Objectives

• Describe the current guidelines for LTBI treatment

• Describe monitoring recommendations for patients on LTBI treatment

• Explain the use of IGRA
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)

1-2% Second Year
3-4% First 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 $\Rightarrow$ US
TB Cases & Case Rates vs. Years in US

~30% Foreign-born coming into US unscreened...
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 TNF$\alpha$ 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
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
Other 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 (eg. 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
TB Testing Upgrade...A Reality
Interferon Gamma Release Assay (IGRA)

Measures interferon-gamma (IFN-\(\gamma\)) 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 3\(^{rd}\) 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)

IGRA Results include control wells

- Negative (Nil) – no antigen (subtract from pt value)
- Positive – mitogen stimulation

<table>
<thead>
<tr>
<th>IGRA</th>
<th>TST</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>In vitro</em></td>
<td><em>In vivo</em></td>
</tr>
<tr>
<td>Specific antigens</td>
<td>Multiple antigens</td>
</tr>
<tr>
<td>Unaffected by BCG</td>
<td>BCG affects results</td>
</tr>
<tr>
<td>No boosting</td>
<td>Boost occurs</td>
</tr>
<tr>
<td>One patient visit</td>
<td>Two pt visits</td>
</tr>
<tr>
<td>No inter-reader variability</td>
<td>Inter-reader variability</td>
</tr>
<tr>
<td>One standard result for all</td>
<td>Different thresholds based on risk</td>
</tr>
</tbody>
</table>
QFT vs T-Spot.TB

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

- **T-Spot.TB:** Lymphocytes (T) incubated w/ specific antigens. ELISPOT-method counts IFN-γ 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</strong></td>
<td>≥0.35*</td>
<td>&lt;0.35*</td>
<td>None</td>
<td>Controls fail: High Nil</td>
</tr>
<tr>
<td><strong>Gold &amp; IT version</strong></td>
<td></td>
<td></td>
<td></td>
<td>Poor 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 CDC Guidelines 2009

- IGRA may substitute for TST
- IGRA preferred:
  - BCG vaccinated persons
  - Clients unlikely to return for TST reading
  - Low risk persons
- Clinical judgment required when interpreting IGRA among immunosuppressed, children <5, & TB suspects
- TST preferred in children <5
- Lab should be reporting quantitative results
Interpreting IGRA Results

- Contact investigation: If initial IGRA negative, Repeat test at 8-10 wks as one would TST
- IGRA conversion = change from neg to pos
- 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
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
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 retesting

Serial testing problems:
  - Unexpected positives that require further review (eg, repeat testing, assessing quantitative results)
  - “Wobblers” = results hovering around cut point
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
- Immunosuppressive Rx
- Overwhelming TB
- Age (newborn, very old)
TST False Positives

• Cross reaction w/ NTM or BCG
• Immediate hypersensitivity misinterpreted as positive
• TST product switch (tubersol vs applisol)

IGRA False Positives

• Cross reaction NTM: M kansasii, M szulgai, M marinum
• Product failure such as endotoxin traces in tubes
• Lab error
LTBI: TST & IGRA ≠ Gospel

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

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


Tuberculosis Screening Flowchart

At-risk person

TST or IGRA & symptom review

- Negative
  - Treatment not indicated
- Positive
  - Chest x-ray
    - Normal
      - Potential candidate for Rx of latent TB
    - Abnormal
      - Evaluate for active TB
...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.?
Treatment of Latent TB Infection

• ATS/CDC/IDSA sanctioned guidelines released 5/2000 (AJRCCM & MMWR)

• Evidence-based recommendations

• 9 months of therapy represent re-interpretation of old data, not failure of previously recommended 6 month regimen.
TB Case Rates vs. No. of Months INH Treatment (Bethal Data)
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.
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)
- *New Regimen* not recommended for the following:
  - Child <2
  - HIV/AIDS taking HART
  - Pregnant women
  - Contacts of INH &/or Rif resistant TB
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 & drug regimen modifying issues

• LTBI diagnosis (TST) and Rx reviewed
  • Decision to test = Decision to treat!
  • Clinical Monitoring role for PHN
  • Drug toxicity issues

• New TB tests: IGRA, QFT-Gold, T-Spot. TB

• (Iowa) Department of Public Health provides TB Rx at no cost to patient

• Call (Iowa) Department of Public w/ any TB question or suspect drug resistant LTBI (link MD TB experts)
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
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
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
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 at risk for exposure to TB who are to receive treatment with TNF alpha antagonists
TNF$\alpha$ Antagonists

- Block TNF$\alpha$ 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
  
  - Remicade (inflixamab)
  - Embril (entanercept)
  - Humira (adalimumab)
  - Cimzia (certolizumab)

- Patients should be evaluated for LTBI with a 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 $\geq 10$ 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