TB Update for Civil Surgeons

April 15, 2010

Robert Belknap, MD
Topics

1. Discuss overseas screening and the importance of civil surgeons in TB elimination
2. Review the new I-693 Technical Instructions for TB screening
3. Who, when and how to refer patients to Public Health for TB follow-up
Objectives

After this course, you will be able to:

1. Describe the role of the civil surgeon in TB elimination
2. Complete the I-693 correctly
3. Explain when and how to refer patients to the Denver Metro TB Clinic
4. Describe when and how to treat latent TB
TB Evaluation – Step 1

Initial Exam
- Detailed hx of prior TB or exposure
- Review prior hospitalizations
- Obtain PMHx of serious illnesses
- Review previous CXRs and lab results
- Review of symptoms
- General Physical – lung exam and LN
25 yr old female

- Born in Mexico
- Had BCG vaccination as a child
- Immigrated to U.S. 5 years ago
- She comes to you for her change of status paperwork
- She is 16 weeks pregnant and asymptomatic
25 yr old female

- Should you do a TST?
- What cutoff would you use? Does the BCG history matter?
- What about an Interferon-\( \gamma \) Release Assay?
- If she tests positive, does she need a chest x-ray?
  - If yes, when would you get it (immediately or post-partum)?
TB Evaluation – Step 2

- Mantoux Tuberculin Skin Test (TST) or
- Interferon-gamma Release Assays (IGRAs)

All applicants ≥ 2 y/o regardless of pregnancy or prior BCG and those < 2 if a known contact to TB **unless**

1. Written documentation of (+) TST or IGRA
2. Report of a severe blistering reaction to a TST
Interferon-gamma Release Assays

- Blood tests for detecting TB infection
- Require only 1 visit to get a result
- Less subject to reader bias and error
- More specific with less cross-reaction with non-tuberculous mycobacterium and BCG than the TST

Lancet 2000;356:1099-104
2 Commercially Available IGRAs

QuantiFERON® - TB Gold
One blood test, one clear answer

A 21st Century Solution for Latent TB Detection
QuantiFERON-TB (Cellestis)

- Measures IFN-\(\gamma\) in stimulated whole blood
- Antigen – nil = IU/mL
- Result \(\geq 0.35\) is considered positive
T-SPOT.TB (Oxford Immunotec)

- Uses isolated peripheral blood mononuclear cells (PBMCs)
- Measures number of cells producing interferon-γ
- Nil, Antigen, and Mitogen
  - \( \leq 4 \) = Negative
  - 5-7 = Borderline
  - \( \geq 8 \) = Positive
What about BCG?

- A history of BCG is not a contraindication for a TST.
- A Positive TST reaction in a BCG vaccinated person usually indicates infection with TB.
- Do not alter your interpretation of the TST because of a history of BCG vaccination.
- The IGRAs appear to be more accurate in BCG vaccinated persons and should be considered where available.
Two-step testing and boosting

![Graph showing two-step testing and boosting.](image-url)
# Tuberculin Skin Test

## Criteria for a Positive Reaction

<table>
<thead>
<tr>
<th>≥5 mm</th>
<th>≥10 mm</th>
<th>≥15 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>Recent immigrants</td>
<td>No risk</td>
</tr>
<tr>
<td>Contact to active TB case</td>
<td>Injection drug users</td>
<td></td>
</tr>
<tr>
<td>Abnormal CXR</td>
<td>Children</td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>High-risk medical conditions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Residents and employees of jails/nursing homes, hospitals</td>
<td></td>
</tr>
</tbody>
</table>

Note: Skin test conversion is an increase of ≥10 mm within a 2-year period.
What if the patient comes back late?

If the patient returns after 72 hours

- Read the test
- If the reaction is large enough to be considered positive, record the result and proceed with the evaluation (ie CXR)
- If there is a small reaction or no reaction, the test should be repeated
25 yr old female

- Should you do a TST? Yes
- What cutoff would you use? 10mm
- What about an Interferon-γ Release Assay? Could Consider if Available

- Her TST is 26 mm, 16 weeks pregnant
- Does she need a CXR? When?
TB Evaluation – Step 3 (1)

- DO a CXR if the TST is ≥ 5mm or (+) IGRA
  - NOTE: applicants with symptoms of active TB should get a CXR regardless of the TST or IGRA
- If the CXR is abnormal
  - Infiltrate, cavity, nodule, pleural effusion, adenopathy, miliary pattern, fibrotic scar, volume loss

REFER to the TB CLinic
TB Evaluation – Step 3 (2)

- You do not need to refer the applicant if the only x-ray findings are
  - Pleural capping
  - Diaphragmatic tenting
  - Blunting of the costophrenic angle in adults
  - Solitary calcified nodule (granuloma) or calcified lymph node
30 y/o female

- from SE Asia
- Applying for permanent resident status
- Reported no symptoms
- TST 15 mm
30 y/o female

Culture (+) Pulmonary TB
Timing of CXR for Pregnant Applicants

1. Symptomatic Patient
   → CXR immediately
   * REGARDLESS of the TST or IGRA; 25% of pts with active TB have a (-) TST and/or IGRA

2. Asymptomatic Patient, TST or IGRA (+)
   → CXR any time after the first trimester
Risk of CXR for Pregnant Women

- Estimated fetal radiation from a PA and Lat CXR with proper shielding = 0.00007 rad

- Accepted maximum cumulative fetal dose during pregnancy = 5 rad

- Conclusion: would need > 71,000 CXR to reach this dose

Toppenberg, Am Family Physician 1999; 59(7): 1813-1818
25 yr old female

Radiology reading: Fibrotic opacity in the right upper lobe with pleural thickening consistent with scarring from old TB
25 yr old female

Now What?
1. Offer INH
2. Refer to pulmonary
3. Recommend a CT
4. Collect sputa for AFB
Tuberculosis Technical Instructions: Effective May 1, 2008 (1)

Major Changes:

1. Sputum cultures and drug susceptibility testing required for applicants with abnormal CXRs suggestive of TB

2. Class A – smear or culture positive TB must complete a full course of treatment before medical clearance can be given
3. A CXR is required for all applicants with a TST > 5mm, including pregnant women.

- “if she wishes, the applicant may defer until after delivery, but the civil surgeon cannot sign the medical exam”
- Can’t defer if symptomatic
4. A CXR is required for applicants with a TST < 5mm if they have:
   1. Signs or symptoms of active dz
   2. Immunosuppression (eg HIV, prednisone ≥ 15mg/d x 1 month, history of transplant)
Changes in TB Classification (1)

- Class A
  - 1991: Abnl CXR & + smear
  - 2007: Active TB (+ smear or culture)
- Class B1-Pulmonary
  - 1991: Active TB, not infectious (- smear)
  - 2007: Abnl CXR, neg Cx
- Class B1-Extrapulmonary
  - 1991: Active TB, not infectious
  - 2007: Extrapulmonary TB (w/o pulmonary)
Changes in TB Classification (2)

- Class B2 – Pulmonary TB, inactive
  - 1991: TB, not clinically active (no sputum required)
  - 2007:
    1. Abnl CXR but not suspicious for active TB (ie no sputum needed) or
    2. Treatment completed for active TB
Changes in TB Classification (3)

NEW

- Class B – Latent TB
  - (+) TST / IGRA, no symptoms, and a normal CXR

- Class B – Other Condition (non-TB)
  - Examples: cardiomegaly, scoliosis in a child
The instructions allow either a TST or IGRA, not both

- If an exception applies:
  - Prior documented (+) TST or IGRA
  - Report of a blistering reaction to a TST mark “Not Administered”
If an exception applies, check the box on page 2 and list the reason for the exception in the Remarks.
Only applicable to QFT

Represents the Antigen minus nil results

Labs may report only the calculated result or each result for Nil, Antigen and Mitogen
NOTE: an indeterminate or borderline result is treated as a negative
Indeterminate results don't actually provide useful info about LTBI
You do not need to refer the applicant if the only x-ray findings are:
- Pleural capping
- Diaphragmatic tenting
- Blunting of the costophrenic angle in adults
- Solitary calcified nodule (granuloma) or calcified lymph node
36 y/o male (1)

- From Philippines, in the U.S. for 15 years
- TST is 6mm
- CXR is normal

What classification is this?
36 y/o male (2)

- Although a CXR is done for anyone with a TST $\geq 5$mm, the TST needs to be 10mm to consider the person infected (ie. Class B, Latent TB Infection)

4. Chest X-Ray: Required based on TST or IGRA result, or if specific TST or IGRA exceptions apply, or for an applicant with TB signs or symptoms or immunosuppression (e.g., HIV). Attach a copy of X-ray report.

Date Chest X-Ray Taken: 4/7/10

Date Chest X-Ray Read: 4/8/10

Results:
- Normal
- Abnormal (Describe results in remarks.)

TB Classification/Findings (check only if chest x-ray was performed):
- No Class A or Class B TB
- Class A Pulmonary TB
- Class B1 Pulmonary TB
- Class B1 Extra Pulmonary TB
- Class B2 Pulmonary TB
- Class B, Latent TB Infection
- Class B, Other Chest Condition (non-TB)
42 y/o female from Vietnam (1)

- Cervical adenopathy
- Normal CXR
- (-) Quantiferon

What classification?

4. Chest X-Ray: Required based on TST or IGRA result, or if specific TST or IGRA exceptions apply, or for an applicant with TB signs or symptoms or immunosuppression (e.g., HIV). Attach a copy of X-ray report.

Date Chest X-R
Taken

4/12/10

Needs Further Work-up
42 y/o female from Vietnam (2)

- Biopsy shows granulomas
- AFB smear negative

B1 extrapulmonary TB - refer to the health dept.
Referral to the Denver Metro TB Clinic

- During business hours, 8:00a-6:00p Mon-Fri
  - Call (303) 602-7240, option 3
  - Ask to speak with the charge nurse

- After hours, page the ID physician on call
  - Call (303) 602-8710 and follow the instructions to reach the answering service
Helpful Information When Referring

- Demographics
  - Name, DOB, address, phone number
  - If available - place of employment, name and phone number of an alternate contact (family or friend)

- Symptoms
  - Cough, hemoptysis, fever, weight loss, night sweats, lymphadenopathy etc.

- Labs
  - HIV, CBC, LFTs, chemistries, AFB smear / culture

- CXR report

- TST or IGRA
Part 3. by civil surgeon
Denver Metro TB Clinic
605 Bannock Street
Denver, CO 80240
(303) 602-7240

Part 4. by TB clinic
Please send them with their current and prior CXRs and copies of any pertinent labs
Active Pulmonary TB, Class A TB (1)

- Smear or culture positive TB
- Mark Class A on the I-693 but don’t sign it until they have completed a full course of TB therapy (at least 6 months)

4. Chest X-Ray: Required based on TST or IGRA result, or if specific TST or IGRA exceptions apply, or for an applicant with TB signs or symptoms or immunosuppression (e.g., HIV). Attach a copy of X-ray report.

<table>
<thead>
<tr>
<th>Date Chest X-Ray Taken</th>
<th>Date Chest X-Ray Read</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>□ Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>□ Abnormal (Describe results in remarks.)</td>
</tr>
</tbody>
</table>

TB Classification/Findings (check only if chest x-ray was performed):

- □ No Class A or Class B TB
- □ Class A Pulmonary TB Disease
- □ Class B1 Pulmonary TB
- □ Class B1 Extra Pulmonary TB
- □ Class B2 Pulmonary TB
- □ Class B, Latent TB Infection
- □ Class B, Other Chest Condition (non-TB)
Active Pulmonary TB, Class A TB (2)

Reclassifying:

- Cross out the class A with a single stroke, initial and date the change
- Mark Class B2 Pulmonary TB

---

4. Chest X-Ray: Required based on TST or IGRA result, or if specific TST or IGRA exceptions apply, or for an applicant with TB signs or symptoms or immunosuppression (e.g., HIV). Attach a copy of X-ray report.

<table>
<thead>
<tr>
<th>Date Chest X-Ray Taken</th>
<th>Date Chest X-Ray Read</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>□ Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>□ Abnormal (Describe results in remarks.)</td>
</tr>
</tbody>
</table>

TB Classification/Findings (check only if chest x-ray was performed):

- [ ] No Class A or Class B TB
- [ ] Class A Pulmonary TB Disease
- [ ] Class B1 Pulmonary TB
- [ ] Class B1 Extra Pulmonary TB
- [ ] Class B2 Pulmonary TB
- [ ] Class B, Latent TB Infection
- [ ] Class B, Other Chest Condition (non-TB)
Reclassify:

- Indicate the following information in the Remarks section of the I-693 form (may attach a separate sheet of paper, if needed):
  - The TB drug regimen used (medication names, dosages, number of doses given).
  - The date treatment began (month/year).
  - The date treatment was completed (month/year).
  - The date and results of the most recent sputum culture tests (month/year).
Class B – Latent TB Infection (1)

- Asymptomatic
- Normal CXR or without findings that could represent active TB (eg. Isolated granuloma, or cardiomegaly)

- Health Department evaluation is not required to complete the I-693
Class B – Latent TB Infection (2)

- CDC recommends referral for LTBI treatment but you should **only** refer applicants if they are interested in taking LTBI treatment.

- We recommend offering LTBI treatment to patients who are either:
  - ≤ 50 y/o or
  - who have other medical illnesses that increase their risk of reactivation.
Class B – Latent TB Infection (3)

Figure 1. Lifetime Risk of Active Tuberculosis among Persons with a Non-conversion Positive Tuberculin Skin Test.

Risks were calculated with the assumption of a decrease in risk of 10 percent per decade.

Horsburgh, NEJM 2004 350; 20: 2060-7
### Table 3. Relative Risk of Reactivation Tuberculosis among Persons with Medical Conditions That Impair Immune Control of *M. tuberculosis*.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Study</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced HIV infection</td>
<td>Pablos-Mendez et al.(^{27})</td>
<td>9.9 (8.7–11.3)†</td>
</tr>
<tr>
<td></td>
<td>Moss et al.(^{26})</td>
<td>9.4 (3.5–25.1)</td>
</tr>
<tr>
<td>Old, healed tuberculosis</td>
<td>Ferebee,(^{13}) Ferebee et al.(^{20})</td>
<td>5.2 (3.4–8.0)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Pablos-Mendez et al.(^{27})</td>
<td>2.4 (2.1–2.8)†</td>
</tr>
<tr>
<td>Infliximab therapy</td>
<td>Keane et al.(^{28})</td>
<td>2.0 (0.7–5.5)†</td>
</tr>
<tr>
<td>Poorly controlled diabetes</td>
<td>Pablos-Mendez et al.(^{27})</td>
<td>1.7 (1.5–2.2)†</td>
</tr>
<tr>
<td>Silicosis</td>
<td>Cowie(^{29})</td>
<td>1.7 (1.3–2.1)†</td>
</tr>
<tr>
<td></td>
<td>Corbett et al.(^{30})</td>
<td>1.3 (1.1–1.7)†</td>
</tr>
<tr>
<td></td>
<td>Kleinschmidt and Churchyard(^{31})</td>
<td>1.2 (1.0–1.5)†</td>
</tr>
<tr>
<td>Underweight (≤10 percent below normal)</td>
<td>Palmer et al.,(^{22}) Edwards et al.(^{23})</td>
<td>1.6 (1.1–2.2)</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>Thorn et al.(^{32})</td>
<td>1.4 (1.1–1.9)†</td>
</tr>
<tr>
<td></td>
<td>Steiger et al.(^{33})</td>
<td>1.3 (1.2–1.4)†</td>
</tr>
</tbody>
</table>

Horsburgh, NEJM 2004 350; 20: 2060-7
- **Part 5** – fill out and sign only after the evaluation is complete
- **Part 6** - is for Refugees who are evaluated at a health dept and will generally be blank
25 yr old female

Now What?
1. Offer INH
2. Refer to pulmonary
3. Recommend a CT
4. Collect sputa for AFB
25 yr old female

- No other PMHx
- HIV (-)
- Sputum AFB smear (-) x 3

Because she has an infant at home, she is started on I/R/Z/E

All 3 Sputa are Culture (+) for MTB
25 yr old female
Referral to the Denver Metro TB Clinic

- During business hours, 8:00a-6:00p Mon-Fri
  - Call (303) 602-7240, option 3
  - Ask to speak with the charge nurse

- After hours, page the ID physician on call
  - Call (303) 602-8710 and follow the instructions to reach the answering service