

- Any HIV infected with unexplained cough and fever
- Any at high risk for TB with dx CAP & not improved >7 days
- Any at high risk for TB with incidental findings on CXR of TB even minimal/no sx

- CXR and collect 3 sputum for AFB smear and culture
- CXR and 3 sputum for AFB smear and culture
- Review prior CXR if available, 3 sputum for AFB smear and culture

Controlling TB in U.S. MMWR: Nov 2005

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**Fever in 7th month of Pregnancy**

- 6 month history of cervical adenopathy
- 6 week history of fever, wt loss and abdominal pain
- Tuberculin skin test negative
- No response to multiple antibiotics
- Pleural effusion and infiltrate on CXR
Missed Diagnosis

Pulmonary consult for thoracentesis:
Cervical node biopsy: AFB+, granuloma
Disseminated disease
  nodes, lung, liver, ascites, multiple
  abdominal masses, **placenta**, ovaries, bowel
Clinical deterioration, hypotension, emergent C section

Missed Diagnosis

M Tb resistant to INH grew from sputum and nodes
Infant also treated for tuberculosis as placenta was positive for AFB
Missed Diagnosis

Pulmonologist consulted for thoracentesis obtained a **history of risk factors** for TB

Born in Mexico
Prior +TST at US entry at age 15
Treated with INH x 6 mo
Exposure to uncle in Mexico who died with TB 2 years ago

**TST usually negative with extensive disease!**
## Treatment of Tuberculosis

**American Thoracic Society, CDC, and Infectious Diseases Society of America**

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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 M Tb 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** (Levofloxacin-agent of choice) 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
Treatment of Culture-Positive Drug Susceptible Pulmonary TB

- 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)

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<tr>
<th>Drugs Currently in Use</th>
<th>First line</th>
<th>Second line</th>
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<tr>
<td>Isoniazid (H)</td>
<td>Ethionamide</td>
<td>Levofloxacin</td>
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<td>Rifampin (Rif)</td>
<td>Amikacin</td>
<td>Moxifloxacin</td>
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<tr>
<td>Rifabutin (RBT)</td>
<td>Capreomycin</td>
<td>Gatifloxacin</td>
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<tr>
<td>Rifapentine</td>
<td>Streptomycin</td>
<td>Clofazamine</td>
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<tr>
<td>Ethambutol (EMB)</td>
<td>Cycloserine</td>
<td>?Linezolid</td>
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<tr>
<td>Pyrazinamide (Z)</td>
<td>PAS</td>
<td>?Imipenem</td>
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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

Treatment of Culture Positive Pulmonary Disease

Regimens Rated \textit{A-1 (HIV Uninfected)}

\textbf{INITIAL PHASE}

2 mo I,R,Z,E daily (56 doses, 8wks) \textbf{or}
2 mo I,R,Z,E 5x/wk (40 doses, 8wks) \textbf{then}

\textbf{CONTINUATION PHASE}

-4 mo - I,R daily (126 doses, 18 wks) \textbf{or}
-4 mo – I,R 5x/wk (90 doses, 18 wks) \textbf{or}
-4 mo – I,R, 2x/wk (36 doses, 18 wks)

Continuation phase increased to 7 mo if initial CXR shows cavities and Sputum culture is positive at 2 mo
Treatment of Culture Positive Pulmonary Tuberculosis

- **Regimens Rated A-II (HIV Uninfected)**
  - Initial phase
    - 2 weeks – I,R,Z,E daily (14 doses) *then*
    - 6 weeks – I,R,Z,E *twice* weekly (12 doses)
  - Continuation phase
    - PLUS (DOT only)
    - -4mo – I,R Twice weekly (36 doses, 18 weeks) *or*

- **Regimens Rated A-III (HIV Uninfected)**
  - Initial phase
    - 2 weeks – I,R,Z,E 5x/week (10 doses) *then*
    - 6 weeks – I,R,Z,E *twice* weekly (12 doses)
  - Continuation phase
    - PLUS (DOT only)
    - -4mo – I,R Twice weekly (36 doses, 18 weeks) *or*
Treatment of Culture Positive Pulmonary TB

– THRICE WEEKLY – “HONG KONG” REGIMEN

» Regimen Rated BI (HIV uninfected)

– Initial phase
  • 2mo – I,R,Z,E 3x/week (24 doses, 8weeks)

PLUS

– Continuation phase
  • 4mo – I,R 3x/wk (54 doses, 18 weeks)

Baseline and Follow-up Evaluation

• Susceptibility testing on all initial isolates to INH, Rifampin & EMB

• For pulmonary TB – Monthly sputum until two consecutive cultures are negative
  – -2 month sputum is crucial
  – 80% should convert by 2 mo, 95% by 3 mo
TBTC STUDY 22: RATE OF FAILURE/RELAPSE, BY REGIMEN, SPUTUM CULTURE, AND CHEST RADIOGRAPH

![Graph showing rate of failure/relapse](image)

- **Rate of Failure/Relapse**
  - Positive: 16.7%
  - Negative: 8.9%
  - Cavitary: 2.5%
  - Non-Cavitary: 2.9%


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Prolongation of Continuation Phase

- **Rational for Extending Therapy**
  - Continuation of PZA for an additional 2 months was not helpful in drug susceptible disease
  - Prolongation of continuation phase by 2 months decreased relapses in silico-tuberculosis from 20% to 2%
Effect of Prolonging Therapy on Treatment Failure or Relapse

Treatment of Silico-tuberculosis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SHRZ - 6mo*</th>
<th>SHRZ – 8mo*</th>
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<tbody>
<tr>
<td></td>
<td>(n=49)</td>
<td>(n=50)</td>
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<tr>
<td>Relapse</td>
<td>20%</td>
<td>2%</td>
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* Three times weekly therapy

Am Rev Respir Dis 1991;143:262-267

New Treatment Guidelines
Tailoring Treatment Regimens

- Prolongation of continuation phase
  - Positive 2 month culture with cavitary disease
  - Extrapulmonary disease
    - Meningitis
    - Disseminated disease in children
  - HIV TB in children and adolescents
New Treatment Guidelines
Tailoring Treatment Regimens

• Consider Prolongation of continuation phase when patient:
  – Slow to clinically or radiographically respond
  – Positive 2 month culture OR cavitary disease?
  – <10% ideal body weight?

Relapse

• Circumstance in which a patient becomes and remains culture-negative while receiving antituberculosis drugs but at some point after completion of therapy, either becomes culture-positive again or experiences clinical and radiographic deterioration consistent with active tuberculosis
Treatment Guidelines 2003

• “Microbiological Confirmation of Relapse Should be Pursued Vigorously”
  – Confirm true relapse
  – Use DNA fingerprinting to identify new infection causing the disease versus relapse
  – Identify drug susceptibility pattern of isolate

Relapsed Tuberculosis

• Most relapses occur within the first 6 – 12 months after stopping therapy but some occur 5 or more years later
• Nearly all drug susceptible patients who were treated with a rifamycin and received DOT will relapse with drug susceptible organisms
  – Treat with standard RIPE regimen
Relapsed Tuberculosis
“situations of concern”

• If no culture or susceptibility studies are done there may be an increased risk of drug resistance as a cause of relapse (foreign born)
  – Usual treatment with RIPE
  – Watch carefully for clinical deterioration, may need to expand the regimen
    • Consider an expanded regimen if immune suppressed and significant disease

• Patients treated with self administered therapy and those non compliant are at risk of resistance
  – Consider expanded regimen, especially if immune suppressed
    • RIPE plus a fluoroquinolone and an injectable
Treatment Related Risk Factors for Early Relapse of TB

• Evaluation of 113 cases of relapsed Tb when matched with case controls
  – Non-cavitary Tb, relapse rate: 1.1%
  – Cavitary Tb relapse rates:
    • Thrice weekly Rx: 7.8%
    • Daily Rx: 3.3%
    • Extended thrice weekly: 0.5%
    • Extended daily: 0.4%
    – Extending either intensive phase or both was beneficial

  » Chang, Am J Respir Crit Care Med. 2004; 170: 1124-30

Dose-Response Relationship
Daily versus Intermittent Therapy

• Review of trials, 200 cases of relapse, 6 mo Rx
• Relapse rates higher when intermittent therapy used especially in initiation phase
  – Daily IP, 3 x/wk CP: 1.6%
  – Daily IP 2x/wk CP: 2.8%
  – 3/wk IP and CP: 5.0%
• Relapse higher especially with cavitary disease and + 2 month cultures
  – Only 6 month daily or 6 mo daily IP and 3/wk CP had relapse rates <5%

  » Chang Am J Respir Crit Care Med 2006; Vol 174 p 1153
Medical Factors Associated With Relapse of Tuberculosis

- Cavitary TB
- Extensive disease on CXR
- Positive 2 month culture
- Associated medical conditions
  - Diabetes
  - HIV
- Tuberculous lymphadenitis
- Underweight at diagnosis and failure to gain
- Drug resistant disease
- Prior treatment for tuberculosis

Treatment Factors Associated with Relapse of Tuberculosis

- Dosing intensity
- DOT
- Adherence
- Duration of therapy
  - Intensive phase
  - Continuation phase
  - Both
- Rifampin containing regimen
In the Treatment of TB, You Get What You Pay For…

- “A consistent theme has begun to appear: more extensive disease requires more treatment, and the fewer total doses, the higher the risk that treatment will prove inadequate”
  - What should we conclude?
    - First: More is more and less is less
      - More treatment means more cures
    - Second: Programs need to consider some individualization of therapy
    - Third: This should not deter us from intermittent therapy but should remind us that sophisticated management based on case-specific circumstances is still needed
      - We should not be surprised that individuals differ in their response.


Case Study

- 47 yr old male, recurrence of TB
  - Weight at Dx 117 pounds (<10% IBW)
  - Two months, 114 pounds
  - Three months, 114 pounds
  - Four months, 115 pounds
- Extensive cavitary disease on CXR
- Sputum smear + 5 ½ months
- Sputum culture + 3 ½ months
Lack of Weight Gain and Relapse Risk, TBTC Study 22

- Relapse risk high in those underweight at diagnosis 19.1 versus 4.8%
- Among pts underweight at Dx, weight gain ≤ 5% after 2 mo Tx:
  - Relapse risk 18.4 vs. 10.3%
  - If also cavitary disease: 18.9%
  - If cavitary and + 2 month culture: 50.5%

Weight as A Risk Factor

- Relative risk of TB during 8-19 yr f/u of 1,717,655 Norwegians in screening program was 5 times greater in the lowest body mass index (BMI) category


Problems with TB Treatment

- Rifampin is the KEY DRUG for all “short course” (≈ 6 month) regimens.

- Rifampin is THE most potent inducer of hepatic microsomal enzymes known.
Rifamycin Drug Interactions

- HAART (Protease inhibitors and efavirenz)
- Medications for other comorbidities
  - Itraconazole, Fluconazole
  - Clarithromycin
  - Methadone
  - Coumadin
  - Immunosuppressive therapy for transplants
  - Chemotherapeutic agents

Rifabutin may be a good substitute to minimize interactions

Extrapulmonary TB

- Treatment regimens similar to pulmonary TB EXCEPT for
  - TB meningitis – optimal therapy still not defined; 9-12 months recommended (AIII)
  - Disseminated TB in children
  - ?? Disseminated TB in adults
    - Can you really use 6 month therapy?
Active TB During Pregnancy

- Treatment:
  - INH, Rifampin, Ethambutol x 9 months
    - Stop ethambutol if susceptible to INH and rifampin
  - Follow carefully for hepatotoxicity
    - During pregnancy
    - Three months postpartum

Therapy in Special Situations
Renal Disease

- No change in dose or dosing interval for INH and Rifampin even with severe renal disease
- If creatinine clearance <30
  - Modify dosing intervals of EMB and PZA
  - If sensitivity known, treat with I,R, +/- Z
- Dose medications after dialysis
- Serum drug levels especially for EMB
TB in Patients treated with TNF-α Antagonists

- TNF-α: key role in control of latent TB
  - Animal models
  - Clinical disease in recipients
- Current agents:
  - Infliximab (Remicade)
  - Etanercept (Enbrel)
  - Adalimumab (Humira)
- Treatment with these agents is associated with the development of active TB, often disseminated with aggressive progression of disease

TB reported more frequently than other OI

Warning: Risk Of Infections Infliximab

- Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation), ...and other opportunistic infections have been observed in patients receiving Remicade some of these infections have been fatal.
- Patients should be evaluated for LTBI with a TST.
- Treatment of LTBI should be initiated prior to therapy with Remicade.
- SEE WARNINGS
Warnings

- Remicade should not be given in patients with a clinically important active infection.
- Caution...when considering the use of Remicade in patients with a chronic infection or a history of recurrent infections.
- Patients should be monitored for signs and symptoms of infection while on or after treatment with Remicade.
- If a patient develops a serious infection Remicade should be discontinued.

TB in Patients treated with TNF-α Monoclonal Antibodies

- 70 cases of active TB reported in patients treated with infliximab (up to 5/29/01)
  - TB developed after median of 12 weeks
    - 48 developed disease after 3 or less infusions
  - 48/70 (69%) had extra pulmonary disease
    - 17 disseminated
    - 11 lymphatic, 4 peritoneal, 2 pleural
    - 1 each meningeal, enteric, paravertebral, bone, genital and bladder
    - Confirmed by biopsy in 33 patients
  - 12 patients died despite stopping TNF-α antagonist

Keane N Engl J Med 2001; 345: 1098-104
TB in Rheumatoid Arthritis and Effect of TNF-α Antagonists

• TB incidence in 6,460 infliximab treated patients followed prospectively in Spanish data base
  – 61.9/100,000
  – No cases with other agents
• TB incidence in 10,782 patients 1998-1999 prior to widespread use of infliximab
  – 6.2/100,000
• Marked decrease in TB with use of screening
  – No cases in patients who had had TST or prophylaxis
  » Gomez-Reino Arthritis Rheum 2003; 48:2122-2127

Management of Patients with Suspected Infection Receiving Treatment with TNF-α Antagonists

• Stop TNF-α antagonist if fever and other signs/symptoms consistent with an infectious process occur in a patient at possible risk for tuberculosis,
• Aggressive evaluation
• Start empiric therapy for suspected pathogens while waiting cultures
  • Dual infections have been reported
• Disagreement about when or whether TNF-α antagonist can be restarted.
Beyond the Guidelines

- **Do not use TNF-α antagonist during active serious infection**
  - Hold Rx at least until smears (cultures?) negative & pt well
  - Attempt to complete TB Rx prior to restarting. (Keane NEJM)
  - RATIO: Resumption of TNF blocker not recommended
    » French cooperative group - Ann Rheum Dis 2003; 62: 791-792
  - In setting of active disease pts must complete RX before infliximab
- **Use the least immunosuppressive agent**
  - Infliximab is associated with highest risk of TB
- **Immunosuppressive effects of infliximab continue for at least 2 months after stopping drug.**
  - Continue to suspect OI’s 6 mo after d/c of drug
- Steroid therapy safe during TB treatment

Management of Delayed Bacteriologic Response

- If cultures positive at 2-3 months:
  - Extend therapy if cavitary disease
  - Evaluate possible causes
    - Non-compliance
    - Unrecognized drug resistance
    - Malabsorption
  - Repeat susceptibility studies
  - Evaluate clinical and radiographic response
Prolonged Positive Smears

- 51 year old male
- Slow clinical and CXR improvement
- Prolonged conversion of cultures (10 weeks)
- Prolonged conversion of smears (7½ months)

W.C. 12-18-01

Significance of Persistent + AFB Smears

- Review of lab data of 428 patients, 30 with smear persistently + >20 weeks
  - 23/30 had a negative culture
  - 7/30 positive culture "treatment failure"
- Of those with negative cultures - none relapsed
- Most received standard therapy for 12 months; PZA was continued for 2-3 months
  » Al-Moamary Chest 1999; 116:726-731
Prolonged Positive Smears

• 12 months of RX
• Culture and smear – 20 months after stopping TB meds
• CXR still extensive cavitary infiltrates

DX and Management of Treatment Failure

• Treatment failure: “Patients whose sputum cultures remain positive after 4 months of treatment are considered to have failed treatment”

• “Patients with treatment failure should be assumed, until proven otherwise, to have drug-resistant organisms and be treated with multiple agents that they have not received before.

• A single drug should never be added to failing RX

• It is “prudent to add at least 3 new drugs”
  » MMWR Treatment of Tuberculosis 2003; 52
Tuberculosis Drug Serum Level Monitoring

• Routine therapeutic drug level monitoring not recommended

• Drugs which exhibit concentration dependent killing (fluroquinolones, rifampin, amikacin and streptomycin) may be more effective and less toxic if dosing is individualized and maximized
  – Especially in toxic or poorly responding patient

Tuberculosis Drug Serum Level Monitoring Recommended

• Delayed response to therapy
• Advanced AIDS with evidence of malabsorption
• Seriously ill patient to maximize therapy
• Toxicity evaluation
• Use of second line drugs
• Acquired drug resistance
• Relapse
• Potential for drug-drug interactions
• Renal and hepatic insufficiency
Low serum INH and Treatment Failure

• In patients treated with once weekly INH/Rifapentine all INH pharmacokinetic parameters lower in pts with failure/relapse
  – Median INH AUC₀-₁₂
    • 36 in 22 pts with failure or relapse
    • 55.9 mcg/hr/ml in 49 with cure.
  – 2 HIV + pts with acquired rifamycin resistance had very low INH levels and pharmacokinetic parameters.

• Twice weekly INH/Rifampin AUC were similar in pt with failure/relapse and cure
  » Weiner AJRCCM 2003

Low Rifabutin Levels Associated with Rifampin Resistance

– Pharmokinetic evaluation of HIV+ patients in rifabutin trial
  – (Rifabutin 300mg/INH 300mg daily)

• Patients with treatment failure or relapse with acquired rifamycin resistance
  – Had significantly lower rifabutin levels measured by area under curve
  – Patients also had significantly lower INH levels
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–, may stop
  – Repeat culture
    • >3 month interruption restart from beginning
    • <3 month interruption, culture + restart
    • <3 month interruption, culture - give an additional 4 months

Lessons

• Clinical TB Issues May Not Be Answered by Prospective Controlled Studies

• Discuss Difficult Case Management with Colleagues with Clinical TB Experience
When to Ask for Consultation

- HIV TB
- Renal Disease
- Drug resistance
- Slow to convert
- Treatment relapse
- Treatment failure
- Toxicity
- Management of treatment interruptions
- When you have a question you need answered

Where to get more information

- HEARTLAND NATIONAL TB CENTER
  - 1-800-TEX LUNG: Medical Consultation and Technical Assistance Line
  - Future training courses
- CDC
- TB Educate
- TBresources.com