Diagnosis and Medical Management of Latent Tuberculosis Infection

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October 8, 2008
Objectives/Overview

- Discuss basic science of TB infection
- Discuss “targeted testing” and risks for progression from infection to active disease
- Discuss tuberculin skin testing and interferon-gamma release assay
- Discuss recommendations for treatment of latent TB infection
- Case studies

Mycobacteria

- Over 120 species
- Named for mycolic acid in their cell wall. Unique to each species
- Most are non-pathogenic
- Acid-fast: resistant to staining, acid and alkali
- Waxy cell wall: resistant to dehydration
- Related to Nocardia and Actinomyces
- Very common in environment and “normal flora”
M. tuberculosis complex

- A group of seven pathogenic Mycobacteria
- M. tuberculosis, M. africanum (humans)
- M. bovis (cattle, deer, many other mammals)
- M. caprae (goats)
- M. pinnipedii (seals)
- M. canetti (mice)
- M. microti (lab)
- M. bovis, BCG vaccine strain (not reportable)

M. tuberculosis

- Obligate aerobe: requires high O2 concentration for growth
- Intracellular parasite
- Very slow growing: 20 hour generation time (E. coli: 20 min)
- Unique, very durable cell wall (major factor in virulence)
- 2-4 microns in length (RBC 6-8 microns)
- 10,000 organisms/ml required to show up as “smear positive”
**Droplet Nuclei**

- Basic infectious particle of TB
- Aerosolized from source case. Dry rapidly and float
- 3-5 microns. Contain 1-3 tubercle bacilli each
- Can float into the alveoli
- From 5 to 200 viable bacilli must impinge on an alveolus for infection to possibly develop

**Day 1-7**

- Droplet nuclei inhaled and impinge on alveolus
- Ingested by non-activated macrophage
- Begins multiplying in macrophage
- Macrophage killed, cytokines released, attracting additional macrophages and lymphocytes from blood
- Or: *Organism is quickly killed if ingested by a previously activated macrophage* (person has a prior +PPD)
- This is why we are not as concerned about previously infected contacts
- Having a + PPD is not all bad. It does offer some protection against re-infection
Day 7-21

- “Stage of logarithmic growth”
- Non-activated macrophages fill with organisms and burst. Many more cells attracted to site.
- Macrophages and organisms move into local lymphatics and eventually to thoracic duct.
- Set up local foci of infection and disseminate throughout the body via circulatory system.
- Prefer sites of high O2 concentration (lung apices, kidney, brain, growth centers of bone).

Day 21-90

- Immune response (CMI) develops. T-lymphocytes and macrophages are able to destroy organisms.
- Tubercles form, walling off and halting multiplication (although some organisms remain viable in a dormant state). “Two-edged sword”
- Skin test becomes positive. Microscopic dormant tubercles can be found along lymphatic channels. Occasionally these are large enough to be seen on x-ray (primary complex). This is LTBI
- This is the end of the story for the majority of people.
Basic algorithm following exposure

Exposure to TB Droplet Nuclei

- No infection develops (80-90%)
- LTBI (90%)
- Infection develops (10-20%)
- Never develop disease

Untreated (from pre-antibiotic era data)
- ~33% die in first 2 years
- ~33% die later due to TB (Class 4 - Class 3)
- 33% spontaneously cured (Class 4)

Adequately treated
- Vast majority cured
- Small number re-activate

Active TB (10%)
- 5% in first 2 years
- 5% many years later

TB Pathogenesis: Progression from LTBI to Disease

Latent TB Infection

- No Disease (90%)  
- ~0.1% per year thereafter
- 2-3% Second Year
- 5% First Year

Disease (10%)
LTBI vs. Pulmonary TB Disease

**Latent TB Infection**
- TST or IGRA positive
- Negative chest radiograph (may see calcified primary complex)
- No symptoms or physical findings suggestive of TB disease

**Pulmonary TB Disease**
- TST or IGRA usually positive
- Chest radiograph usually abnormal
- Symptoms may include one or more of the following: fever, cough, night sweats, weight loss, fatigue, hemoptysis, decreased appetite
- Respiratory specimens may be smear or culture positive

Targeted Tuberculin Testing
- An essential TB prevention and control strategy
- Identify persons with LTBI who are at high risk of developing active disease
- Emphasizes treatment of those who would benefit most
- Once active disease is excluded, treatment is offered regardless of age
- Testing discouraged for those at low risk
- Reduces the waste of resources and prevents inappropriate treatment
Increased Risk for Developing Active TB Disease

2 categories:

- Recent Infection
- Medical Conditions

More likely to have been recently infected:

- Close contacts to infectious TB case
- Skin test converters*
- Immigrants from TB-endemic regions of the world (within 5 years of arrival to the U.S.)
- Children ≤ 5 years with a positive TST
- Residents and employees of high-risk congregate settings (correctional facilities, homeless shelters, health care facilities)

*TST conversion is considered an increase of 10 mm induration within a 2 year period, regardless of age
More likely to progress from LTBI to TB disease:

- HIV-infected persons
- Those with a history of prior untreated TB or fibrotic lesions on chest radiograph
- Low body weight (> 10% below ideal body weight)
- Injection drug users
- Conditions that require treatment with TNF-alpha antagonists, prolonged corticosteroids or other immunosuppressive agents

More likely to progress from LTBI to TB disease:

Persons with certain medical conditions

- Silicosis
- Diabetes mellitus
- Chronic renal failure +/- hemodialysis
- Solid organ transplantation
- Carcinoma of head or neck
- Gastrectomy or jejunoilial bypass

* All tuberculosis screening should be performed in conjunction with risk assessment
Tuberculosis Screening Flowchart

At-risk person

TST (or IGRA) + symptom review

Negative

Positive

Chest x-ray

Normal

Abnormal

Treatment not indicated

Potential candidate for Tx of LTBI

Evaluate for active TB

Tuberculin Skin Testing

Basic immunology, methodology and pearls
Classification of Immunologic Responses

- Immune responses provide specific protection against infection with bacteria, viruses, fungi and parasites
- A two-edged sword: Provides protection. Necessary for survival. Also the cause of mild to life-threatening reactions (hay fever to anaphylactic shock)
- Hypersensitivity: excessive or inappropriate immune response to antigen
- Coombs and Gell Classification of Immunologic Hypersensitivity Reactions (Type I-IV)
- Useful guide to understanding immune reactions

Type I Immediate Hypersensitivity

- Mediated by IgE antibody to specific antigens
- Mast cells stimulated and release histamine
- Reaction within one hour of exposure

Examples
1. Urticaria (hives)
2. Angioedema
3. Anaphylaxis (e.g. penicillin allergy)
4. Atopic Allergy
**Type II**

**Cytotoxic Antibody Reaction**

- Mediated by IgG and IgM to specific antigens
- Antibodies directed against cell surface antigens
- Damage is restricted to specific cells or tissues
- B-lymphocytes (produce antibody). Have ~3 year memory

**Examples**
1. Transfusion Reaction
2. Rhesus Incompatibility (Rh Incompatibility)
3. Hashimoto’s Thyroiditis
4. Goodpasture’s Syndrome
5. Delayed transplant graft rejection

**Type III**

**Immune Complex Reaction**

- Antigen-antibody complexes deposit in tissue
- Most reactions within 1-3 weeks after exposure

**Examples**
1. Systemic Lupus Erythematosus
2. Erythema Nodosum
3. Polyarteritis nodosa
4. Arthus Reaction
5. Rheumatoid Arthritis
6. Elephantiasis (Wuchereria bancrofti reaction)
7. Jarisch-Herxheimer Reaction
8. Serum Sickness
Type IV
Delayed-Type Hypersensitivity

- Cell mediated immunity/Delayed-type hypersensitivity are 2 sides of the same sword. Helpful and harmful at the same time.
- Mediated mainly by T-lymphocytes sensitized to specific antigens
- Involves major histocompatibility complex (MHC)
- Reaction within 2-7 days after exposure
- T-lymphocytes have ~15 year memory. Basis for the “booster” effect

Examples
1. Mantoux Test (PPD)
2. Cachexia and caseous necrosis due to tuberculosis
3. Allergic Contact Dermatitis (e.g. Nickel allergy)

Tuberculin Skin Test

- One of two primary methods of testing for *M. tuberculosis* infection
- TST is used for:
  - Targeted testing for LTBI
  - Contact investigation
  - Evaluation of persons with signs and symptoms of TB
Administering the TST

- Inject 0.1 ml (5 TU) PPD tuberculin solution intradermally on volar surface of forearm using a 27-gauge needle
- Produce a wheal 6 to 10 mm in diameter

Reading the TST

- Measure reaction in 48 to 72 hours
- Measure induration, not erythema
- Record reaction in millimeters, not “negative” or “positive”
- Ensure trained health care professional measures and interprets the TST
Reading the TST

- Educate patient and family regarding significance of a positive TST result
- Positive TST reactions can be measured accurately for up to 7-10 days
- Negative reactions can be read accurately from 48 to 72 hours only

TST Interpretation

5-mm induration is interpreted as positive in:

- HIV-infected persons
- Close contacts to an infectious TB case
- Persons with chest radiograph consistent with prior untreated TB
TST Interpretation

5-mm induration is interpreted as positive in:

- Organ transplant recipients
- Other immunosuppressed patients (those taking the equivalent of >15 mg/day of prednisone for >1 month or those taking TNF-alpha antagonists)

TST Interpretation

10-mm induration is interpreted as positive in:

- Recent immigrants
- Injection drug users
- Residents or employees of congregate settings
- Mycobacteriology laboratory personnel
TST Interpretation

10-mm induration is interpreted as positive in:

- Persons with clinical conditions that place them at high risk
- Children < 4 years
- Infants, children, and adolescents exposed to adults at high-risk for TB disease

Although skin testing programs should be conducted only in high-risk groups, certain low-risk persons do require testing for employment or school.

TST Interpretation

15-mm induration is interpreted as positive in:

- Persons with no known risk factors for TB
Tuberculin Skin Test

- False negative tests
  - Quality and stability of reagents
  - Poor technique
  - Anergy (common with HIV infection)
- False positive tests
  - Reader error
  - Presence of cross-reacting antigens
    - Nontuberculous mycobacteria
    - BCG vaccination

Factors That May Cause False-Positive TST Reactions

- Nontuberculous mycobacteria
  - Reactions caused by nontuberculous mycobacteria are usually ≤ 10 mm of induration
- BCG vaccination
  - Reactivity in BCG vaccine recipients wanes over time; positive TST result is likely due to TB infection if risk factors are present
Factors That May Cause False-Negative TST Reactions

- Anergy
  - Inability to react to a TST because of an altered immune response
  - Usefulness of anergy testing in TST negative persons who are HIV infected has not been demonstrated

- Recent TB infection
  - Defined as 2 to 10 weeks after exposure

- Very young age

- Live-virus vaccination
  - For example, MMR or varicella
  - Can temporarily suppress TST reactivity

- Overwhelming TB disease
Factors That May Cause False-Negative TST Reactions

- Poor TST administration technique
  - Injection too shallow or deep
  - Wheal too small
- Reagent problem
  - Poor quality or degraded PPD
  - Wrong substance injected

“Never has such a simple test been done so poorly by so many”  Harold Muchmore, M.D.

Tuberculin Skin Testing

- A 100 year-old, very imperfect test. Poorly understood by many health care providers. Each reaction should be interpreted in context.
- A negative PPD does not rule out TB. 15-20% of active TB cases have a negative PPD
- In PPD reactors, T-lymphocytes recognize the antigen and start to migrate to the PPD site 4 to 6 hours after injection.
- The induration is caused by a dense accumulation of activated T-lymphocytes at the injection site.
Tuberculin skin testing

- The only absolute contraindications to PPD application are previous ulceronecrotic reaction or a prior true anaphylactic reaction to PPD.
- Can safely be administered to newborns, pregnant women, AIDS patients, persons who have received BCG vaccination and to prior PPD reactors.
- Arthus Reaction: rapid immune complex (Type III) reaction at PPD site. Redness and edema at site 12-24 hours after injection. NOT a positive reaction.
- In persons with atrophic skin (or diseased/damaged skin) on the arms and those who attempt to feign reactions (by scratching the site), place PPD between the shoulder blades.

Tuberculin skin testing

- For large, painful and/or ulcerating PPD reactions, document the result and treat with a Medrol DosePak and topical corticosteroids (extremely effective, rapid-acting therapy).
- Most of the time, “allergic reactions” to PPD are actually misinterpretations of positive tests.
- When “allergic” persons require documentation of PPD status for employment, a screening chest x-ray and symptom review are adequate most of the time.
- In these instances, IGRA testing will eventually become standard.
Boosting/Anamnesis

- Some people with LTBI may have a negative skin test reaction when tested years after infection because of a waning response.
- The initial skin test may stimulate (boost) the ability to react to tuberculin.
- The booster effect is also known as “anamnesis” (forgetting to forget).
- Without two-step testing, a positive reaction with subsequent testing may be misinterpreted as new infection rather than true old LTBI.

Two-Step Testing

- A strategy to determine the difference between boosted reactions and reactions due to recent infection.
  - If first TST is positive, consider the person infected
  - If first TST is negative, give second TST 1–3 weeks later
  - If second TST is positive, consider the person infected
  - If second TST is negative, consider the person uninfected at baseline
Two-Step Testing

- Use two-step test only for initial baseline skin testing of adults who will be retested periodically (health care workers, residents of long term care facilities, etc)

- Two-step testing should not be used for follow-up testing

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**BOX 1. Indications for two-step tuberculin skin tests (TSTs)**

<table>
<thead>
<tr>
<th>Situation</th>
<th>Recommended testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous TST result</td>
<td>Two-step baseline TSTs</td>
</tr>
<tr>
<td>Previous negative TST result (documented or not)</td>
<td>Two-step baseline TSTs</td>
</tr>
<tr>
<td>&gt;12 months before new employment</td>
<td>Single TST needed for baseline testing; this test will be the second-step</td>
</tr>
<tr>
<td>Previous documented negative TST result =&lt; 12 months before new employment</td>
<td>Single TST; two-step testing is not necessary</td>
</tr>
<tr>
<td>&gt;2 previous documented negative TSTs but most recent TST &gt;12 months before new employment</td>
<td>No TST</td>
</tr>
<tr>
<td>Previous documented positive TST result</td>
<td>Two-step baseline TST(s)</td>
</tr>
<tr>
<td>Previous BCG vaccination</td>
<td>Two-step baseline TST(s)</td>
</tr>
<tr>
<td>Programs that use serial BACTEC® lines including QFT® (or the previous version QFT), including†</td>
<td>See Supplement, Use of QFT-G® for Diagnosing M. tuberculosis Infections in Health Care Workers (HCWs)</td>
</tr>
</tbody>
</table>

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* For newly hired healthcare workers and other persons who will be tested on a routine basis (e.g., residents or staff of correctional or long-term care facilities), a previous TST is not a contraindication to a subsequent TST, unless the test was associated with severe reactions or anaphylactic shock, which are substantially rare adverse events. If the previous positive TST result is not documented, administer two-step TSTs or offer BACTEC. SOURCES: Aventis Pasteur, Tuberculin purified protein derivative (Mannheim) Tuberculosis diagnostic antigen. Toronto, Ontario, Canada: Aventis Pasteur, 2001. Patholele Pharmaceuticals, ML250, Tuberculin purified protein derivative, dilution (1:1000). Diagnostic antigen for intradermal injection only. Roche, Ltd, Patholele Pharmaceuticals, 2003. Procione Hz, Rabon Hz, Beb AM. Immediate hypersensitivity reactions after use of tuberculin skin testing. Clin Infect Dis 2003;34;813-8.

† BACTEC Calmette Guerin

‡ Blood test for Mycobacterium tuberculosis

§ Quantiferon® TB test

**QuantiFERON®-TB Gold test.**
**Blood Assay for MTB (BAMT)**

**Interferon-gamma release assay (IRGA)**

- Quantiferon-TB Gold In-tube™ (QFT-GIT)
- Current test being used in the U.S.
- A blood test to diagnose the presence or absence of tuberculosis infection
- An in-vitro enzyme-linked immunosorbent assay (ELISA) measuring release of IFN-γ from sensitized T-lymphocytes after stimulation with specific antigenic peptides from MTB
- Advantages and disadvantages compared to the tuberculin skin test. Can be used in all circumstances in which the TST is currently used. Not a perfect test

**CDC Recommendations for QFT-GIT**

- CDC recommends that QFT-GIT may be used in all circumstances in which the TST is currently used, including:
  - Contact investigations
  - Evaluation of recent immigrants
  - Sequential testing in surveillance programs for infection control
- Caution should be used in interpreting the results in selected populations such as:
  - Young children
  - Immunocompromised persons
Advantages of IGRA over TST

- Increased specificity and negative predictive value*
- No cross reactivity with BCG and MAC antigens (and the majority of other non-tuberculous mycobacterial antigens)‡
- Prevalence of pulmonary disease and colonization with NTM is increasing**

‡ Does cross react with M. kansasii, M. marinum and M. szulgai antigens

* Chest 2007;132(3) ** Thorax 2007;62:661-666

Advantages of IGRA over TST

- Studies suggest possible improved sensitivity in immunocompromised persons (including HIV)* and better prediction of those more likely to progress to disease
- Single patient encounter, result every time
- No booster effect, application variables, reader bias or alleged “allergic reactions”
- Automated lab reporting. Decreased lab entry errors. Better analysis potential

* Am J Resp Crit Care Med 2008;177
Disadvantages of IGRA

- Strict processing timetable/limited availability
  - Must get specimen to reference lab or initiate incubation of specimen (at 37° C) within 16 hours
  - Errors in collecting/transporting specimens and in interpreting results can decrease accuracy
  - No labs in Oklahoma are currently performing test commercially
- Limited data on use in children, recent contacts and immunocompromised persons
- Expensive
- Venipuncture on young children can be difficult

LTBI Treatment Regimens
History of Treatment of LTBI

- Preventive therapy/chemoprophylaxis/treatment of LTBI have been essential components of tuberculosis control in the U.S. for 43 years.
- 1965: ATS recommends preventive therapy for those with previously untreated TB, skin test converters, and young children.
- 1967: Recommendations expanded to include all TST positive reactors (≥10 mm).
- 1974: CDC and ATS guidelines recommend preventive therapy only for persons ≤35 years of age in order to decrease risk of hepatitis.
- 1983: CDC recommends clinical and laboratory monitoring of persons ≥35 who require preventive therapy.
- 1998: CDC recommends 2 months of RIF/PZA as an option for HIV-infected patients.
- 2000: ATS/CDC updates recommendations for “treatment of latent TB infection”.
- 2001: Due to cases of severe liver injury associated with a 2-month regimen of RIF/PZA, use of this option de-emphasized in favor of other regimens.
- 2003: 2-month regimen of RIF/PZA not recommended.
Initiating Treatment

Before initiating treatment for LTBI:
- Rule out TB disease!!
- Determine prior history of treatment for LTBI or TB disease
- Assess risks and benefits of treatment
- Determine current and previous drug therapy

Isoniazid Regimens
- 9-month regimen of isoniazid (INH) is the current CDC “preferred” regimen
- 6-month regimen is slightly less effective but may be used if unable to complete 9 months
- May be given daily or intermittently (twice weekly)
  - Use directly observed therapy (DOT) for intermittent regimen
Isoniazid Regimens

- INH daily for 9 months
  (270 doses within 12 months)
- INH twice/week for 9 months
  (76 doses within 12 months)
- INH daily for 6 months
  (180 doses within 9 months)
- INH twice/week for 6 months
  (52 doses within 9 months)

Rifampin Regimens

- Rifampin (RIF) given daily for 4 months is an acceptable alternative in HIV – and HIV + persons
- Shorter regimen leads to greater completion rates*
- In situations where RIF cannot be used (HIV-infected persons receiving protease inhibitors), rifabutin may be substituted.

* “The best preventive therapy is the one the patient completes” Harold Muchmore, M.D.
Rifampin Regimens

- RIF daily for 4 months
  
  (120 doses within 6 months)

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

* If 60 doses have been completed, can be considered adequate treatment for LTBI

Other regimens

- INH and RMP for 4 months.
  - Reassuring if subtle active disease has not been completely excluded
  - Rapid completion of full course (TNF-alpha, etc)

- INH and RMP for 3 months
  - Used in Great Britain and other countries

- Rifapentine and INH once weekly
  - Currently being studied
Completion of Therapy

Completion of therapy is based on the total number of doses administered, not on duration alone.

Management of Interrupted Therapy

- Extend or re-start treatment if interruptions were frequent or prolonged enough to preclude completion
- When treatment has been interrupted for more than 2 months, patient should be examined to rule out TB disease
- Recommend and arrange for DOPT as needed
- Rule of Thumb - “off for longer than on, start from scratch. On for longer than off, continue as if no break occurred”.
Monitoring During Treatment

Instruct patient to report signs or symptoms of adverse drug reactions

- Rash
- Anorexia, nausea, vomiting, or abdominal pain in right upper quadrant
- Fatigue or weakness
- Dark urine
- Persistent numbness in hands or feet

Clinical Monitoring
Clinical Monitoring

Monthly visits should include a review of

- Rationale for treatment
- Adherence with therapy
- Symptoms of adverse drug reactions
- Plans to continue treatment

Clinical Monitoring

- Incidence of hepatitis in persons taking INH is lower than previously thought (0.1 to 0.15%)
- Hepatitis risk increases with age
  - Uncommon in persons < 20 years old
  - Nearly 2% in persons 50 to 64 years old
- Risk increased with underlying liver disease or heavy alcohol consumption
Laboratory Monitoring

Baseline liver function tests (AST, ALT, and bilirubin) are not necessary except for patients with the following risk factors:

- HIV infection
- History of liver disease
- Alcoholism
- Pregnancy or in early postpartum period

Repeat laboratory monitoring if patient has:

- Abnormal baseline results
- Current or recent pregnancy
- High risk for adverse reactions
- Symptoms of adverse reaction
- Liver enlargement or tenderness during examination
Laboratory Monitoring

- Asymptomatic elevation of hepatic enzymes seen in 10%-20% of people taking INH
  - Levels usually return to normal after completion of treatment
- Some experts recommend withholding INH if transaminase level exceeds 3 times the upper limit of normal (if symptomatic) and 5 times the upper limit of normal if patient is asymptomatic

Meeting the Challenge of TB Prevention

For every patient:
- Assess TB risk factors
- If risk is present, perform TST or IGRA
- If TST or IGRA is positive, rule out active TB disease
- If active TB disease is ruled out, initiate treatment for LTBI
- If treatment is initiated, ensure completion
Case Studies

Case Study #1

Patient history
- 36 year-old Native American female
- History of diabetes
- 35 weeks pregnant
- TST = 18 mm induration
- No symptoms of TB disease
- CXR, CBC, LFTs normal
- No known contact to active case
Case Study #1

Questions
1. What are this patient’s risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

- 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 Study #1

- 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

Case Study #1

- In the absence of risk factors, wait until after delivery to start therapy (to avoid unnecessary medication during pregnancy)
- Consider immediate treatment for LTBI if HIV+ or recent contact
Case Study #2

Patient history

- 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

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 Study #2

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

Discussion of risk factors

- 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
- Persons who immigrate from TB-endemic countries have increased rates of TB
Case Study #2

Discussion of management

• Recent immigrants should be treated for LTBI if TST ≥ 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 Study #3

Patient history

■ 56 year-old White male
■ Works in a mycobacteriology lab
■ TST (1 year ago) = 0mm
■ M. marinum infection in his hand 8 months ago
■ TST (current) = 5 mm induration
■ IGRA (QFT-GIT) test “positive”
■ No symptoms of TB disease, CXR normal
■ No contact to TB case and no spills / accidents in the lab
Case Study #3

Questions:

- Is treatment of LTBI indicated?
- What about positive QFT test?
- Current skin test positive?
- What if TST one year from today measures 15 mm induration?