TB Intensive
San Antonio, Texas
April 6-8, 2011

Tuberculosis and Co-Morbidities
Barbara Seaworth, MD
Friday April 8, 2011

Barbara Seaworth, MD has the following disclosures to make:

• Has received research funding from Otsuka Pharmaceuticals.

• No relevant financial relationships with any commercial companies pertaining to this educational activity.
Tuberculosis and Co-Morbidities

Barbara J. Seaworth MD
Medical Director, Heartland NTBC
Professor of Medicine, UT Tyler

Objectives

• Discuss the impact of diabetes on TB

• Identify impact of rifampin on blood sugar and oral agents for treatment of diabetes

• Identify risk of active TB in patients on anti-Tumor Necrosis Factor (TNF) agents

• Evaluate and manage chronic kidney disease patients with tuberculosis exposure or disease
Type 2 Diabetes

• Increased risk has been noted in many racial and ethnic populations

  – African Americans
  – Hispanic/Latino Americans
  – Native Americans
  – Asian Americans

• Globally urbanization has fueled an increasing incidence in Africa, India, Asia
  • Areas of world with high rates of tuberculosis

Prevalence of Diagnosed Diabetes by Race/Ethnicity and Age in Persons 18 & Older

<table>
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<tr>
<th>AGE</th>
<th>White non-Hispanic</th>
<th>Black, non-Hispanic</th>
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<td>8.3</td>
<td>13.0</td>
<td>11.1</td>
<td>8.1</td>
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</table>

» Texas Diabetes Fact Sheet, 2009
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008


Age-adjusted percentage of adults aged ≥20 years with diagnosed diabetes, 2007

MMWR 58:1259-1263, 2009
Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

Obesity (BMI ≥ 30 kg/m²)

<table>
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<th>Year</th>
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<th>&lt;14.0%</th>
<th>14.0-17.9%</th>
<th>18.0-21.9%</th>
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</table>

Diabetes

<table>
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<tr>
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<th>4.5-5.9%</th>
<th>6.0-7.4%</th>
<th>7.5-8.9%</th>
<th>&gt;9.0%</th>
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<td>2008</td>
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</table>


Does Diabetes Predispose to TB?

DOES TB INCREASE THE RISK OF DIABETES?
Diabetes: a Moderate to Strong Risk Factor for TB

- 2008 Meta analysis
  - 13 studies many areas of world showed increased risk of TB in persons with diabetes
    - 3 prospective cohort studies showed RR 3.1
    - 8 case-control studies and 2 other types- OR 1.2-7.8
  - Association of Diabetes and TB stronger
    - With higher background TB incidence
    - In younger age groups
    - In Central America, Asia, Europe
    - Among North Americans the RR for Hispanics 2.69

  Jeon, PLoS Medicine, 2008

Diabetes Predisposes to TB

- Hong Kong prospective study of 4661 close contacts of active TB cases
  - RR 3.4 in diabetics for both
    - early – primary progressive disease (3month)
    - and late– reactivation (within 5 years) disease

  Lee MS, Int J Tuberc Lung 2008
Risk of TB Related to Degree of Diabetic Control

- Actuarial probability of developing TB was 24% in IDDM and 4.8% in NIDDM

- 1592 diabetics in Chili followed prospectively from 1959-1982

Prospective study in Tanzania, diabetic patients followed 1 – 7 years

- 9.0% IDDM versus 2.7% NIDDM developed pulmonary TB

Growing Diabetic Epidemic Will Have a Significant Impact on TB Control
Global Prevalence of Tuberculosis and Diabetes, 2008

**Tuberculosis**
- 12.7 million people
- (9.4 WHO 2010)
- 95% in developing countries

**Diabetes Mellitus**
- 171 million people
- (285 WHO 2010)
- 70% in developing countries

(Source: World Health Organization, 2008)

Projected prevalent DM incidence & TB Incidence

Figure: Projected prevalent diabetes cases and current worldwide tuberculosis incidence. Estimated number of individuals with diabetes mellitus in 2005 compared with WHO projections are shown. Tuberculosis incidence per 100,000 population in 2005 and 2030 are shown. Data from International Diabetes Federation and WHO.17

Dooley, & Chaisson, Lancet ID, Dec, 2009
At Risk Populations and Behaviors for TB and Diabetes

TB
- HIV/AIDS
- Immune Suppression
- Alcohol and Drug Abuse
- Homeless Population
- Refugees
- Prisoners
- Migrant Farm Workers
- Health Care Workers

Diabetes
- Overweight / Obesity
- Cardiovascular Disease
- Family History
- Polycystic Ovary Syndrome (PCOS)
- Native Americans
- Hispanics
- Asian / Pacific Islanders
- Blacks
- Older Age
- Unhealthy Diet
- Smoking
- Vitamin D deficiency

Other risk factors for TB and Diabetes

- **Smoking**
  - Active smoking associated with significant increase in risk of diabetes RR 1.4
    » Will, JAMA 2007
  - Exposure to passive smoke increases RR 1.81
    » Hayashino, Diabetes Care, 2008
  - Asia 50-60% of male population smokes

- **Vitamin D deficiency**
  - Increases risk of type 1 and type 2 diabetes
  - Also associated with active TB
    - Odds ratio 2.9
    - Deficiency may lead to TB and vice versa
      » Wilkinson, Lancet 2000
TB and Diabetes: Is Vitamin D the Missing Link?

- 1 billion people worldwide are Vitamin D deficient due to decreased sun exposure or inadequate intake

- Vitamin D is thought to affect pancreatic β cell function and immune response
  - Low concentrations associated with insulin resistance and glucose intolerance
  - Deficiency increases risk of type 1 & type 2 diabetes
  - Supplementation is protective against both types

- Vitamin D deficiency is associated with active TB
  - Actions of monocytes and phagocytes on M TB dependent on Vitamin D
    » Handel & Ramagopalan, Sept 2010, Lancet Inf Dis

Vitamin D Deficiency in Adults

- CDC notes decline in adults who have adequate levels of Vitamin D
  - 30% whites, 5-10% blacks

- Who should be tested?
  - Decreased intake (poor nutrition)/Limited sun exposure
  - Gastrointestinal illness with malabsorption
  - Hepatic disease
  - Chronic renal disease (GFR < 60%, nephrotic syndrome
  - Aging
  - Diabetics?
    » Kennel et al, Mayo Clinic Proc; August 2010
Linkage Between Tuberculosis and Diabetes

Latent TB Infection (LTBI) in Diabetic Patients

- Persons with diabetes should be screened for TB with an IGRA or TST
  - Communicate risk of progression to disease to community physicians caring for diabetics
  - If LTBI is found, treat for latent infection
  - INH for 9 months is best approach
  - Be sure to include Vitamin B6
    • Neuropathy is complication of diabetes and a side effect of INH
Presentation of TB in Diabetics

- Various reports of more severe disease

- Varying findings as to the radiographic presentation
  - ? More cavities
  - ? Isolated lower lung involvement

Classic Article Prior to Availability of TB Medications
Howard Root MD, Deaconess Hospital, Boston
NEJM, 1934

Autopsy series of 126 patients: no pathological findings unique to “the tubercular diabetic”

245 TB cases in diabetic patients, "no special insidiousness" of signs or symptoms and similar CXR findings to non-diabetics

Noted that TB developed most frequently in patients with poor diabetic control

Dooley, & Chaisson, Lancet ID, Dec, 2009
## TB and Diabetes, CXR Findings

<table>
<thead>
<tr>
<th>Year</th>
<th>Study location</th>
<th>Participants (n)</th>
<th>With diabetes</th>
<th>Without diabetes</th>
<th>Lower lung more commonly involved</th>
<th>More scattered lesions?</th>
<th>More diffuse involvement?</th>
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<td>USA</td>
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<td>1996</td>
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<td>1998</td>
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<td>2008</td>
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<td>2009</td>
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<td>57</td>
<td>78</td>
<td>-</td>
<td>-</td>
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</table>

*Apart from the study by Lawrence et al., high computed tomography was used. Patients with diabetes mellitus or who were immunocompromised. Patients with tuberculosis, of whom 15 had lower lung disease, result in dependent diabetes mellitus had more centriac disease than non brain dependent diabetes mellitus. In subgroup analysis, diabetes mellitus was a risk factor for lower lung disease in patients aged ≥60 years. — Not reported.

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### Does Diabetes Impact TB Treatment and Cure?

- Previously thought not to affect treatment

- Four new studies from Baltimore, Texas, Taiwan and Indonesia reveal:
  - Delayed culture conversion
  - Higher mortality
    - Dooly, 2009; Restrepo 2008; Wang 2008; Alisahlanda, 2007
Response to Treatment

• Relapse may be more frequent
  – Recent Shanghai study 203 diabetics with TB followed for 2 years after standard treatment

  • 20% relapse rate in patients with DM (most Type 2)
  • 5% relapse rate in patients without DM

Zhang et al. Jpn J Infect Dis, 2009

Hyperglycemia in Patients with TB

• Blood glucose control may worsen while patients are taking Rifampin
  – Rifampin augments intestinal absorption of glucose
  – Does so in both diabetics and non-diabetics

• Infections impair glucose tolerance early in disease in both diabetics and non-diabetics
  – Independent of rifampin, infection can lead to poor glucose control
Does Diabetes Increase the Risk of TB?

Does TB Increase the Risk of Diabetes?

No evidence to suggest that having tuberculosis or taking medications for tuberculosis increases the risk for diabetes.

Increased hyperglycemia with active disease and with rifampin-induced medicine interactions, does not lead to development of diabetes.
Low Blood Levels of Rifampin in Diabetics: Indonesia

- 17 Patients with Diabetes and Tuberculosis
- Rifampin levels decreased 50%
  - Perhaps related to higher BMI in diabetics
- Is a different dose of rifampin needed?
  - Mg/kg?
  - Hanneke M. J. Nijland *Clinical Infectious Diseases*, 43 2006

Treatment Issues – Rifampin

- Rifampin induces CYP450 enzyme system increasing production of enzymes that metabolize many drugs
  - Increased metabolism results in lower blood levels of drug (20 – 40+%)
  - Affects many classes of diabetic medications
Induction of Cytochrome P450 (CYP) by Rifampin

![Graph](image)

**Fig. 1.** Effects of rifampin on cytochrome P450 (CYP) enzyme mRNA expression in primary human hepatocytes as determined by oligonucleotide-based microarrays. Induction was calculated as the normalised ratio of expression in rifampin-treated versus vehicle control-treated cells (from Rae et al., 2004 with permission).

Effects of Rifampin on Anti-diabetic Drugs

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Subjects (n), Study Design</th>
<th>Rifampin (mg/d)</th>
<th>Results</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Glibenclamide (glyburide)†</td>
<td>Healthy (10), randomised crossover</td>
<td>600 x 5d</td>
<td>36% ↓ in AUC, 22% ↓ in C_max, 17% ↓ in t½g; 44% ↓ in blood glucose decremental AUC, 36% ↓ in maximum ↓ of blood glucose</td>
<td>Monitor blood glucose carefully and increase dosage as necessary</td>
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<tr>
<td>Glimepiride‡</td>
<td>Healthy (10), randomised crossover</td>
<td>600 x 5d</td>
<td>34% ↓ in AUC, 25% ↓ in t½g</td>
<td>Monitor blood glucose carefully and increase dosage as necessary</td>
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<tr>
<td>Glipizide§</td>
<td>Healthy (10), randomised crossover</td>
<td>600 x 5d</td>
<td>22% ↓ in AUC, 18% ↑ in C_max, 35% ↓ in t½g</td>
<td>Monitor blood glucose carefully and increase dosage as necessary</td>
</tr>
<tr>
<td>Repaglinide†</td>
<td>Healthy (8), randomised crossover</td>
<td>600 x 5d</td>
<td>57% ↓ in AUC, 41% ↓ in C_max, 21% ↓ in t½g, blood glucose decremental AUCg ↓ by 1.2 mmol • h/L, 37% ↓ in maximum ↓ of blood glucose</td>
<td>Monitor blood glucose carefully and increase dosage as necessary</td>
</tr>
</tbody>
</table>

*AUC = area under the concentration-time curve, C_max = peak concentration, d = days, t½g = elimination half-life, ↑ indicates increase; ↓ indicates decrease.*

Clin Pharmacokinet 2003; 42 (9)
TB and Diabetes - Treatment Issues

- **Diabetic neuropathy** at baseline complicates therapy due to INH-related neuropathy
  - Baseline assessment of neuropathy
  - Vitamin B6 (pyridoxine) to all diabetics on INH or ethionamide

- **Renal insufficiency** is associated with diabetes, especially long standing or poorly controlled diabetes
  - Adjust dose and dosing interval of EMB & PZA in those with Creatinine Cl < 30

TB and Diabetes - Treatment Issues

- Diabetics have an increased risk of hepatotoxicity
  - Multiple medications
  - Fatty liver

- Monitoring and education are very important
  - Baseline and monthly liver enzymes
  - Educate regarding risk of liver toxicity, symptoms to watch for, and what to do should these occur
    - Contact provider
    - Hold TB medications until liver injury excluded
Impact of Diabetes on TB Epidemic

- A transition is occurring in many countries as development increases -- the most common cause of morbidity and mortality is changing from "Infectious" to "Chronic" diseases
  - The impact of diabetes on TB threatens to cause an overlap that adds infectious disease to an increasing tide of chronic disease
  - Urbanization increases risk of both TB and diabetes

How Big?

- TB has never been big enough to really grab the world’s interest except for outbreaks of MDR in the 1990’s and now XDR TB in recent years
- HIV is really big as it affects many more people but-----
- Diabetes is hugh and it’s impact on TB incidence and control may be greater than the impact of HIV
Diabetes cases may double by 2050

And perhaps triple, with 1 in 3 having the disease

--By Mary Brophy Marcus, USA TODAY

October 22, 2010

The future of diabetes in America looks bleak, according to a new Centers for Disease Control and Prevention report out today, with cases projected to double, even triple, by 2050, according to the report, one in 10 U.S. adults have diabetes now. The prevalence is expected to rise sharply over the next 40 years with as many as one in three having the disease, primarily type 2 diabetes, according to the report, published in the journal Population Health Metrics.

“There are some positive reasons why we see prevalence going up. People are living longer with diabetes due to good control of blood sugar and diabetes medications, and we’re also diagnosing people earlier now,” says Ann Albright, director of the CDC’s Division of Diabetes Translation.

A more diverse America — including growing populations of minority groups such as African Americans and Hispanics, who are more at risk for the disease — factors into the increase as well, Albright says. But an increasing number of overweight Americans is also fueling the stark predictions for diabetes, which should be taken seriously, Albright says.

Diabetes and Tuberculosis: Mexico

• Prospective population based evaluation of pulmonary TB in Veracruz Mexico, using molecular epidemiological data
  – Risk of TB in diabetics was increased 7 times
  – Risk was increased in both reactivation and new infection

• Authors concluded that:
  – Increased risk due to diabetes is comparable to that found in other studies attributable to HIV
  – “When HIV prevalence in the study area was estimated based on national HIV prevalence, tuberculosis-attributable risk due to HIV was 2% compared with 25% due to diabetes”

  » Ponce-de-Leon, 2004 “TB and Diabetes in Southern Mexico”, Diabetes Care
Impact of Diabetes Epidemic on TB Incidence

• Epidemiological model to assess potential impact of diabetes as risk factor for incident pulmonary TB using India as example

• 2000 there were 20.7 million adults with diabetes and 900,000 with pulmonary TB
  – Model suggests diabetes accounts for 14.8% of pulmonary TB
  – And for 20.2% of smear positive TB

  – Increased TB in urban areas
    • is associated with a 15.2% greater smear + TB incidence vs rural

  » Stevenson et al, BMC Public Health, 2007

Impact of Diabetes Epidemic on TB Incidence

• “In India, HIV accounts for 3.4% of adult tuberculosis incidence, the proportion we estimate to be attributable to diabetes is 14.8%”

• “The current diabetes epidemic may lead to a resurgence of tuberculosis in endemic regions, especially in urban areas”

• “It is time that the “unhealthy partnership” of tuberculosis and diabetes receives the attention it deserves”

  » Stevenson et al, BMC Public Health, 2007
Recommendations from 2009 Consultation Meeting TB and DM

- Collaboration between diabetes and TB care and control initiatives

- Screening diabetics for active TB
  - Screening for LTBI benefit unclear
  - Screening for LTBI for increased risk

- Screening TB patients for diabetes
  - Initial diagnosis and at 3 months

- Management of TB and diabetes co-morbidity
  - Optimize case management, education, monitoring for adverse outcomes
Expert Meeting November 2009
Research Agenda for TB & DM

• IF and when to screen for TB in patients with DM and vice versa

• Impact of DM and non diabetes hyperglycemia on TB treatment outcomes and deaths

• Implementation and evaluation of the TB DOTS model for diabetes management

• Development and evaluation of better point of care diagnostic and monitoring tests for diabetes

What Can We Offer in TB Clinics?

• Include glucose or HB A1C on blood work.

• Educate on need to follow a healthy eating plan.

• Encourage physical activity for 30 to 60 minutes/day.

• Stress the importance of taking medicines as directed.

• Encourage patients to quit smoking.

• Refer for regular physician visits

• Educate on need for daily foot check for cuts, blisters, sores, swelling, redness, or sore toenails.
TB and Diabetes

- DM growing in prevalence world-wide
- Uncontrolled DM increases risk of TB
- TB often presents in more advanced stage in DM
- Treatment time may need to be longer in DM patients
- Implications in populations with high prevalence
- Screening across clinics for DM and TB is needed

TB in Patients treated with TNF-á Antagonists

- TNF-á: key role in control of latent TB
  - Animal models
  - Clinical disease in recipients
- Current agents:
  - Infliximab (Remicade)
  - Etanercept (Enbrel)
  - Adalimumab (Humira)
  - Certolizumab (Cimzia)
- Treatment with these associated with the development of active TB, often disseminated with aggressive progression
- TB reported more frequently than other opportunistic infections (OI)
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 database
  - 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
  - Gomez-Reino Arthritis Rheum 2003; 48:2122-2127

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
  - PDR 2004
### Table 3: Time to onset of tuberculosis after initiation of TNF antagonist therapy

<table>
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<tr>
<th></th>
<th>Infliximab</th>
<th>Etanercept</th>
<th>I:E</th>
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<tr>
<td>Wallis et al (AERS)</td>
<td>17 weeks</td>
<td>48 weeks</td>
<td>1:2.8</td>
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<tr>
<td>Wolfe et al (NDB)</td>
<td>21 weeks</td>
<td>...</td>
<td>n/a</td>
</tr>
<tr>
<td>Keane et al (AERS)</td>
<td>12 weeks</td>
<td>...</td>
<td>n/a</td>
</tr>
<tr>
<td>Askling et al (ARTIS)</td>
<td>19 weeks</td>
<td>32 weeks</td>
<td>1:1.7</td>
</tr>
<tr>
<td>Brassard et al (PharMetrics)</td>
<td>17 weeks</td>
<td>79 weeks</td>
<td>1:4.6</td>
</tr>
<tr>
<td>Total (weighted mean)</td>
<td>16.2 weeks</td>
<td>59.6 weeks</td>
<td>1:3.7</td>
</tr>
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</table>

Data are median time to onset (number of cases). Patients treated for any indication are included. AERS = Adverse Event Reporting System (US Food and Drug Administration). ARTIS = Anti-Rheumatic Treatment in Sweden. I:E = Infliximab to etanercept ratio. NDB = National Databank for Rheumatic Diseases. RATIO = Recherche sur Anti-TNF et Infections Opportunistes.

### Figure 2: Progression of M tuberculosis infection

- **All Anti-TNF α**
- **Anti-TNF α antibodies except Entanercept**
Risk of TB from Anti TNF Antibody Infliximab versus Etanercept

Wallis, Lancet Inf Dis, 2008

Development of Active TB by Drug

- New infections shortly after start of TNF alpha antagonist - Reactivation TB
  - Infliximab 20%/month
  - 12 to 1 times greater than with etanercept

- Both drugs caused an equally high proportion of new infections that progressed directly to TB disease

- Excess cases of TB with Infliximab due to more efficient reactivation of latent TB infection.

Wallis, Lancet Inf Dis, 2008
Risk of travelling to the country of origin for TB among immigrants living in a low-incidence country

- Moroccan patients had travelled more often (26/32 = 81%) in the preceding year than Moroccan controls (472/816 = 58%).

- The travel-associated odds ratio (OR) for TB among Moroccans was 3.2 (95%CI 1.3–7.7), and increased to 17.2 (95%CI 3.7–79) when the cumulative duration of travel exceeded 3 months.

- The corresponding population fraction of Moroccan TB cases attributable to recent travel was 56% (95%CI 19–71).

- Among Turkish immigrants TB was not associated with travel (OR 0.9, 95%CI 0.3–2.4).

Management of Patients with Suspected Infection Receiving 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.
Paradoxical Upgrading in TNF Alpha Blocker Recipients

- Reactions similar or worse in intensity to those noted in HIV infected individuals
- Anti-inflammatory treatment important therapeutic intervention
  - Steroids reported beneficial by Garcia et al in CID, 2005
  - Steroid use controversial by others

TB in Chronic Kidney Disease

- Increased risk of progression from latent to active TB with chronic kidney disease (CKD)
- Difficulty diagnosing & treating dialysis patient
  - Symptoms often mistaken for complications of dialysis
    - Cough (congestive heart failure, fluid overload), fever (bacterial infection)
  - Atypical presentation
    - Extrapulmonary TB, especially abdominal TB common
- Contact investigation in a dialysis center is challenging
  - Interpretation of TST and/or IGRA (BCG vaccinated persons)
  - Excluding active TB
    - Interpretation of symptoms
    - Interpretation of chest x-ray (heart failure, chronic infiltrates)
California TB Controller Association (CTCA) Recommendations

• TB skin test or IGRA
  – at diagnosis of CKD
  – When diagnosed with DM
  – Thirty days prior to admission to HD Unit
  – Thirty days prior to scheduled renal transplant
  – Annual/periodic
    • If TST – Two step should be done

TB Presentation in Dialysis Patient

• Pulmonary Atypical presentation
  – Fever – most common sign!
  – Weight Loss
  – Anorexia
  – Cough (may be present)

• TB Disease considered in ANY patient with
  – Recurrent pneumonia
  – Pneumonia not improved within 2 weeks of antibiotics – avoid fluoroquinolones May mask TB!
TB Presentation in Dialysis patients

• Extra pulmonary TB
  – More common in dialysis patients
  – Don’t forget to do SPUTUMS!!
  – Abdominal – (Peritoneal, liver, bowel, adenopathy)
    • TB peritonitis can be difficult to distinguish from bacterial
  – Any other site possible, evaluate if abnormal

TB Screening for CKD Patients

• TB Risk Assessment Questionnaire (RAQ)
  – Rule Out - Active TB!
  – Use Standardized risk assessment tool (RAQ)
CXR Findings of TB in CKD

- Cavitations, typical nodules and upper lobe infiltrates less common in late stage CKD
- Dialysis patients and transplant patients are immunocompromised and may have atypical findings on chest x-rays
  - Any lung region, especially lower lobes, miliary, diffuse, resembling pulmonary edema, or NORMAL
- Pleural effusions
Pleural Effusions

- Delay in TB Diagnosis can occur
  - If assumed that pleural effusions reflect volume overload or under dialyzed
  - Consider diagnostic thoracentesis
  - Pleural fluid or specimen biopsy
    - Expert consultation with TB doctor

Treatment Regimen: Active TB

- Initial Phase (first two months):
  - INH 300mg po daily or 900 mg thrice weekly
  - Rifampin 600mg po daily or thrice weekly
  - Ethambutol 15-25mg/kg po thrice weekly
  - PZA 25-35mg/kg po thrice weekly
  - Vitamin B6 50mg thrice weekly

- Continuation
  - INH and Rifampin x 4 – 7 months

- All doses should be given AFTER DIALYSIS
Airborne Infection Isolation (AII)

- Consider isolating patient during evaluation phase

- If dialysis center does not have isolation room patient may need to have inpatient dialysis

- Sputa Smear Positive patients should be isolated until
  - 3 consecutive negative sputum specimens at least 8 hrs apart
  - On appropriate treatment as indicated by drug susceptibilities
    - minimum of 14 days
  - Responding clinically to treatment