TB Screening and Diagnosis

Douglas B. Hornick, MD

Pulmonologist w/ Infectious Attitude
Division of Pulm/Crit Care/Occ Med
UI Carver College of Medicine

Disclosures: None
Objectives

• Rural (US) TB epidemiology indicates treating LTBI is an appropriate strategy

• Describe Screening for LTBI: TST and IGRA

• Describe current treatment for LTBI

• Describe monitoring recommendations
TB Nomenclature

• Latent TB Infection (~90% TB infections):
  – Positive TST (or IGRA eg, QFT-G)
  – No symptoms
  – Negative or chronic CXR changes
  – Can not transmit disease to others.

• Active TB Infection (~10% TB infections):
  – TST (or IGRA) may be positive
  – Symptoms present
  – CXR changes & sputum smear positive in most cases
  – Disease transmission to others

• Treatment for both latent and active infections

• Avoid terms: Prophylaxis, Preventive therapy
TB Pathogenesis
Progression to Disease

- Infection (LTBI)
  - 3-4% First Year
  - 1-2% Second Year
  - ~0.1% per year thereafter

Disease (Active Infection)

No Active Disease (~90%)
Epidemiology of Tuberculosis
TB in Foreign-Born Immigrants to US

- Proportion of TB cases foreign-born increased from <25% to 57% (1986-2006)
- US-born TB cases decreased by 45% (1993-2006)
- ~70% MDR TB occur among Foreign-born
  - Anticipate XDR TB & TDR TB
- SE Asians, Sub-Saharan Africans, & Latin Americans
- Concentrated in NY, NJ, Ca, Fl, IL, Tx
- Active cases most often arise from prior infection
- ~55% occur within 5 yrs of immigration
  - ≤ 2 yrs in US 75/100,000
  - > 2 yrs in US 16/100,000

CDC; Cain et al: JAMA 2008
Foreign-Born ⇒ US
TB Cases & Case Rates vs. Years in US

~30% Foreign-born coming into US unscreened...

Cain et al: JAMA 2008
Refugee & Immigrant TB Screening

• Within Country of Origin
  – Adults: Evaluated for Active TB only
  – Children (<15 yrs) & TB contacts screened (TST) in some countries but no LTBI Rx

• Arrival within US
  – TB Suspects are expected to f/u w/ local health dept (not mandated)
  – Applicants for adjustment of status evaluated for LTBI (Rx not mandated)

• Not evaluated…Estimates ~30%
  – Visitors, Temp Workers, Undocumented
  – Student visa

Immigration process doesn’t deal with LTBI for you…
“Tuberculosis is a social disease with medical implications”

–Sir William Osler
How do Rural TB rates compare to the National TB rates?
US vs. Foreign-Born TB Cases – Iowa 2012

US: 3.2 /100,000
Iowa: 1.5 /100,000
~1/yr drug resistant
Focus of TB Control in the US: Targeted Testing & Rx for LTBI

- Few cases due to transmission from other active cases (↓ HIV related cases)
- High rates of TB among foreign-born immigrants to US (including rural locales) from high incident countries
- “Targeted tuberculin testing” is the theme of the LTBI guidelines
- One of the main targets must be the foreign-born immigrants from high incident countries
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Estimate (vs. control w/ +TST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced HIV</td>
<td>9.9</td>
</tr>
<tr>
<td>Anti-TNF Rx</td>
<td>7.9</td>
</tr>
<tr>
<td>Old, healed TB</td>
<td>5.2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.1</td>
</tr>
<tr>
<td>Tobacco abuse</td>
<td>2.7</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
<td>2.4</td>
</tr>
<tr>
<td>Silicosis</td>
<td>1.7</td>
</tr>
<tr>
<td>Underweight (10% &lt; IBW)</td>
<td>1.6</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Targeted TB Testing
Decision to Test = Decision to Treat

- Patients at highest risk for progression to active TB
- Patients with medical conditions that increase risk for active TB
- Patients in whom active TB is more prevalent
Targeted TB Testing
Decision to Test = Decision to Treat

- Patients at highest risk for progression to active TB
- Patients with medical conditions that increase risk for active TB
- Patients in whom active TB is more prevalent
Targeted TB Testing

Decision to Test = Decision to Treat

Patients at highest risk for progression to active TB

• HIV infection, or risk factors for HIV infection
• Receiving TNFα antagonist for RA or Crohn’s
• Fibrotic lesion on CXR c/w prior pulmonary TB
• Close contact of persons with infectious TB (e.g., pulmonary, laryngeal TB)
• New TB infection (TST conversion within prior 2 years)
• IV drug abuser (HIV negative)
Targeted TB Testing
Decision to Test = Decision to Treat

• Patients at highest risk for progression to active TB
• **Patients with medical conditions that increase risk for active TB**
• Patients in whom active TB is more prevalent
Targeted TB Testing
Decision to Test = Decision to Treat
Medical conditions ↑ risk for progression to active TB

- Diabetes mellitus
- Tobacco abuse (NEW)
- Silicosis
- Jejunoileal bypass surgery or gastrectomy
- Solid organ transplant (e.g. renal, heart)
- Chronic renal failure/hemodialysis
- Head/neck carcinoma
- Hematologic malignancies (e.g. leukemia, Hodgkin’s)
- Immunosuppressed, particularly steroid treatment (≥15 mg/day, ≥ 1 month)
- Substantial weight loss: >10% ideal body weight
Targeted TB Testing
Decision to Test = Decision to Treat

• Patients at highest risk for progression to active TB
• Patients with non-HIV medical conditions that increase risk for active TB
• Patients in whom active TB is more prevalent
Targeted Skin Testing
Decision to Test = Decision to Treat
Patients in whom active TB is more prevalent

- Recent arrivals (< 5 years) from high TB prevalence countries (Africa, SE Asia, Pacific Isles, Latino, E. Europe, Russia)

- Resident or employee of high-risk congregate settings: prisons/jails, nursing homes/other long term facilities, hospitals/other health care facilities, residential facilities for AIDS patients, and homeless shelters

- Mycobacteriology lab workers
Case S. B.

• 56 yo female
• Asymptomatic
• TST+ (estranged husband had TB 20 years ago)
• On no drugs, no HIV risk factors, no EtOH
• Chest x-ray unremarkable
What is the diagnosis?

Latent TB Infection (LTBI)
New technology replacing old...
Mantoux Tuberculin Skin Test (TST)

• Standard (old) method of skin testing for *M. tuberculosis* infection
• Produces delayed-type hypersensitivity reaction
• TST is useful for:
  – Detecting LTBI
  – Contact investigation: Determining how many people in a group are infected
  – Evaluating persons who have symptoms of active TB
Administering the TST

• Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally on volar surface of lower arm using a 27-gauge needle
• Produce a wheal 6 to 10 mm in diameter
Low (Old) Tech…TST
Delayed-type Hypersensitivity Reaction @ 48-72 hrs

- Positive: 18 mm **Induration**
- A positive test may be measured up to 7 days out
- A negative reaction can be read accurately @ 48-72 hrs
Reading a TST

- Measure induration, not erythema by 48 to 72 hours
- Record induration size in millimeters, in addition to interpretation ("negative" or "positive")
- Ensure trained health care professional measures & interprets the TST
- Educate patient & family about the significance of a positive test
**TST Interpretation**

Positive classification based on pre-test probability of TB:

- $\geq 5\text{ mm} = \text{positive}$
  - HIV positive
  - Household or close contact to patient with infectious, active TB
  - CXR consistent with old/healed TB
  - Organ transplant or other immunosuppressed patient

- $\geq 10\text{ mm} = \text{positive}$
  - Foreign born (e.g. Africa, SE Asia, Hispanic, India, China, E Europe)
  - IV drug abusers
  - Residents or employee of high risk congregate setting
  - Non-immunosuppressive medical conditions known to increase risk of active TB
  - Mycobacteriology lab workers

- $\geq 15\text{ mm} = \text{positive}$
  - Persons in regions of low TB incidence
Limitations for TST

- **Interpretation variability; False positives:** NTM, BCG...
- **BCG Vaccine effect on TST Interpretation**
  - Induces 3-19 mm TST reaction in 1st few mos.
    - Reaction wanes significantly by 10 years
    - Reaction size does not correlate with protection
  - Positive TST most likely due to TB infection:
    - Persons from regions of high TB prevalence (e.g. hispanic, asian)
    - Large reaction (>15 mm)
  - Prior BCG, should be Tested and Treated if positive
- **Booster Phenomenon**
  - False negative TST, becomes positive as a result of skin testing
  - Most common situations:
    - Initial TB infection many years previous
    - Prior BCG immunization
  - Two Step Skin Testing (TST x 2, one week apart)
    - Elderly nursing home population
    - Prior BCG immunization
LTBI Testing Upgrade…
Interferon Gamma Release Assay (IGRA)

Measures interferon-gamma (IFN-γ) released by lymphocytes in response to specific TB antigens: ESAT-6, CFP-10

- QuantiFERON® Family:
  - QuantiFERON® -TB test 1999
  - QuantiFERON® - TB Gold 2005
  - QuantiFERON® - TB Gold In-Tube (GIT) 2007
    Added 3rd antigen TB7.7 (RD4) & travel time

- T-Spot. TB® Aug 2008:
TST vs IGRA

Presentation of TB antigens
- TST (Multiple = PPD)
- IGRA (Specific = ESAT-6, CFP-10)

IFN-γ
IL-8, etc.
TNF-α

TST

IFN-γ
IL-8, etc.
TNF-α

IGRA

Antigen Presenting Cell

Memory T-Cell


IGRA Results include control wells
- Negative (Nil) – no antigen (subtract from pt value)
- Positive – mitogen stimulation
IGRA vs TST

**IGRA**
- *In vitro*
- Specific antigens
- Unaffected by BCG
- No boosting
- One patient visit
- No inter-reader variability
- One standard result for all

**TST**
- *In vivo*
- Multiple antigens
- BCG affects results
- Boost occurs
- Two pt visits
- Inter-reader variability
- Different thresholds based on risk
QFT vs T-Spot.TB

- **Quantiferon TB (QFT):** Whole blood incubated w/ TB specific antigens. ELISA measures IFN-\(\gamma\) release

- **T-Spot.TB:** Lymphocytes (T) incubated w/ specific antigens. ELISPOT-method counts IFN-\(\gamma\) releasing cells
## IGRA Interpretation

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
<th>Gray Zone</th>
<th>Indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>QFT-TB Gold &amp; IT version</strong></td>
<td>≥0.35*</td>
<td>&lt;0.35*</td>
<td>None</td>
<td>Controls fail:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• High Nil</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Mitogen response</td>
</tr>
<tr>
<td><strong>T Spot.TB</strong></td>
<td>≥8 spots*</td>
<td>&lt;8 spots*</td>
<td>5-7 spots*</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

*TB Ag – Nil, assuming appropriate control response
• IGRA may substitute for TST
• IGRA preferred:
  – BCG vaccinated persons
  – Clients unlikely to return for TST reading
  – Low risk persons
• TST preferred in children <5
• Clinical judgment required when interpreting IGRA among immunosuppressed, children <5, & TB suspects
• Lab should be reporting quantitative results
Indeterminate IGRA Results

• Poor response to mitogen that resolves with repeat assay
  - Delayed specimen processing
  - Technical errors
• Persistent poor response to mitogen
  - Anergy from immunosuppression
  - May occur in healthy persons
• High background IFN-γ levels (high NIL response)
  - Often persistent, reasons unclear
  - IGRA not useful
Interpreting IGRA Results

• Contact investigation: If initial IGRA negative, Repeat test at 8-10 wks as one would with TST
• IGRA conversion = change from neg to positive
• Indeterminate result: Repeat IGRA or do nothing (don’t recommend TST generally)

Areas of uncertainty:
• Quantification of IGRA conversion (serial testing)
• Possible quantitative assessment of Rx response
Host Factors Creating False Negative TST & IGRA

- HIV (low CD4, no HART)
- <10 wks since TB infection
- Other infections (viral, fungal, bacterial)
- Lymphoma
- Live virus vaccination (eg, measles, smallpox)
- Immunosuppressive Rx
- Overwhelming TB (eg, miliary TB)
- Age (newborn, very old)
TST False Positives

- Cross reaction w/ NTM or BCG
- Immediate hypersensitivity misinterpreted as positive
- TST product switch (Tubersol vs Aplisol)

IGRA False Positives

- Cross reaction NTM: *M kansasii*, *M szulgai*, & *M marinum*
- Product failure such as endotoxin traces in tubes
- Lab error
Can IGRA Replace TST?

- Contact investigation: YES
- BCG vaccine Hx: YES
- Low risk person: yes
- Screening homeless & other unreliable persons: YES
- Serial Testing: Yes, but…
Real Life with IGRA

• Significant reduction in positive rate vs TST
• Increased frequency of retesting

• Serial testing issues:
  – Unexpected positives that require further review (eg, repeat testing, assessing quantitative results)
  – “Wobblers” = results hovering around cut point
LTBI: TST & IGRA ≠ Gospel

- Reassess TB risk factors
- Review symptoms
- Review CXR... evidence suggest old TB (Upper lobe fibrosis, Gohn lesion, Hilar Ca++)

- LTBI Rx decision should be based on complete certainty that active TB not present
Key Recent References

CDC. Updated Guidelines for Using IGRAs to detect M tuberculosis infection, US 2010. MMWR Recommendations and Reports June 25, 2010

Is This Really True?

- Apples, not Caffeine, are more efficient at waking you up in the morning
- You burn more calories sleeping than you do watching TV
- Donkeys kill more people annually than plane crashes and/or shark attacks…

So watch your ASS…
Tuberculosis Screening Flowchart

At-risk person

TST or IGRA & symptom review

Negative

Positive

Chest x-ray

Normal

Potential candidate for Rx of latent TB

Abnormal

Evaluate for active TB

Treatment not indicated
Back to SB, the case of LTBI

- Obtained:
  - TST (Mantoux) Positive
  - Chest x-ray Negative

- Do you need sputum smear and culture?
  
  Only if suspicious for active disease
  Not necessary in asymptomatic patient, positive TST, normal CXR
What Treatment for S. B.?

Optimal LTBI Rx…

- Short as possible to enhance completion rates (programmatic advantages)
- Minimally toxic
Treatment of Latent TB Infection
HIV Neg. & Pos. Adults
(Dept of Public Health provides meds)

1. Daily INH for 9 months (270 doses w/in 12 mos)*,+  
2. Daily INH for 6 months (100 doses w/in 9 mos)+  
   Exclude any w/ old healed fibrotic TB lesions on CXR  
3. 1*,+ or 2+ above, administered as DOT, twice weekly  
   76 doses w/in 12 months or 52 doses w/in 9 months  
4. Daily rifampin for 4 months (120 doses w/in 6 m)  
   Alternative for those who are known contacts with INH  
   resistant TB or INH not feasible  

Completion = Total # doses, not duration alone  
If > 2 month interruption, re-evaluate for active TB before  
restarting  

*Recommended for children < 18 years  
+Recommended for pregnant women.

ATS/CDC/IDSA 5/2000; Update 8/2003
TB Case Rates vs. No. of Months INH Treatment (Bethal Data)

Comstock GW: *Int J Tuberc Lung Dis* 1999
Even Shorter Treatment = Reality…

- **New regimen**: INH 900 mg plus Rifapentine 900 mg weekly x 3 months (12 doses, DOT)
- Open Label, Randomized Noninferiority trial 2011:
  - *New regimen* (DOT) vs INH x 9 mos (not DOT)
  - N ~ 8000 US & Canada x 33 mos (few HIV, children)
  - Target population: TST converters & +TST old healed TB chest x-ray
  - Result: *New Regimen* equivalent to 9 mos INH
    - Drug d/c d/t adverse events 4.9 vs 3.7%
    - Increased hypersensitivity (*New*) vs hepatotoxicity (INHx9)
    - Trend toward *New regimen* better than INHx9
      - *New Regimen* group: TB rate ~50% lower
      - Rx completion rate 82% vs 69%

Sterling TR et al. *NEJM* 2011;365:2155-66
New Regimen vs INHx9

Sterling TR et al. NEJM 2011;365:2155-66
Real World Recommendation

- *New Regimen* (DOT) does not replace INHx9, but equal option for Rx LTBI
- (Iowa) Dept Public Health provides INHx9 at no cost for anyone diagnosed w/ LTBI
- IDPH agrees *New Regimen* equivalent to INHx9
  - *New Regimen* costs 10x the standard INHx9 regimen
  - IDPH able to cover high cost of *New Regimen* (not DOT)
  - Policy for your state?
- *New Regimen* not recommended for the following:
  - Child <2
  - HIV/AIDS taking HART
  - Pregnant women
  - Contacts of INH &/or Rif resistant TB
Real World Dosing

• **INH:** 900 mg max for those ≥ 60 kg or 15 mg/kg rounded up to the nearest 100 mg
  Formulations: 300 & 100 mg tabs

• **Rifapentine:** 900 mg max for ≥ 50 kg
  10.0–14.0 kg  300 mg
  14.1–25.0 kg  450 mg
  25.1–32.0 kg  600 mg
  32.1–49.9 kg  750 mg
  Formulation: 150 mg tabs (others in development)

• INH-Rifapentine combo being developed
Rifamycins Better Than INH?

• INH monotherapy (6 or 9 mos) plagued by low completion rates, programmatic challenges & hepatotoxicity

From > 20 yrs of studies (~1500 trials), 53 RCTs LTBI Rx systematically selected & reviewed

• Each included relative efficacy & adverse events

• Applied Bayesian network meta-analysis [Allows comparison two distinct Rx regimens when no trials directly compare them]

LTBI Rx: Rifamycins Better Than INH?

Comparison to standard INH monotherapy:
• Rifampin x3-4 months ranked highly for both efficacy & hepatotoxicity
• INH & Rifampin x3-4 months also ranked well
• INH & Rifabutin trended well but data NS
• Surprise: INH & Rifapentine not as well as above

Regimens containing rifamycins more effective alternative?  

More Real Data Coming

• HALT trial: Evaluates Non-DOT Rifapentine vs INH monotherapy

• CDC trial: INH x 9 mos vs Rifampin x 4 mos
Treatment for S.B.

- INH daily x 9 months
- County public health department supervised treatment:
  - PHN performed Clinical Monitoring
  - 30 day supply aliquots of INH provided
  - Completed 9 months w/in 9 months
Summary Points

• Screen persons at high risk for TB (eg, foreign born)
• Seek to distinguish active vs. latent TB infection
• LTBI diagnosis reviewed
  – Decision to test = Decision to treat!
  – Highest risk subgroups identified
• Role for IGRA: QFT-Gold, T-Spot.
• LTBI treatment update
  – Can be shortened to 3 months (INH/rifapentine x 12 doses)
  – Data re-evaluation → Rifamycin better than INH?
• (Iowa) Department of Public Health provides TB Rx at no cost to patient
Monitoring on INH Treatment

• Educate the patient
  – Liver disease symptoms & signs
  – Stop meds until contact made with health care

• The critical element for preventing INH toxicity is Clinical monitoring…PHN
  – Absolutely necessary to do, absolutely necessary to do well & absolutely necessary to document well.

• LFTs (ALT, AST) at baseline in selected cases
  – Hx of liver disease, EtOH, pregnancy, HIV
  – Repeat monthly if abnormal at baseline, symptomatic, or pregnant
  – Stop meds:
    • Symptomatic, LFTs 3x upper limit of normal (ULN)
    • Asymptomatic, LFTs 5x

ATS/CDC/IDSA 5/2000
Clinical Monitoring

• Instruct patient to report following adverse drug reactions (ADRs):
  – Rash
  – Anorexia, nausea, vomiting, or pain in RUQ
  – Fatigue or weakness
  – Dark urine
  – Persistent numbness in hands or feet

• Monthly visits should include review of:
  – Rationale for treatment
  – Adherence to therapy
  – Symptoms consistent with ADR(s)
  – Plans to continue treatment
Liver Safety Issues for INH

• Deaths from INH hepatitis in 1960s
• 1971-72 PHS Study (14,000 pts)
  – 1% overall rate of INH related hepatitis
  – Age related increase
    • 0.3% (<35)
    • 2.3% (>50)
  – 4x increase a/w EtOH
  – 8 deaths due to INH hepatitis
• Review of PHS data (Comstock JAMA 1986)
  – 7/8 deaths occurred in Baltimore
  – Death certificate review: XS deaths due to cirrhosis in 1972
  – Unidentified co-factor related to cluster of cirrhosis cases?
• Subsequent studies: risk is lower
Latest CDC Data on INH Liver Toxicity

• SAEs during LTBI Rx, 2004-2008
• 17 patients with SAEs, all hepatotoxicity
  – 2 children < 15 yrs of age; Adults median age 39
  – One patient HIV seropositive for Hep C, HIV
  – 5/17 liver transplant (one child), 5/17 died (one transplant)
• 10/17 patients with CDC on-site investigation
  – Prescribers followed ATS/CDC guidelines for Clinical Monitoring
  – Symptoms 1-7 months after INH started
  – Fatigue, nausea, abdominal pain in 7 patients who waited for jaundice to seek medical attention
  – 2 patients INH discontinued within 3 days of symptoms, 8 stopped at least one week after symptom onset; all after medical instruction
• Death & liver transplantation ~1/150,000 - 1/220,000
• SAEs idiosyncratic reaction, independent of dosing, possible anytime during treatment, can occur in children

MMWR 2010 59(08):224-229
Deaths from INH Hepatitis

• Rates in women increased
  – Pregnancy & immediate post-partum period (3 mos)

• Concurrent acetaminophen questionable

• INH death rate reduced by Clinical Monitoring
  – Stopping INH at symptom onset reduces deaths
  – 7/8 liver transplants for INH hepatitis: Pts continued INH >10 d beyond symptom onset
    (CDC: *MMWR* 1993)
Safety Issues for INH: Current Practice Outcomes

- Most PHD practice Clinical Monitoring vs. biochemical monitoring
- Clinical Monitoring:
  - Educate for Rx related ADRs & Reviews adherence
  - Stop INH if any question until consult with clinician
  - CDC: “Medical providers should emphasize to patients that INH treatment should be stopped immediately upon the earliest onset of symptoms (e.g. excess fatigue, nausea, vomiting, abdominal pain, or jaundice), even before a clinical evaluation has been conducted, and that initial symptoms might be subtle and might not include jaundice.”
Monitoring on Treatment

- Educate the patient
  - Liver disease symptoms & signs
  - Stop meds until contact made with health care
- Clinical monitoring monthly…PHN
- LFTs (ALT, AST) at baseline in selected cases
  - Hx of liver disease, EtOH, pregnancy, HIV
  - Repeat monthly if abnormal at baseline, symptomatic, or pregnant
  - Stop meds:
    - Symptomatic, LFTs 3x upper limits of normal (ULN)
    - Asymptomatic, LFTs 5x ULN

ATS/CDC/IDSA 5/2000
More Case Examples & Discussion
Factors Causing False-Negative TST

- Anergy = Weakened immune system $\Rightarrow$ Inability to react to TST
  - Anergy testing utility in TST-negative persons not demonstrated in clinical trials
- New TB infection (eg, 2-10 weeks post exposure)
- Newborns
- Live virus vaccination (eg, measles, smallpox) suppresses TST response
- Overwhelming disease (eg, miliary TB)
- Poor TST administration technique
How Should Immunosuppressed Persons at Risk for TB Be Managed?

Empiric treatment for LTBI even when TST or IGRA neg on repeat testing 8-10 weeks after exposure

- Advanced HIV infected contacts
- Children < 5 years who are contacts
- Contacts with other causes of immunosuppression
- Persons who are to receive treatment with TNF alpha antagonists
TNFα Antagonists

- Block TNFα activity which is required for granuloma formation & containment of *M tuberculosis*
- Used for RA, Crohn’s disease, Psoriasis and a variety of other immune mediated diseases
  - Remicaid (inflixamab)
  - Embril (entanercept)
  - Humira (adalimumab)
  - Cimzia (certolizumab)
- Patients should be evaluated for LTBI w/ IGRA or TST
- Treatment of LTBI should be initiated prior to therapy
Questions Remain

• Unknown
  – Does treatment of LTBI need to be completed prior to use of TNF-α antagonist?

• Unknown
  – Does a person at risk of TB who is TST negative need to be treated?
    • Consider treatment of high risk TST negative patients

• No need to continue INH after completion of treatment for LTBI
Case 2

- 36-year-old Native American female
- History of diabetes
- 35 weeks pregnant
- TST = 18 mm of induration
- No symptoms of TB disease
- CXR, CBC, LFTs normal
- No known contact with TB patient
Case 2

Questions

1. What are this patient’s risk factors for TB infection or disease?

2. What is the appropriate management for this patient?
Case 2

Discussion of risk factors

• Persons with diabetes mellitus are 2 to 4 times more likely to develop TB disease than those without diabetes

• Risk may be higher in insulin-dependent diabetics and those with poorly controlled diabetes
Case 2

Discussion of management

• Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progressing to disease
• Pregnant women should be targeted for TB testing only if they have specific risk factors for LTBI or progression to disease
• Some experts prefer to delay treatment until after the early postpartum period, unless the woman has recent TB infection or HIV infection
Case 3

- 41-year-old Hispanic male
- Moved to U.S. from Mexico 4 years ago
- Known contact of infectious TB case
- TST = 5 mm of induration
- 3 months later TST = 23 mm of induration
- No symptoms of TB disease
- Normal CXR, CBC, AST, and bilirubin
Case 3

Questions

1. What are the patient’s risk factors for TB infection or disease?

2. Has the management of this patient to date been appropriate?
Case 3

Discussion of risk factors

• Patient is a contact of an infectious TB case
• Recent immigrant to the U.S. from a country with a high prevalence of TB. Such persons have increased rates of TB
• If the patient had not been a contact, the recent immigration (less than 4 years) would have made him a candidate for TB testing, but the 5-mm reaction would not be considered positive
Case 3

Discussion of management

• Should be treated for LTBI if TST reactions ≥ 10 mm of induration
• As a contact of an active TB case, 5 mm of induration is considered positive
• This patient should have been treated for LTBI immediately after the first TST
Case 4

- 56-year-old White male
- Works in a mycobacteriology lab
- TST result negative 1 year ago
- M. marinum infection in his hand 8 months ago
- TST result 5mm
- QFT-G test positive
- No symptoms of TB disease, CXR normal
- No known contact with a TB patient & no known spills or accidents in the lab