New TB Diagnostic Guidelines

Connie A. Haley, MD MPH
Southeast National TB Center
University of Florida
Division of Infectious Diseases and Global Medicine

Objectives

At the completion of this session, the participant will be able to:

• Explain how to select the appropriate diagnostic test for patients suspected of TB as an initial step in the clinical management of the disease to improve the timeliness and accuracy of diagnosing TB.
• Outline the current recommendations published by the CDC, ATS, and IDSA for the diagnosis of TB in adults and children to improve the timeliness and accuracy of diagnosing TB.
• Describe the guidelines for the diagnosis of LTBI using the TST or an IGRA to improve the accuracy of diagnosing TB infection.
• Recognize that NAAT are recommended as an adjunct to mycobacterial culture and AFB smear microscopy to enable rapid, timely diagnosis of TB.

Many of these slides have been kindly shared by Dr. David Lewinsohn, MD, PhD from his presentation at the American Thoracic Society meeting May 18, 2016.
• Published in AJRCCM, 2000
• Joint statement of ATS and CDC with endorsement by IDSA
• Predated availability of interferon-gamma release assays (IGRAs) and molecular tests for drug resistance

New Statement

• Joint statement of ATS, IDSA, CDC
  - One Chair from each
  - Equal Representation on Writing Committee
  - Funded through MTPI Assembly starting in 2007
  - Matching funding or in-kind contributions from IDSA and CDC
  - Organizational meeting ATS International Conference May 2007
• Partners
  - American Academy of Pediatrics
  - Association of Public Health Laboratories
• Harmonization with Concurrent and Overlapping Guidelines
  - AAP Red Book
  - CDC IGRA Guidelines Update
  - CDC Nucleic Acid Amplification Testing Guidelines Update

https://www.cdc.gov/tb/publications/guidelines/testing.htm
**GUIDELINE STATEMENT**

“These guidelines are not intended to impose a standard of care. They provide the basis for rational decisions in the diagnostic evaluation of patients with possible latent tuberculosis or tuberculosis. Clinicians, patients, third-party payers, stakeholders, or the courts should never view the recommendations contained in these guidelines as dictates. Guidelines cannot take into account all of the often compelling unique individual clinical circumstances. Therefore, no one charged with evaluating clinicians’ actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion. Qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines.”

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**Grading, Recommendations, Assessment, Development and Evaluation (GRADE) approach**

- Key diagnostic questions identified, pragmatic evidence synthesized and summarized.
- Recommendations formulated and quality of evidence and strength of each recommendation rated using GRADE approach (not a systematic review).
- The quality of evidence is the extent to which one can be confident that estimated effects are close to the actual effects and was rated as high, moderate, low, or very low.

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**Approach to Use of GRADE in the TB Diagnostics Statement**

- Benefits of Diagnostic Testing
  - Prevention of TB (TST, IGRA)
  - Detection of TB
- Studies of TB diagnostics are generally observational studies of diagnostic accuracy.
  - There is no Gold Standard for LTBI
  - No RCTs
- No direct linkage to management outcomes
- Recommendations could be rated at best as having a moderate quality of evidence.
- Certain issues/questions were given a GRADE recommendation where evidence basis was incomplete.
- In some cases, usual practice/options were described without a formal GRADE recommendation.
Guideline Content

- Testing for LTBI (4 recommendations-in LTBI lecture)
  - Adults (age ≥ 5y)
  - Children <5y
- Testing for TB Disease (16 recommendations)
  - Smear Microscopy
  - Bacterial Culture
  - Rapid Molecular Drug Susceptibility Testing
  - Testing for TB in Children
  - Sputum Induction
  - Bronchoscopy
  - Evaluation of Extra-pulmonary Specimens

Testing for *M. tuberculosis* infection

Methods for Detecting *M. tb* Infection

- Mantoux tuberculin skin test (TST)
- Interferon Gamma Release Assays (IGRAs):
  - QuantiFERON-TB Gold In-Tube (QFT-GIT)®, and
  - T-Spot.TB®
- Indirect measures of infection (cellular immune response)
- These tests do not exclude LTBI or TB disease
- Decisions about medical/public health management should not rely only on TST/IGRA results, but consider TB risk, setting, patient and source case factors
Testing for LTBI

• Recommendations for diagnostic testing for LTBI are based upon the likelihood of infection with M. tuberculosis and the likelihood of progression to TB disease if infected.
• Considering pre-test probability is essential

Paradigm for evaluation of those with LTBI based on risk of infection, risk of progression to TB, and benefit of therapy.

Question 1: Should an IGRA or a TST be performed in individuals 5 years or older who are likely to be infected with Mtb, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted?

• Evidence Basis
  - Sensitivity: IGRAS equal or better than TST (active TB as reference)
    • QFT-GIT  81-86 %
    • TSPOT  90-95 %
    • TST  71-83%
  - Specificity: IGRAs better than TST if BCG, same if no BCG (Individuals unlikely to be exposed to Mtb as reference)
    • QFT-GIT  >95%
    • TSPOT  85-97%
    • TST
      • Had BCG  60%
      • No BCG  97%
Recommendation 1a:
Perform an IGRA rather than a TST in individuals 5 years or older who meet the following criteria:

- Are likely to be infected with Mtb.
- Have a low or intermediate risk of disease progression.
- It has been decided that testing for LTBI is warranted.
- Either have a history of BCG vaccination or are unlikely to return to have their TST read.

**Strong recommendation, moderate quality evidence**

- Remarks: A TST is an acceptable alternative, especially in situations where an IGRA is not available, too costly, or too burdensome.

Recommendation 1b:
Perform an IGRA rather than a TST in all other individuals 5 years or older who are likely to be infected with Mtb, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted.

**Conditional recommendation, moderate quality evidence**

- Remarks: A TST is an acceptable alternative, especially in situations where an IGRA is not available, too costly, or too burdensome.

Question 2: Should an IGRA or a TST be performed in individuals ≥5 years who are likely to be infected with Mtb, who have a high risk of progression to disease, and in whom it has been decided that testing for LTBI is warranted?

- **Evidence Basis**
  - Heterogeneous population
  - Very limited data in high income settings
  - TSPOT may be less affected by low CD4 counts
  - Immunosupression is associated with impaired test performance for all cellular assays
  - Sensitivity in HIV (active TB as reference standard)
  - QFT-GIT / TSPOT 65-100% (65,100)
  - TST 43% (25,85)
**Recommendation 2:**
There are insufficient data to recommend either a TST or an IGRA as the preferred first-line diagnostic test in individuals 5 years or older who are likely to be infected with Mtb, who have a high risk of progression to disease, and in whom it has been determined that diagnostic testing for LTBI is warranted.

Remarks:
To maximize sensitivity, the clinician may wish to consider dual testing where a positive result from either test would be considered evidence of infection with *M. tuberculosis*.

**Question 3:**
Should an IGRA or a TST be performed in individuals 5 years or older who are unlikely to be infected with *Mtb*, but in whom it has been decided that testing for LTBI is warranted?

**Evidence Basis**
- Specificity of IGRA is superior to TST, particularly in those with a history of BCG vaccination.
- IGRA contain only antigens not found in BCG
- IGRA distinguish NTM except *M. kansasii*, *M. marinum*, *M. szulgai*, and *M. flavescens*

**Question 3 (Continued)**
“Guidelines recommend that persons at low risk for Mtb infection and disease progression NOT be tested for Mtb infection.

*We concur with this recommendation.*
Question 3 (cont.):
However, we also recognize that such testing may be obliged by law or credentialing bodies. If diagnostic testing for LTBI is performed in individuals who are unlikely to be infected with Mtb despite guidelines to the contrary:

Recommendation 3a:
Perform an IGRA instead of a TST test in individuals 5 years or older.

Conditional recommendation, low quality evidence

Remarks:
A TST is an acceptable alternative in settings where an IGRA is unavailable, too costly, or too burdensome.

Question 3:
Individuals unlikely to be infected (Cont.)

Recommendation 3b:
Perform a second diagnostic test if the initial test is positive in individuals 5 years or older.

Conditional recommendation, very low quality evidence

Remarks:
The confirmatory test may be either an IGRA or a TST. When such testing is performed, the person is considered infected only if both tests are positive.

Longitudinal Testing
(eg. For Health Care Workers)

- Do not routinely test persons at low risk.
- Committee felt that there was not sufficient evidence to make a specific recommendation.
  - Criteria for TST boosting and conversions have been established.
  - While FDA has established criteria for positive and negative tests, criteria for conversions and reversions are not established for IGRA.
  - However, IGRA has not proven to be the solution to the problem of falsely positive results associated with serial testing in low risk individuals.
  - In 2563 HCW IGRA conversions occurred at a rate of 6.8% with many not confirmed on repeat testing.
- Therefore, TST and IGRA are both acceptable in this setting.
- May consider confirmatory (dual) testing in this setting

Question 4: Should an IGRA or a TST be performed in healthy children <5 years of age in whom it has been decided that testing for LTBI is warranted?

Evidence Basis

- Limited evidence regarding IGRA performance in young children (fewer studies, esp. in low TB prev. areas)
- Sensitivity of IGRA in young children with TB 52% - 100%, is comparable to adults.
- Sensitivity of TST reported as equivalent or increased compared with IGRA in children; young age associated with decreased IGRA positivity.
- Specificity of IGRA appears in children 90%-100%, higher than TST (in children with NTM)

Recommendation 4: Perform a TST rather than an IGRA in healthy children <5 years of age for whom it has been decided that diagnostic testing for LTBI is warranted.

Conditional recommendation, very low-quality evidence

Summary of recommendations for testing for LTBI

<table>
<thead>
<tr>
<th>Group</th>
<th>Testing Strategy</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely to be infected High Risk of Progression (TST &gt; 10mm)</td>
<td>Acceptable: IGRA OR TST</td>
<td>Consider dual testing when positive result</td>
</tr>
<tr>
<td></td>
<td>Acceptable: IGRA OR TST</td>
<td>Consider dual testing when positive result</td>
</tr>
<tr>
<td>Likely to be infected Low Risk of Progression (TST &lt; 5mm)</td>
<td>Preferred: IGRA when available</td>
<td>Acceptable: IGRA OR TST</td>
</tr>
<tr>
<td>Likely to be infected Low Risk of Progression (TST &gt; 10mm)</td>
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</tbody>
</table>
## Screening for LTBI in Adults. US Preventive Services Task Force (USPSTF) Recommendation Statement

**Evidence Review:** The USPSTF reviewed the evidence on screening for LTBI in asymptomatic adults seen in primary care, including evidence dating from the inception of searched databases.

**Finding:** The USPSTF found adequate evidence that accurate screening tests for LTBI are available, treatment of LTBI provides a moderate health benefit in preventing progression to active disease, and the harms of screening and treatment are small. The USPSTF has moderate certainty that screening for LTBI in persons at increased risk for infection provides a moderate net benefit.

### Screening for LTBI in Adults. US Preventive Services Task Force (USPSTF) Recommendation Statement

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
</tr>
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<tbody>
<tr>
<td>Asymptomatic adults seen in primary care</td>
<td>Screening for LTBI is recommended.</td>
<td>B</td>
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## Diagnostic Tests for TB

### Bacteriologic examination has 5 parts

1. Specimen collection
2. AFB smear classification
3. Nucleic acid amplification testing (NAA, NAAT, PCR etc., DNA probe)
4. Culture and identification
5. Drug-susceptibility testing (DST)
Diagnostic Testing for TB

- In US, up to 80% of initial TB-related laboratory work (eg, AFB smear/culture) performed in hospitals, clinics, labs outside public health system
- But, >50% of species identification and DST is performed in public health laboratories
- PH lab workers should take a leadership role in developing networks and flow of information among lab workers, clinicians and TB controllers
**Question 5:** Should AFB smear microscopy be performed in persons suspected of having pulmonary TB?

**Evidence Basis:**
- 70% overall sensitivity of 3 sputum smears for AFB; each increases sensitivity
  - 1st smear 54%
  - 2nd + 11%
  - 3rd + 2.5%
- Sensitivity of first morning specimen 12% > single spot specimen
- Concentrated specimens have mean increase 18% in sensitivity vs nonconcentrated specimens
- Sensitivity of fluorescence microscopy ~ 10% > conventional micro.
- Specificity of smears >90%

**Recommendation 5:** AFB smear microscopy should be performed, rather than no AFB smear microscopy, in all patients suspected of having pulmonary TB.

*Strong recommendation, moderate quality evidence*

**Remarks:**
- A negative AFB smear result does not exclude pulmonary TB.
- A positive AFB smear result does not confirm pulmonary TB.
- At least 2 respiratory specimens should be tested, at least one first morning specimen
  - CDC and NTCA strongly recommend 3 sputum specimens

**Question 6:** Should both liquid and solid mycobacterial cultures be performed in persons suspected of having pulmonary TB?

**Evidence Basis:**
- Meta-analysis comparing 2 liquid culture methods with solid
- Both liquid methods more sensitive (88% and 90%) than the solid culture method (76%)
- 2 liquid methods had shorter time to detection (13.2d and 15.2d) vs 25.8d for the solid method.
- Specificity of all 3 was 99%
- 4-9% contamination rate of growth other than mycobacteria in liquid culture method
Recommendation 6: **Both liquid and solid** mycobacterial cultures should be performed for every specimen obtained from an individual with suspected TB disease.

*Conditional recommendation, low quality evidence*

**Remarks:**
- Liquid cultures alone are reasonably sensitive and highly specific, but limited by bacterial contamination
- Solid cultures alone are not sufficiently sensitive to reliably diagnose TB and take longer to yield results; however, some Mtb isolates are detected only on solid medium.

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**Question 7:** Should NAAT be performed on the initial respiratory specimen in persons suspected of having pulmonary TB?

**Evidence Basis**
- AFB Smear Positive\(^1\)
  - Sensitivity of NAAT is 96%, Specificity is 85%
- AFB Smear Negative\(^2\)
  - Sensitivity 66%, Specificity 98%
- Not stratified by AFB smear results\(^2\)
  - Sensitivity 85%, Specificity 97%
- Positive NAAT beneficial in AFB smear (-) individuals when clinical suspicion of TB intermediate or high, Negative NAAT is of little use in excluding TB\(^3\)


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**Recommendation 7:** A diagnostic **NAAT should be performed on the initial respiratory specimen** from patients suspected of having pulmonary TB

*Conditional recommendation, low quality evidence*

**Remarks:**
- Laboratory-based diagnostic tests are not a replacement for clinical judgment and experience. A diagnosis of pulmonary TB can be made in the absence of laboratory confirmation, especially in children.
Question 8: Should rapid molecular drug susceptibility testing for isoniazid and rifampin be performed as part of the initial diagnostic evaluation for all patients suspected of having pulmonary TB or only in selected subgroups?

Evidence Basis:
• Line probe assays detect RIF resistance with sensitivity ≥97% and specificity of ≥98% (e.g., MTBDRplus, Hain Lifesciences)
• Molecular-beacon based method (XPERT MTB/RIF) >92% sensitive and >99% specific for detection of rifampin resistance when performed on single specimen; sensitivity >97% for 3 specimens
• PPV of rapid molecular DST to detect rifampin resistance low in populations with low prevalence of drug resistance

Recommendation 8: Perform rapid molecular DST for rifampin with or without isoniazid using the respiratory specimens of persons who are either AFB smear positive or Hologic Amplified MTD positive and who meet one of the following criteria:
(1) have been treated for TB in the past,
(2) were born in or have lived for at least 1 year in a foreign country with at least a moderate TB incidence (≥20 per 100,000) or a high primary MDR-TB prevalence (≥2%),
(3) are contacts of patients with MDR-TB, or
(4) are HIV infected

Strong recommendation, moderate-quality evidence

Remarks: CULTURES STILL REQUIRED for growth-based DST!

Question 9: Should respiratory specimens be collected from children with suspected pulmonary TB disease?

Evidence Basis:
• Respiratory specimens that can be collected from children:
  - Gastric aspirates on 3 consecutive mornings, yield 40%-50%, up to 90% for infants, and up to 77% children with extensive disease
  - Nasopharyngeal aspiration or sputum induction with a bronchodilator has yield of 20%-30%
  - Bronchoalveolar lavage (BAL) has yield 10%-22%
  - Spontaneous expectoration

See http://www.currytbcenter.ucsf.edu/pediatric_TB/
Recommendation 9: **All children** suspected of having pulmonary TB **should have mycobacterial culture** of respiratory specimens

*Strong recommendation, moderate-quality evidence*

Remarks:
- Benefits include confirmed diagnosis, isolate for DST enables appropriate TB therapy, genotyping
- Downsides: cost, burden, risk of procedures, false results
- Selection of appropriate respiratory specimen based upon expertise of the clinic and provider, the patient’s age and developmental level, and likelihood of an alternative diagnosis

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Question 10: Should sputum induction or flexible bronchoscopic sampling be the initial respiratory sampling method for individuals with suspected pulmonary TB who are either unable to expectorate sputum or whose expectorated sputum is AFB smear microscopy negative?

**Evidence Basis:**
- Induced sputum has equal or greater diagnostic yield than bronchoscopic sampling,
  - Detection by AFB smear 91%-98% and culture 99-100% when 3 or more specimens obtained
- Induced sputum also has fewer risks and is less expensive than bronchoscopy

Recommendation 10: **Use sputum induction** rather than flexible bronchoscopic sampling as the *initial* respiratory sampling method for individuals with suspected pulmonary TB who are either unable to expectorate sputum or whose expectorated sputum is AFB smear microscopy negative.

*Conditional recommendation, low-quality evidence*

Remarks:
- Potential advantage of bronchoscopy is possibility of making rapid presumptive diagnosis of TB through biopsies and histopathologic findings, but balance of upsides to downsides of induced sputum outweighed bronchoscopic sampling.
Recommendation 11: Use flexible bronchoscopic sampling, rather than no bronchoscopic sampling, in individuals with suspected pulmonary TB from whom a respiratory sample cannot be obtained via induced sputum

*Conditional recommendation, very low-quality evidence*

**Remarks:**
- Bronchoscopy in a patient with possible pulmonary TB can:
  - Differentiate TB disease from alternative diseases
  - Obtain specimens for cultures, DST, histopathology
- Consider costs, delays in referrals to pulmonology, risk of procedure, etc.

Recommendation 12: Postbronchoscopy sputum specimens be collected from all individuals with suspected pulmonary TB who undergo bronchoscopy

*Conditional recommendation, low-quality evidence*

**Evidence Basis:**
- Postbronchoscopy AFB smears have diagnostic yield 9%–73%, postbronchoscopy cultures have yield of 35%–71%
- In one study of HIV infected patients, the yield of postbronchoscopy sputum cultures was 80%
- Specimens can be tested with AFB smear microscopy, mycobacterial culture, NAAT, DST.

**DIAGNOSTIC APPROACH:**
**TESTING FOR SUSPECTED EXTRAPULMONARY TB**
Extrapulmonary TB

- Specimens other than sputum may be obtained
- Depends on part of body affected

Recommendation 13: If induced sputum is AFB smear negative or a respiratory sample cannot be obtained via induced sputum, use flexible bronchoscopic sampling in individuals with suspected miliary TB and no alternative lesions that are accessible for sampling.

*Conditional recommendation, very low-quality evidence*

Remarks:
- Sampling should include bronchial brushings and/or TBB, as yield from washings is substantially less and yield from BAL is unknown
- Can get rapid presumptive diagnosis by identifying histopathologic findings consistent with TB

Recommendation 14: Cell counts and chemistries should be performed on amenable fluid specimens collected from sites of suspected extrapulmonary TB

*Conditional recommendation, very low-quality evidence*

Remarks:
- No studies reported sensitivity and specificity, based on clinical experience
- Cell counts and chemistries can be obtained for pleural, cerebrospinal, ascitic, and joint fluids.
- Performed in hours, are inexpensive, technically simple
- Risks related to sampling procedure
Recommendation 15a: Adenosine deaminase (ADA) levels should be measured on fluid collected from patients with suspected pleural TB, TB meningitis, peritoneal TB, or pericardial TB

Conditional recommendation, low-quality evidence

Recommendation 15b: Free IFN-γ levels should be measured on fluid collected from patients with suspected pleural TB or peritoneal TB

Conditional recommendation, low-quality evidence

Remarks: For both ADA and free IFN-γ levels, sensitivity and specificity depend on definition of elevated level and type of body fluid tested, but found to be moderate to high in multiple studies

Recommendation 16: AFB smear microscopy should be performed on specimens collected from sites of suspected extrapulmonary TB

Conditional recommendation, very low-quality evidence

Recommendation 17: Mycobacterial cultures should be performed on specimens collected from sites of suspected extrapulmonary TB

Strong recommendation, low-quality evidence

Remarks: Diagnostic yield and sensitivity of AFB smear microscopy and culture in extrapulmonary TB lower than pulmonary TB because often paucibacillary; specificity is high.

Recommendation 18: NAAT should be performed on specimens collected from sites of suspected extrapulmonary TB

Conditional recommendation, very low-quality evidence

Evidence and Remarks:
- NAAT on pleural and CSF had sensitivity of 56% and 62%, respectively
- Specificity of NAAT 98% for both pleural and CSF
- Sensitivity and specificity variable for other disease sites
- Positive test suggests TB, negative does not exclude TB
- NAAT is off label on specimens other than sputum
<table>
<thead>
<tr>
<th>Recommendation 19: Histological examination be performed on specimens collected from sites of suspected <strong>extrapulmonary TB</strong></th>
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<td><strong>Conditional recommendation, very low-quality evidence</strong></td>
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<tr>
<td><strong>Evidence and Remarks:</strong></td>
</tr>
<tr>
<td>• Sensitivity moderate to high, depends on tissue type</td>
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<tr>
<td>• Specificity tends to be low because necrotizing and nonnecrotizing granulomas seen in other infectious and noninfectious diseases.</td>
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<tr>
<td>• Both positive and negative results should be interpreted in the context of the clinical scenario</td>
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<thead>
<tr>
<th>Recommendation 20: Submit one culture isolate from each mycobacterial culture–positive patient to a regional genotyping laboratory for <strong>genotyping</strong></th>
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<tbody>
<tr>
<td><strong>Strong recommendation, very low-quality evidence</strong></td>
</tr>
<tr>
<td><strong>Evidence and Remarks:</strong></td>
</tr>
<tr>
<td>• No evidence, based on clinical experience</td>
</tr>
<tr>
<td>• Genotyping useful in detecting false-positive results due to lab cross-contamination, investigating outbreaks, evaluating contact investigations, determining whether new episodes of TB are due to reinfection or reactivation, and elucidating sites and patterns of Mtb transmission within communities</td>
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<table>
<thead>
<tr>
<th>THINK TB!!!</th>
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<tr>
<td><em>(then evaluate appropriately)</em></td>
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TB Diagnosis Guidelines Writing Committee Members

- David Cohn
- Charles Daley
- Ed Desmond
- Joe Keane
- Deborah Lewinsohn
- Ann Loffler
- Jerry Mazurek
- Rick O’Brien
- Madhu Pai
- Luca Richeldi

- Max Salfinger
- Tom Shinnick
- Tim Sterling
- Dave Warshauer
- Gail Woods
- Michael Leonard (IDSA)*
- David Lewinsohn (ATS)*
- Philip LoBue (CDC)*

References and Resources


Summary of Recommendations: Pulmonary TB Disease

- We recommend that AFB smear microscopy be performed, rather than no AFB smear microscopy, in all patients suspected of having pulmonary TB.
- We suggest that both liquid and solid mycobacterial cultures be performed, rather than either culture method alone, for every specimen obtained from an individual with suspected TB disease.
- We suggest performing a diagnostic NAAT, rather than not performing a NAAT, on the initial respiratory specimen from patients suspected of having pulmonary TB.

Summary of Recommendations: Pulmonary TB Disease

- We recommend performing rapid molecular drug susceptibility testing for rifampin with or without isoniazid using the respiratory specimens of persons who are either AFB smear positive or Hologic Amplified MTD positive and who meet one of the following criteria:
  1) have been treated for TB in the past
  2) were born in or have lived for at least one year in a foreign country with at least a moderate tuberculosis incidence (≥ 20 per 100,000) or a high primary multi-drug resistant (MDR) TB prevalence (≥ 2%),
  3) are contacts of patients with MDR tuberculosis, or
  4) are Human Immunodeficiency Virus (HIV) infected.

Summary of Recommendations: Pulmonary TB Disease

- We recommend mycobacterial culture of respiratory specimens for all children suspected of having pulmonary TB.
- We suggest sputum induction rather than flexible bronchoscopic sampling as the initial respiratory sampling method for individuals with suspected pulmonary TB who are either unable to expectorate sputum or whose expectorated sputum is AFB smear microscopy negative.
- We suggest flexible bronchoscopic sampling, rather than no bronchoscopic sampling, in individuals with suspected pulmonary TB from whom a respiratory sample cannot be obtained via induced sputum.
### Summary of Recommendations: Pulmonary TB Disease

- We suggest that **postbronchoscopy sputum specimens** be collected from all individuals with suspected pulmonary TB who undergo bronchoscopy.
- We suggest **flexible bronchoscopic sampling**, rather than no bronchoscopic sampling, in individuals with suspected **miliary TB** and no alternative lesions that are accessible for sampling whose induced sputum is AFB smear microscopy negative or from whom a respiratory sample cannot be obtained via induced sputum.

### Summary of Recommendations: Extrapulmonary TB Disease

- We suggest that **cell counts and chemistries** be performed on amenable fluid specimens collected from sites of suspected extrapulmonary TB.
- We suggest that **adenosine deaminase levels** be measured, rather than not measured, on fluid collected from patients with suspected pleural TB, TB meningitis, peritoneal TB, or pericardial TB.
- We suggest that **free IFN-γ levels** be measured, rather than not measured, on fluid collected from patients with suspected pleural TB or peritoneal TB.
- We suggest that **AFB smear microscopy** be performed, rather than not performed, on specimens collected from sites of suspected **extrapulmonary TB**.

### Summary of Recommendations: Extrapulmonary TB Disease

- We recommend that **mycobacterial cultures** be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB.
- We suggest that **NAAAT** be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB.
- We suggest that **histological examination** be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB.
- We recommend one culture isolate from each mycobacterial culture-positive patient be submitted to a regional genotyping laboratory for **genotyping**.

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2017 National TB Conference - Atlanta, Georgia
**NAAT and AFB Smear Results**

- If NAAT and AFB smears are both positive:
  - Patient presumed to have TB and should begin treatment
  - NAAT yields false-negative results only 4% of the time, so a negative NAAT makes TB disease unlikely
- If NAAT positive and AFB smear is negative:
  - If clinical suspicion for TB is intermediate to high:
    - Positive NAAT result can be used as presumptive evidence of TB (few false-positive results); start therapy
    - Negative NAAT cannot be used to exclude pulmonary TB because false-negative results are common
- If NAAT is negative and AFB smears are positive:
  - Patient may have nontuberculous mycobacteria infn (NTM)