Diagnosis & Treatment of Latent TB Infection (LTBI)

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Latent TB Infection (LTBI)

- Infection with *Mycobacterium tuberculosis* without manifestations of active disease
  - Asymptomatic
  - Normal or stable chest radiography
- >80% TB disease in the US is due to reactivation of latent infection
- Reactivation is preventable
- TB elimination focuses on targeting people with a high risk of LTBI for screening and treatment

Horsburgh and Rubin, NEJM, 2011

LTBI Diagnosis

Testing for TB

- Limited by inability to identify *Mycobacterium tuberculosis* in people with latent infection
- Diagnosis is indirect and based on detecting host immune response to infection
  - Tuberculin skin test (TST)
  - Interferon gamma release assays (IGRA)
Tuberculin Skin Test
- 4.2% of all tested with TST in US between 1999-2000 had LTBI
- Measures cell-mediated immunity via delayed type hypersensitivity response to tuberculin PPD
- A sensitive test
- Not able to accurately predict risk of reactivation

Risk of reactivation with +TST – 5%
Lengthy (4-9 months) treatment

Tip the Scale: Targeted Testing for LTBI
- Identify groups at highest risk for testing:
  - High prevalence of latent infection
  - More likely to reactivate or progress to disease once latently infected
- Reduce likelihood of screening groups at low risk and lessen false positives
  - Low risk groups likely to be exposed in future (e.g., HCW) is one exception
- Decision to test = decision to treat

High Prevalence of LTBI
- Close contacts of patients with TB disease
  - Over half lifetime risk of reactivation occurs in 1-2 years post-conversion
- Foreign-born (recent immigrants <5 years)
  - In one series, 43% of foreign-born cases with TB disease had no indication for testing by current guidelines, 65% had been in US > 5 years
- Injection drug users
- Homeless
- Prisoners

Horsburgh and Rubin. NEJM, 2011; Cain and Macenzie. CID, 2008; Walter et al. CID 2008

Increased likelihood of progression from LTBI to TB disease

<table>
<thead>
<tr>
<th>Risk Factor and Study</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced, untreated HIV infection</td>
<td>9.3 (7.7-11)</td>
</tr>
<tr>
<td>Moore et al.</td>
<td>9.3 (7.7-11)</td>
</tr>
<tr>
<td>Patients with progressive tuberculosis</td>
<td>8.5 (5.8-12)</td>
</tr>
<tr>
<td>Horsburgh and Rubin</td>
<td>8.5 (5.8-12)</td>
</tr>
<tr>
<td>Radiographic evidence of old, healed tuberculosis that was not treated</td>
<td>6.1 (3.6-10)</td>
</tr>
<tr>
<td>Horsburgh and Rubin</td>
<td>6.1 (3.6-10)</td>
</tr>
<tr>
<td>Treatment with at least 25 mg of prednisone per day</td>
<td>3.8 (2.3-6.4)</td>
</tr>
<tr>
<td>Jick et al.</td>
<td>3.8 (2.3-6.4)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>3.4 (2.3-1.8)</td>
</tr>
<tr>
<td>Patients with TMT 1+ induration</td>
<td>3.4 (2.3-1.8)</td>
</tr>
<tr>
<td>Adding et al.</td>
<td>3.4 (2.3-1.8)</td>
</tr>
<tr>
<td>Poorly controlled diabetes</td>
<td>2.0 (1.3-3.1)</td>
</tr>
<tr>
<td>Patients with TMT 2+ induration</td>
<td>2.0 (1.3-3.1)</td>
</tr>
<tr>
<td>Walter et al.</td>
<td>1.7 (1.5-2.9)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.4 (1.2-3.2)</td>
</tr>
<tr>
<td>Rais et al.</td>
<td>1.4 (1.2-3.2)</td>
</tr>
<tr>
<td>Horsburgh and Rubin</td>
<td>1.5 (1.2-3.2)</td>
</tr>
</tbody>
</table>

Horsburgh and Rubin. NEJM, 2011
Lifetime Risk of Active TB by Age and TST Response

Horsburgh, NEJM, 2004

Cut points for TST interpretation

<table>
<thead>
<tr>
<th>Size of induration</th>
<th>5 mm</th>
<th>10 mm</th>
<th>15 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>=&lt;1.5 mm</td>
<td>HIV-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-1.4 mm</td>
<td>Recent contacts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5-9 mm</td>
<td>CXR with fibrotic lesions c/w prior TB</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Organ transplants, immunosuppressed patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TNF alpha blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prednisone ≥ 15mg x1 month</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Recent immigrants (&lt;5 years) from high prevalence countries</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Injection drug user</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Residents/employees of congregate settings</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mycobacteriology lab</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High-risk medical conditions*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children exposed to adults at high-risk</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No risk factors

Interpret the TST Results

The following measurements of induration are classified as positive, based on individual risk factors:

- **5 mm**: Positive cut-off for:
  - Persons with HIV infection
  - Persons with known contacts with active TB disease
  - Persons with active or history of latent TB
  - Persons with lesions on chest X-rays
  - Persons with organ transplants and other immunosuppressed persons, including those receiving immunosuppressant medication (e.g., cyclosporine 200 mg x 1 month of prednisone equivalent)

- **10 mm**: Positive cut-off for:
  - Persons who have immigrated within the past 5 years from areas with high TB rates
  - Injection drug users
  - Persons who live or work in institutional settings where exposure to TB is likely (e.g., hospitals, prisons, nurses, shelter workers, EBC, and nursing homes)
  - Mycobacteriology laboratory personnel
  - Persons with chronic conditions associated with a increased risk of progression to active disease (e.g., HIV/AIDS, silicosis, diabetes, advanced age, chronic kidney disease, end-stage renal disease, cancer, and weight loss of >10% of body weight in 6 months)
  - Persons with active or latent TB disease
  - Persons with a history of TB disease

- **15 mm**: Positive cut-off for:
  - Persons at high risk for active TB disease for whom testing is not routinely indicated

High-risk Medical Conditions

- Silicosis
- Diabetes
- Chronic renal insufficiency
- Malignancy (head/neck, lung, leukemia, lymphoma)
- Weight loss
- Gastrectomy, jejunoileal bypass
- Other epidemiologically defined high-risk groups, may vary based on area

*Countries with high rates of TB include China, Democratic Republic of Congo, Ethiopia, India, Indonesia, Kenya, Mexico, Pakistan, Peru, Philippines, South Korea, and all of Africa.
**TST Do’s and Don’ts**

- **Do test:**
  - Prior to immunosuppression
  - 8-10 weeks after prior negative TST for a contact
- **Don’t test:**
  - Previous positive result
  - <6 weeks after live virus vaccine (can be done at same time as vaccine)
  - Prior severe reaction

**False TST Results**

- **False positive**
  - BCG vaccination
  - Nontuberculous mycobacteria infection
  - Improper administration or interpretation
- **False negative**
  - Very young (<6 months)
  - Inability to mount an immune response (e.g., HIV or TB itself)
  - Recent infection (<10 weeks since exposure)
  - Very remote infection
  - Recent live virus vaccination
  - Improper administration or interpretation

**TST Administration & Interpretation**

**Two Step Testing**

*Use two step testing for initial skin testing of adults who will be retested periodically*

- If first test positive, consider the person infected
- If first test negative, give second test 1-3 weeks later
- If second test positive, consider person infected
- If second test negative, consider person uninfected
**Tuberculin Testing**

True Infection vs. Booster Effect (mm induration)

<table>
<thead>
<tr>
<th>Situation</th>
<th>Time</th>
<th>0</th>
<th>1 week</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>4</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>2</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>12</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

**Interferon Gamma Release Assays (IGRA)**

- Approved by FDA
  - QuantiFERON®-TB GOLD
  - QFT-GIT
  - T-SPOT®.TB
- *In vitro* blood test
- Use antigens not found in BCG or most NTM (ESAT-6, CFP-10, TB7.7)
- More specific, less cross-reaction with NTM
- Can cross-react with *M. kansasi*, *M. marinum*, *M. szulgai*

**QuantiFERON®-TB Gold Method**

*Stage 1 Whole Blood Culture*

1. Draw blood with heparin
2. Make 1 ml aliquots & add antigen
3. Incubate overnight IFN-γ from sensitized lymphs

*Stage 2 IFN-gamma ELISA*

1. Harvest plasma from above settled cells
2. Measure [IFN-g] in ‘Sandwich’ ELISA
3. Measure OD and determine IFN-g levels

**QuantiFERON®-TB Gold In Tube (QFT-GIT)**

1. Blood Collection
2. Tube Shaking
3. Incubation/Shipping

[www.cellestis.com](http://www.cellestis.com)
QFT-GIT Interpretation

TABLE 2. Interpretation criteria for the QuantiFERON-TB Gold In-Tube Test (QFT-GIT)

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Nil*</th>
<th>TB Response†</th>
<th>Mitogen Response§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive**</td>
<td>≤8.0</td>
<td>≥0.35 IU/ml and ≥25% of Nil</td>
<td>Any</td>
</tr>
<tr>
<td>Negative***</td>
<td>≤8.0</td>
<td>&lt;0.35 IU/ml or &lt;25% of Nil</td>
<td>≥0.6</td>
</tr>
<tr>
<td>Indeterminate††</td>
<td>&gt;8.0</td>
<td>Any</td>
<td>Any</td>
</tr>
</tbody>
</table>


T-SPOT®.TB Interpretation

TABLE 3. Interpretation criteria for the T-SPOT.TB Test (T-Spot)

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Nil*</th>
<th>TB Response†</th>
<th>Mitogen§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive**</td>
<td>≤10 spots</td>
<td>≤8 spots</td>
<td>Any</td>
</tr>
<tr>
<td>Borderline**</td>
<td>≤10 spots</td>
<td>≤5, 6, or 7 spots</td>
<td>Any</td>
</tr>
<tr>
<td>Negative††</td>
<td>≤10 spots</td>
<td>≤4 spots</td>
<td>Any</td>
</tr>
<tr>
<td>Indeterminate‡‡</td>
<td>&gt;10 spots</td>
<td>≤5 spots</td>
<td>&lt;20 spots</td>
</tr>
</tbody>
</table>

IGRA Sensitivity and Specificity

<table>
<thead>
<tr>
<th></th>
<th>TST</th>
<th>T-SPOT.TB</th>
<th>QFT-GIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity†</td>
<td>95%</td>
<td>91%</td>
<td>84%</td>
</tr>
<tr>
<td>Specificity*</td>
<td>85%</td>
<td>88%</td>
<td>99%</td>
</tr>
</tbody>
</table>

†Pooled estimate, low incidence countries
*Pooled estimate, patients unlikely to have M. tb infection


Comparison of IGRAs and TST

<table>
<thead>
<tr>
<th>IGRAs</th>
<th>TST</th>
</tr>
</thead>
<tbody>
<tr>
<td>• In vitro test</td>
<td>• In vivo test</td>
</tr>
<tr>
<td>• Specific antigens</td>
<td>• Single antigen</td>
</tr>
<tr>
<td>• No boosting</td>
<td>• Boosting</td>
</tr>
<tr>
<td>• 1 patient visit</td>
<td>• 2 patient visits</td>
</tr>
<tr>
<td>• Minimal inter-reader variability</td>
<td>• Inter-reader variability</td>
</tr>
<tr>
<td>• Results possible in 1 day</td>
<td>• Results in 2-3 days</td>
</tr>
<tr>
<td>• Requires phlebotomy</td>
<td>• May be more sensitive in detecting remote infections</td>
</tr>
<tr>
<td>• May be decline in response to test after treatment</td>
<td></td>
</tr>
</tbody>
</table>

IGRA Cautions

- Children < 5 years of age
- Immunocompromised
- System in place for blood collection, transport, etc.
- “Wobblers”
- Cost – overcome with structured implementation

IGRA Indications – 1

- May be used in place of (but not in addition to) a TST in all situations for which CDC recommends tuberculin skin testing
- IGRA preferred
  - Hard to reach populations (e.g., homeless, migrant workers)
    - Only one visit required
  - People who have received BCG (either as vaccine or cancer therapy)
    - TB specificity higher
**IGRA Indications – 2**

- **Both TST and IGRA may be considered**
  - At high risk for infection or progression (e.g., HIV)
  - Suspicion for TB disease exists
  - Further evaluation of positive TST results in individuals at low risk for infection and progression
  - Confirming questionable TST results
  - Other reasons: immediate hypersensitivity to PPD, convincing high risk patient with strongly positive TST to take LTBI treatment, indeterminate/borderline IGRA

**IGRA Indications – 3**

- **Use either TST or IGRA**
  - Contacts
  - Periodic screening for those with occupational exposure, surveillance programs etc.
- **TST preferred**
  - Children < 5 yrs

**LTBI Screening Guidelines**

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>U.S. Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Close contacts of persons with infectious TB</td>
<td>TST or IGRA, but not both</td>
</tr>
<tr>
<td>Persons who may not return for TST reading be-</td>
<td>IGRA preferred</td>
</tr>
<tr>
<td>cause of circumstances (e.g., homelessness or</td>
<td></td>
</tr>
<tr>
<td>methadone use) or logistic difficulties</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressed persons (e.g., those infected</td>
<td>TST or IGRA; use both if first is</td>
</tr>
<tr>
<td>with HIV or receiving treatment with prednis-</td>
<td>negative and suspicion is high</td>
</tr>
<tr>
<td>lone or TNF inhibitors)</td>
<td></td>
</tr>
<tr>
<td>Foreign-born persons</td>
<td>Screening only for those who</td>
</tr>
<tr>
<td></td>
<td>have immigrated in past 5 yrs,</td>
</tr>
<tr>
<td></td>
<td>use TST or IGRA, but not both</td>
</tr>
<tr>
<td>BCG vaccine recipients (if they belong to</td>
<td>IGRA preferred</td>
</tr>
<tr>
<td>another risk group)</td>
<td></td>
</tr>
<tr>
<td>Health care workers (screening program)</td>
<td>TST or IGRA, but not both</td>
</tr>
<tr>
<td>Children &lt; 5 yr old</td>
<td>TST preferred</td>
</tr>
<tr>
<td>Other risk groups</td>
<td>TST or IGRA, but not both</td>
</tr>
</tbody>
</table>

Horsburgh and Rubin, NEJM, 2011

**IGRA Summary**

- **IGRAs are a significant advancement because of high specificity and operational advantages to TST**
  - Like TST, it is not a perfect test. Cases will be missed if relying exclusively on an IGRA result
  - Provider and patient misconceptions need to be met with widespread education and access to consultation
  - Training, QA and maintaining IGRA proficiency of laboratory are feasible, achievable, and may be preferable to maintaining TST proficiency of thousands of clinic personnel
  - Cost-benefit advantage
**LTBI Treatment**

Before initiating treatment for LTBI:
- Rule out TB disease
  - Wait for culture result if specimen obtained
  - Assess/evaluate for symptoms
- Determine prior history of treatment for LTBI or TB disease
- Assess risks and benefits of treatment
  - Active liver disease
- Ascertain current and previous drug therapy and side effects

**Initiating Treatment: Patient Education**

- Counsel and educate patient
- Discuss patient’s risk for progressing to TB disease
- Emphasize benefits of treatment
- Assess whether patient willing to be treated for full treatment period
- Review common side effects
- Establish treatment plan

**Baseline Medical Evaluation**

- Medical history
  - History of TB or HIV treatment
  - TB exposure
  - Risks for drug toxicity
    - e.g., alcoholism, liver disease, pregnancy
  - Complete medication list
- Chest x-ray
  - Rule out TB disease
- Laboratory tests
  - CBC and chemistry panel, if indicated
  - 3 sputum samples for AFB smear, culture, & DST if TB symptoms or findings on chest x-ray
Treatment Regimens for LTBI

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Months of Duration</th>
<th>Interval</th>
<th>Minimum Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>9*</td>
<td>Daily</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td>2x wkly**</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>INH</td>
<td>6</td>
<td>Daily</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>2x wkly**</td>
<td></td>
<td>52</td>
</tr>
<tr>
<td>RIF</td>
<td>4</td>
<td>Daily</td>
<td>120</td>
</tr>
</tbody>
</table>

*Preferred ** Intermittent treatment only with DOT
INH=isoniazid; RIF=rifampin

How Much INH Needed for Prevention of TB?

- Longer duration corresponded to lower TB rates if took 0 – 9 mos.
- No extra increase in protection if took > 9 mos.


Isoniazid Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Doses</th>
<th>Ideal Duration</th>
<th>Complete Within</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily</td>
<td>270</td>
<td>9 months</td>
<td>12 months</td>
</tr>
<tr>
<td>Twice weekly*</td>
<td>76</td>
<td>9 months</td>
<td>12 months</td>
</tr>
<tr>
<td>Daily</td>
<td>180</td>
<td>6 months</td>
<td>9 months</td>
</tr>
<tr>
<td>Twice weekly*</td>
<td>52</td>
<td>6 months</td>
<td>9 months</td>
</tr>
</tbody>
</table>

*Rifampin Regimens

- RIF daily for 4 months is an acceptable alternative when treatment with INH is not feasible
  - INH resistant or intolerant
  - Patient unlikely to be adherent for longer treatment period
- In situations where RIF cannot be used (e.g., HIV-infected persons receiving protease inhibitors), rifabutin may be substituted
- Children should receive 6 months
- Rif + PZA for 2 months

*via Directly Observed Therapy
Comparison of INH vs. RIF for Treatment of LTBI

<table>
<thead>
<tr>
<th>Regimen Feature</th>
<th>9H</th>
<th>4R</th>
</tr>
</thead>
<tbody>
<tr>
<td>High efficacy</td>
<td>X</td>
<td>*</td>
</tr>
<tr>
<td>Lower hepatotoxicity</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Lower overall cost</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Higher adherence</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>More effective against INH-resistant strains</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>(e.g., among foreign-born persons)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shorter duration</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Fewer drug-drug interactions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Good evidence that 3R is at least as efficacious as 6H. Inferential reasoning from other evidence suggests that efficacy of 4R may approach that of 9H.

Weekly INH + Rifapentine x 12 weeks

- PREVENT TB study – Preliminary results
  - INH x 9 months vs. INH + Rifapentine weekly x 12 weeks via DOT
- Efficacy and safety similar
- 82% in INH/Rifapentine vs. 69% completion in standard therapy group

Special Situations – 1

- CXR consistent with old TB disease:
  - i.e., old fibrotic lesions consistent with prior tuberculosis – e.g. dense nodules, scar, volume loss, sharp margins, ‘hard’, bronchiectasis
  - TST reaction 5mm or greater
  - In addition to standard LTBI regimens, some prefer INH + RIF for 4 months, if previously untreated

Special Situations – 2

- CXR with evidence of old healed primary TB:
  - i.e., calcified solitary pulmonary nodule, apical pleural capping, calcified hilar lymph node
  - Not at increased risk of developing TB disease
  - Use other risk factors and appropriate TST size to determine treatment with standard regimen
LTBI and Tumor Necrosis Factor-alpha Inhibitors

- TNF alpha is a pro-inflammatory cytokine, often implicated in autoimmune diseases
- Necessary for host response to mycobacterial infections
- TNF alpha blockers increasingly used for rheumatoid arthritis, inflammatory bowel disease, psoriatic arthritis, ankylosing spondylitis
- One of the major complications is reactivation of *M. tuberculosis*

LTBI and TNF-alpha inhibitor: Management

- Rigorous screening for TB risk factors (e.g. country of origin, exposure, radiographic evidence of prior TB) prior to TNF alpha blocker
- Can use multiple modalities to increase sensitivity of recognizing LTBI (TST, IGRA, CXR)
- LTBI treatment is effective
- Concurrent LTBI treatment and TNF alpha inhibitor initiation is generally accepted
- Consider periodic re-testing
**Vitamin B₆ Supplementation**
- Uremia
- Malnutrition
- Alcoholism
- Diabetes
- Seizure disorder
- HIV infection
- Pregnancy

**Baseline Laboratory Evaluation**
- Not indicated routinely
- Indicated for:
  - Persons with HIV infection
  - Pregnant & postpartum women (up to 2-3 mos. after delivery)
  - Individuals with history/risk of liver disease
    - Heavy alcohol use
    - Chronic hepatitis
    - History of injection drug use
    - On two or more meds
    - On medications for other medical conditions

**Monthly Monitoring During LTBI Treatment – 1**
- Reinforce patient’s understanding of LTBI and its treatment
- Evaluate for signs and symptoms of active TB and drug reactions
- Monitor adherence to prescribed regimen
- Educate patient about signs and symptoms of hepatotoxicity
- Review all medications and assess for potential drug interactions

**Monthly Monitoring During LTBI Treatment – 2**
- Repeat liver function tests for
  - Patients with abnormal baseline
  - Persons with HIV infection
  - Pregnant and post-partum women
  - History/risk of liver disease
    - Heavy alcohol ingestion
    - Chronic hepatitis
    - History of injection drug use
    - On two or more meds
Management of the Patient Who Misses Doses

- Extend or re-start treatment for frequent or prolonged interruptions that preclude completion within recommended time frame
- Examine patients to rule out TB disease when treatment interruption > 2 months
- Recommend and arrange for DOT as needed

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

Re-treatment of LTBI

- Re-infection can occur and is especially of concern in immunocompromised individuals
- Re-treatment should be considered based on underlying medical conditions, severity of exposure and age

Take Home Points

- Decision to test = decision to treat
- Multiple diagnostic tools available, none are perfect
- IGRA can be used in place of TST in almost all situations
- Rule out TB disease
- Choose treatment regimen based on individualized evaluation of each patient
- Monthly clinical assessments and ongoing patient education important
- Use DOT for high-priority patients

Case #1

- 49 y.o. man emigrated from Nigeria 1 year ago
- History of daily alcohol use until 6 months ago, abstinent since
- Hypertension, Hypercholesterolemia
- Hepatitis B core antibody positive
- No known TB contacts
- QFT-Gold – positive
- Asymptomatic
- CXR normal
Case #1

Which of the following is an indication to recommend LTBI treatment to the patient?

A. Alcoholism
B. Recent emigration from a country with high TB prevalence
C. Hepatitis B
D. Cardiac co-morbidities

Case #1

- Baseline LFTs:
  - AST was at ULN
  - ALT was 2x ULN
- Repeat hepatitis markers revealed only HBV core Ab+
- He reported abstaining from alcohol
- INH 300 mg and vitamin B6 were started
- Patient discontinued INH 3 weeks later due to epigastric pain but did not seek medical attention
- 2 weeks later, symptoms improved, presents to clinic
  - AST 2x ULN, ALT 3x ULN

Case #1

- Transaminases were monitored off INH and slowly improved to baseline values (ALT 2x ULN)
- He was seen by Hepatology
- He presented to clinic after a 4 month gap for re-initiation of LTBI treatment

Aside from repeating LFTs, what else must be done prior to initiating treatment for LTBI?

A. Repeat QFT-Gold
B. Check sputum for AFB x 3
C. Re-interview the patient and assess for signs or symptoms of TB disease
**Case #2**

- 56 y.o. woman from Jamaica
- Emigrated 22 years ago
- TST 14 mm
- TST 1 year ago “negative”
- Contact of an active case
- Medical history: Autoimmune hepatitis, SLE
- Medications include prednisone 7.5 mg daily, Azathioprine 50 mg daily, Abatacept monthly
- Weight 48 kg, Height 152 cm, BMI = 20
- CXR normal
- AST, ALT are slightly above ULN

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**Case #2**

Which of the following is least likely to influence the decision to treat this patient for LTBI?

A. Recent TST conversion
B. Immigrant from an endemic country
C. Contact of an active case
D. Use of immunosuppressants

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**Case #2**

The patient wishes to discuss alternatives to INH. Which of the following discussion points should be raised regarding treatment with RIF?

A. Twice weekly RIF with DOT is an option
B. The duration of treatment is 9 months
C. Higher prednisone dose may be necessary
D. None of the above

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**Case #3**

65 y.o. homeless man with bladder cancer has received several doses of intravesicular BCG in the past year. He presents to you with documentation of a 12 mm TST (TST 18 months ago was 0 mm). You perform an IGRA which is positive. Which of the following is most likely true?

A. Results are compatible with sensitization to BCG and no further work-up is required
B. IGRA is a false positive and no further work-up is needed
C. Positive IGRA suggests *M.tbc* infection and additional history regarding exposure should be sought
D. Positive TST represents conversion which may be due to BCG
E. Both C and D are correct
Case #4

A 25 y.o. HIV infected, pregnant woman comes to see you with a TST reaction of 8 mm. She is a known contact to an active case. She is asymptomatic and has a normal CXR. The best course of action is:

A. Repeat the TST in 8-10 weeks
B. Begin INH and B6
C. Defer treatment until she is 2 months post delivery
D. Perform an IGRA

Each patient below has a TST of 6mm. Which one should be treated for LTBI, based on radiograph as sole risk factor?