Positive Tuberculin Skin Test (TST) for TB – What Next?
Wisconsin Tuberculosis Control Program, Wisconsin Department of Health Services

NOTE: Approximately one-half of positive TSTs found in Wisconsin are thought to be due to sensitization with non-tuberculous mycobacteria such as *M. avium* or *M. fortuitum*, based on our experience switching from only TSTs to use of Quantiferon (QFT) and T-Spot tests. Thus our primary recommendation in the event of a positive TST, in the absence of risk factors and symptoms during a screening exam, is to get a QFT or T-Spot. This will be negative in approximately one-half of those with a positive TST, and will save getting a chest X-ray and medical exam when not needed.

Assess patient for risk factors

**Risk factors for tuberculosis (TB) infection?**

*If there’s no risk of infection, a positive test is probably a false positive.*

- Close contacts of persons known or suspected to have active TB
- Foreign-born persons from areas that have a high incidence of active TB (any country other than the US, Canada, Australia, New Zealand, or a country in Western or Northern Europe)
- Persons who visit areas with a high prevalence of active TB, especially if visits are frequent or prolonged for more than 1 month
- Populations defined locally as having an increased incidence of latent *M. tuberculosis* (MTB) infection or active TB, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol
- Infants, children, and adolescents exposed to adults who are at increased risk for latent MTB infection or active TB
- **Wisconsin-specific note:** Congregate settings, Wisconsin State prisons and local jails are generally NOT high-risk areas in Wisconsin. The risk of TB is primarily in those inmates who have been in jails in other states, especially in the southern states.
- **Wisconsin-specific note:** The highest rate of TB in Wisconsin is in the City of Milwaukee; thus the Milwaukee Detention Center and health care and residential facilities within the City and within Milwaukee County can be considered high-risk areas, both for employees and for those served.

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Yes

<table>
<thead>
<tr>
<th>2 or more symptoms? (cough &gt; 2 weeks, fevers, night sweats, weight loss, sputum production, hemoptysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

Possible options:

a) Evaluate and offer treatment based on the test results you have.

b) Get Quantiferon™ or T-Spot™ test (IGRA) to assess for true infection with MTB if patient has contraindications to treatment or does not believe test; otherwise, don’t retest. Because the TST can potentially boost an IGRA response, the IGRA should be drawn on the same day the TST is read or wait 3-6 months from date of TST is administered.

c) After repeat assessment the patient and risk profile, assume the person is not infected and do not treat.

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Have medical evaluation and chest X-ray (PA and lateral) to assess for active TB disease; if CXR normal and medical exam negative, patient may have TB infection and should be offered preventive treatment.

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Evaluate for active TB disease: chest X-ray (PA and lateral), medical evaluation (including looking for extrapulmonary disease), sputum daily X 3 if CXR abnormal (send to Wisconsin State Lab of Hygiene for single day testing with rapid PCR; fee-exempt for TB suspects when submitted by local health department); if no active pulmonary or extrapulmonary disease, patient has TB infection and should be offered preventive medication.

Your local health department can assist with medications (the State TB Program has funds available if needed).

* No restriction on movements or work (*i.e.*, no quarantine or isolation) is needed during evaluation for +IGRA UNLESS patient is symptomatic and has risk factors for active TB disease. Your local health department can assist with this evaluation.
Positive Interferon Gamma Release Assay (IGRA) for TB – What Next?  
Wisconsin Tuberculosis Control Program, Wisconsin Department of Health Services

Assess patient for risk factors

**Risk factors for tuberculosis (TB) infection?  
(If there’s no risk of infection, a positive test is probably a false positive.)**

- Close contacts of persons known or suspected to have active TB
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### Evaluate for active TB disease:

- **chest X-ray (PA and lateral), medical evaluation (including looking for extrapulmonary disease), sputum daily X 3 if chest X-ray abnormal (send to Wisconsin State Lab of Hygiene for single day testing with rapid PCR; fee-exempt for TB suspects when submitted by local health department);** if no active pulmonary or extrapulmonary disease, patient has TB infection and should be offered preventive medication. Your local health department can assist with medications.

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### Flowchart:

1. **If 2 or more symptoms? (cough > 2 weeks, fevers, night sweats, weight loss, sputum production, hemoptysis)**
   - **Yes**
     - Have medical evaluation and chest X-ray (PA and lateral) to assess for active TB disease; if CXR normal and medical exam negative, patient may have TB infection and should be offered preventive treatment.
   - **No**
     - **If option b is accepted**
       - There is a possibility of a FALSE positive for MTB, due to cross-reaction, test variability (see note) or a test error. The test may also be TRULY positive due to an unrecognized exposure or extrapulmonary TB. Possible options:
         - a) Retest in 1-8 weeks;
         - b) Accept the positive test and proceed to evaluate with chest X-ray and exam and treat for infection; or
         - c) After repeat assessment of the patient and risk profile, assume the person is not infected and do not treat.

### Notes:

- **NOTE:** Serially tested low-risk health care workers who have a positive IGRA should be re-tested using >1.00 IU/mL TB antigen NIL to delineate true-positive.
- **NOTE:** IGRA tests provide an equally sensitive, but much more specific test of the body’s immune response to *Mycobacterium tuberculosis* complex. There can be no false positives caused by BCG vaccination. However, it is important to realize that there IS cross reaction (i.e., you can get a positive test) with *M. kansasii, M. szulgai,* and *M. marinum* infections--these are rare, but they do happen. Test variability in pre-analytical phase can also cause false-positives.

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* No restriction on movements or work (i.e., no quarantine or isolation) is needed during evaluation for +IGRA UNLESS patient is symptomatic and has risk factors for active TB disease. Your local health department can assist with this evaluation.

P-01182 (11/2015)
Proposed Assessment of Combined IGRA and TST for LTBI Diagnosis
Wisconsin Tuberculosis Control Program, Wisconsin Department of Health Services

Note: Consider carefully before using a second test. A second test should be used when there is evidence to believe the first test result was inaccurate due to risk for progression to disease, likelihood of previous exposure to infectious TB or likelihood of an error in original test method. Patients with signs, symptoms or radiographic evidence of TB disease may undergo further evaluation despite negative TST/IGRA.

Careful assessment of risk factors for TB infection and TB progression

TST+ / IGRA+

TST+ / IGRA- (*)

TST- / IGRA+ (*)

TST- / IGRA-

High Risk

Low Risk

LTBI

Document TST is likely false + and act on IGRA result

LTBI

Assess IGRA levels Possible LTBI

False + IGRA? Reversion?

No LTBI (**)

Repeat IGRA at 3 months

IGRA+

IGRA-

(*) Either TST+ or IGRA+ test can be significant in immunosuppression.

(**) TST- / IGRA- does not rule out TB in immunosuppression.

Adapted from Lalvani A, Pareek M Brit Med Bull 2010 & NTCA Use of IGRA’s Best Practice Recommendations 2015
<table>
<thead>
<tr>
<th>IGRA</th>
<th>TST</th>
<th>Risk for Progression</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Positive or Borderline | Unknown/not done     | High                 | Consider the individual infected with *M. tuberculosis* and treat accordingly   | Low positive: Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. (see section xxx)  
Borderline: Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample.                                                                                       |
|                      |                      | Low                  | Consider repeating the IGRA as soon as feasible, especially if low positive (QFT) or borderline (T-Spot). If repeat test negative, treat first IGRA as a false positive. If a first IGRA is NOT low positive or if second IGRA is positive on retesting, consider the individual infected with *M. tuberculosis* and treat accordingly |                                                                                                                                                                                                                                                                                                                                               |
| Unknown/not done     | Positive             | High                 | Consider the individual infected with *M. tuberculosis* and treat accordingly   | In individuals who are BCG-vaccinated, testing with an IGRA offers increased specificity over testing with TST  
In US-born individuals, there is no data to suggest increased utility of one test over the other.                                                                                                                                                                                                                                           |
|                      |                      | Low                  | Consider testing with an IGRA to increase specificity, especially if the patient is likely BCG-vaccinated or likely infected with an NTM |                                                                                                                                                                                                                                                                                                                                               |
| Positive or Borderline | Negative             | High                 | Consider the individual infected with *M. tuberculosis* and treat accordingly   | Low positive: Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. **Borderline:** Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample. |
|                      |                      | Low                  | Consider repeating the IGRA as soon as feasible, especially if low positive (QFT) or borderline (T-Spot). If repeat test negative, treat first IGRA as a false positive. If a first IGRA is NOT low positive or if second IGRA is positive on retesting, consider the individual infected with *M. tuberculosis* and treat accordingly |                                                                                                                                                                                                                                                                                                                                               |
| Positive or Borderline | Positive             | High                 | Individuals who test positive by both tests can be considered as infected with *M. tuberculosis* and should be treated accordingly | **Low positive:** Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. **Borderline:** Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample.                                                                                       |
|                      |                      | Low                  | Consider repeating the IGRA as soon as feasible if low positive (QFT) as boosting effects and variability or borderline (T-Spot). In a low risk person a positive test is more likely to be false positive. Consider the risk/benefits of treatment vs evaluation. |                                                                                                                                                                                                                                                                                                                                               |
| Negative              | Negative             | High                 | The greater likelihood is the individual can be considered not to be infected with *M. tuberculosis* Patients with signs, symptoms or radiographic evidence of infection may undergo further evaluation despite negative TST/IGRA. Neither test should be the deciding factor for children <5 at risk for progression or immunocompromised individuals are evaluated as they may be infected with Mtb and test negative | Children < 5 years of age who are part of a contact investigation who are screening test/exam/radiographically negative should receive window prophylaxis until the test can be repeated 8-10 weeks after break in contact.                                                                                     |
|                      |                      | Low                  | The individual can be considered not to be infected with *M. tuberculosis* |                                                                                                                                                                                                                                                                                                                                               |
| Negative              | Positive             | High                 | Consider the individual potentially infected with *M. tuberculosis* and treat accordingly based on clinical assessment weighing the risk/benefit of treatment vs. non-treatment. If BCG-vaccinated, may be false positive TST | In individuals who are BCG-vaccinated, testing with an IGRA offers increased specificity over testing with the TST.                                                                                                                                                                                                                         |
|                      |                      | Low                  | Consider the individual infected with *M. tuberculosis* and treat accordingly   |                                                                                                                                                                                                                                                                                                                                               |
|                      |                      |                      | Document that the TST is likely a false-positive and act on the IGRA result. Recommend that the individual be tested with an IGRA for future testing. |                                                                                                                                                                                                                                                                                                                                               |

*This table is reproduced from the NTCA IGRA workgroup document that can be found at: http://www.tbcontrollers.org/ntca-2/workgroups/igra-workgroup/#.VpQc5f5IhFo*