

Mycobacterium tuberculosis - TB

Clinical Background

Mycobacterium tuberculosis, as well as other non-tuberculosis species, can be infectious agents in humans.

Mycobacterium tuberculosis

- Epidemiology
 - Incidence and prevalence
 - 4-6/1,000,000 (CDC 2006)
 - 8-9 million new cases occur per year
 - 3-4 million cases of infectious pulmonary disease (smear positive)
- Organism
 - Mycobacteria belong to the order Actinomycetales and the family Mycobacteriaceae
 - *Mycobacterium tuberculosis* – rod-shaped aerobic bacterium with acid-fast staining properties
 - *Mycobacterium tuberculosis* complex (MTB) – *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. microti* and others
 - Transmission is via inhalation of droplet nuclei
- Risk Factors
 - Once the patient has been infected, the risks for developing active tuberculosis (TB) include:
 - Comorbidity present (HIV, immunosuppression, fibrotic lung disease, chronic renal failure, diabetes mellitus)
 - Recent tuberculosis infection (<1 year)
 - Malnutrition, alcoholism
 - Fibrotic lesions on chest x-ray
- Clinical Presentation
 - Primary disease
 - Ranges from mild, self-limited illness to severe disseminated disease
 - Post primary disease
 - Reactivation of latent infection
 - Moderate to severe, progressive and often fatal disease
 - Extrapulmonary TB
 - Gastrointestinal disease
 - Genitourinary
 - Lymphadenitis
 - Meningitis, central nervous system tuberculoma
 - Miliary
 - Pericarditis
 - Pleural disease
 - Skeletal (Pott disease)
 - TB in patients with HIV
 - Extrapulmonary disease is common
 - Atypical chest x-ray findings
 - Delays in diagnosis and treatment are common
 - Increased risk of reactivation of latent disease and rapid progression of newly acquired infection

Nontuberculous (atypical) mycobacteria (NTM)

- Epidemiology

- Age – usually isolated
- Transmission via cutaneous, inhalation, or parenteral routes
 - Widely distributed in water, soil and animal species
 - Person-to-person transmission has not been reported
- Organisms
 - Free-living organisms; more than 125 species of NTM
 - Nontuberculous organisms
 - *M. avium* complex, *M. kansasii*, *M. fortuitum*, *M. abscessus*, *M. chelonae*, *M. marinum*, *M. haemophilum*
 - Rare new organisms
 - *M. nebraskerise*, *M. parmense*, *M. saskat-chewanense*, *M. arupense*, *M. caprae*, *M. colombiense*, *M. florentium*, *M. montefiorensis*
 - Pathogenicity and clinical significance vary with species and host
 - Asymptomatic infections are common
- Clinical Presentation
 - Cutaneous – *M. fortuitum*, *M. abscessus*, *M. chelonae*, *M. marinum*, *M. haemophilum*
 - Nodular or ulcerating chronic lesions that fail to respond to standard antimicrobial therapy
 - Lymphadenitis - *M. avium* complex, especially in children
 - Pulmonary – *M. avium* complex, *M. kansasii*, *M. abscessus*
 - Chronic cough usually present
 - Immunocompromised and immunocompetent hosts
 - Increased in elderly and patients with underlying pulmonary disease
 - Bronchiectatic, nodular or cavitory disease
 - Disseminated
 - Weight loss, fever, fatigue, lymphadenopathy, hepatosplenomegaly, gastrointestinal complaints
 - Usually immunocompromised patients (advanced HIV, transplant)
 - Other (catheter-related, skeletal)

Diagnosis

Mycobacterium tuberculosis

- Diagnosis
 - Indications for testing – cough, fever, weight loss in at-risk patients
 - Laboratory testing
 - Based on acid-fast bacilli (AFB) smear, culture and nucleic acid amplification testing
 - Culture provides the definitive diagnosis
 - Susceptibility testing is mandatory
 - Latent *M. tuberculosis* – Interferon alpha release assays (QuantiFERON®)
 - Adenosine deaminase (ADA)
 - Adjunctive test for use in the evaluation of suspected extrapulmonary tuberculosis involving body cavities (or cerebrospinal fluid [CSF])
 - Reported sensitivity and specificity vary
 - Meta-analysis derived summary receiver operator curves (ROC) from pleural fluid: sensitivity 92%; specificity 92%
 - Not specific for tuberculosis
 - AFB culture should always be performed
 - Imaging studies

- Chest x-ray confirmation is required (may have been performed prior to TB testing)

Nontuberculous (atypical) mycobacteria

- Diagnosis
 - Indications for testing – clinical setting suspicious for disease
- Laboratory testing
 - Concentrated AFB smear
 - Traditional standard screening method (sputum)
 - Not as sensitive as culture (requires approximately 10^4 bacilli/mL sputum for detection)
 - Not specific for *Mycobacterium tuberculosis* complex
 - Mycobacterial culture
 - Most sensitive test for detection of mycobacteria (gold standard)
 - Slow (2-8 weeks)
 - Should be performed on any specimen for which mycobacteria are a consideration
 - Required to make the diagnosis of disseminated disease
 - Positive culture from a normally sterile site
 - Nucleic acid amplified testing (NAAT)
 - Emerging recommended method for rapid, sensitive and specific detection of MTB complex
 - Less sensitive than culture
- Imaging studies
 - Chest x-ray – cavities, frank parenchymal infiltrates, bronchiectasis, pulmonary nodules
 - Does not distinguish between TB and NTM
 - CT – may give better global picture of disease present

Screening

(*Mycobacterium tuberculosis*)

- Targeted tuberculin testing for latent TB infection for foreign-born persons entering the U.S. within the past 5 years

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
<p>AFB Culture (Includes AFB Stain 0060151) 0060152</p> <p>Method: Standard reference procedures for stain and culture. Identification of AFB is ordered and billed separately. DNA probes are available for <i>M. tuberculosis</i> complex and <i>M. avium-intracellulare</i> complex as indicated. DNA sequencing and other molecular techniques are used for identification. For drug susceptibilities, refer to Antimicrobial Susceptibility - AFB Mycobacteria (0060217).</p>	<p>Gold standard, most sensitive test for diagnosing mycobacteria</p> <p>Use for detection in sputum, tissues, urine and other body fluids</p>	<p>Time to detection (mycobacteria are slow growing organisms)</p>	<p>DNA probes are available for <i>M. tuberculosis</i> complex and <i>M. avium-intracellulare</i> complex as indicated. DNA sequencing and other molecular techniques are used for identification of other mycobacteria species. For drug susceptibilities, refer to Antimicrobial Susceptibility - AFB Mycobacteria (0060217)</p>
<p><i>Mycobacterium tuberculosis</i> Amplified Direct Detection 0060095</p> <p>Method: Transcription Mediated Amplification (Gen-Probe®)</p>	<p>Order as adjunct to AFB culture in untreated patients with smear-positive and smear-negative respiratory samples</p> <p>Rapid, sensitive and specific detection of MTB complex from respiratory specimens</p>	<p>AFB culture should always be ordered with this test</p> <p>Low level false-positive results can occur in specimens with high concentration of mycobacteria other than <i>M. tuberculosis</i></p> <p>A negative result does not exclude <i>M. tuberculosis</i> infection</p>	

<p>QuantiFERON®-TB Gold In Tube 0051729</p> <p>Method: Cell Culture/Enzyme-Linked Immunosorbent Assay</p>	<p>Detect latent TB infections among persons who are at increased risk for TB</p> <p>Specific for <i>M. tuberculosis</i>, not nontuberculous mycobacteria or the BCG vaccine</p>	<p>Diagnosing or excluding tuberculosis disease and assessing the probability of latent tuberculosis infection require a combination of epidemiological, historical, medical, and diagnostic findings that should be taken into account when interpreting the results of this test</p>	
<p>QuantiFERON®-TB Gold In Tube & <i>Mycobacterium tuberculosis</i> Antibody, IgG 2001627</p> <p>Method: Cell Culture/Enzyme-Linked Immunosorbent Assay</p>	<p>Detect latent TB infections among persons at increased risk for TB</p> <p>Components include QuantiFERON®-TB Gold in Tube and <i>Mycobacterium tuberculosis</i> Antibody, IgG by ELISA</p>		
<p><i>Mycobacterium tuberculosis</i> Complex Speciation 0060771</p> <p>Method: Polymerase Chain Reaction</p>	<p>Identify species of the <i>M. tuberculosis</i> complex (<i>M. tuberculosis</i>, <i>M. bovis</i>, <i>M. bovis</i> BCG-vaccine strain, <i>M. africanum</i>, <i>M. microti</i>, <i>M. caprae</i>) to species level by comparing genomic deletion patterns</p>	<p>Non-tuberculous mycobacteria may have indeterminate patterns of the genomic deletions used as targets in this assay</p> <p>Changes in DNA sequence at the primer annealing sites may affect genomic deletion pattern determination and speciation</p>	
<p><i>Mycobacterium tuberculosis</i> Antibody, IgG by ELISA 0051698</p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Order this rapid serologic assay when clinical symptoms and the possibility of exposure indicate MTB infection</p> <p>Detect IgG antibodies against MTB in patients with active infection</p> <p>Monitor the success of therapeutic intervention</p> <p>Differentiate active and latent cases of TB</p> <p>Can also be used in previously BCG vaccinated individuals since the antigens utilized are not present in <i>Mycobacterium bovis</i></p>	<p>Not intended for use as a screening assay</p> <p>Results should be interpreted in conjunction with PPD or QuantiFERON® testing as well as the complete history of the patient</p> <p>Assay has not been validated for use on patients with HIV/TB co-infection and is not recommended for this population</p>	

<p>AFB Culture (Includes AFB Stain 0060151) with Reflex to <i>Mycobacterium tuberculosis</i> Amplified Direct Detection (0060095) 0060738</p> <p>Method: Standard reference procedures for stain and culture. Identification of AFB is ordered and billed separately. DNA probes are available for <i>M. tuberculosis</i> complex and <i>M. avium-intracellulare</i> complex as indicated. DNA sequencing and other molecular techniques are used for identification. For drug susceptibilities, refer to Antimicrobial Susceptibility - AFB Mycobacteria (0060217). For AFB stain positive respiratory specimens, <i>Mycobacterium tuberculosis</i> Amplified Direct Detection (0060095) will be added at an additional charge.</p>	<p>Single order test incorporating culture and stain with reflex to amplified testing for MTB complex when smear positive</p>	<p>Available for respiratory specimens only</p> <p>Low-level false-positive results can occur in specimens with high concentration of mycobacteria other than <i>M. tuberculosis</i></p> <p>A negative result does not exclude <i>M. tuberculosis</i></p>	
<p>Blood Culture, AFB 0060060</p> <p>Method: Bactec® 9240, continuous monitoring systems. Standard reference procedures for identification of positive cultures.</p>	<p>Order for AFB culture of blood or bone marrow specimen</p>		

<p><i>Mycobacterium tuberculosis</i> Amplified Detection , CSF 0060063</p> <p>Method: Transcription Mediated Amplification (Gen-Probe®)</p>	<p>Amplified test offers rapid and specific detection of MTB complex from CSF</p>	<p>AFB culture should always be ordered with test</p> <p>The <i>Mycobacterium tuberculosis</i> Amplified Direct test does not differentiate among members of the MTB complex</p> <p>Low level false-positive results can occur in specimens with high concentration of mycobacteria other than <i>M. tuberculosis</i> (rare in CSF)</p> <p>Limited sensitivity</p> <p>A negative result does not exclude the possibility of isolating MTB from the specimen (eg culture)</p>	
<p>AFB Identification with Reflex to Susceptibility 0060997</p> <p>Method: Standard reference procedures for identification and susceptibility testing of AFB. DNA probes available for <i>M. tuberculosis</i> complex and <i>M. avium-intracellulare</i> complex. DNA sequencing and other molecular techniques are used for other mycobacteria species.</p>	<p>Identification of AFB isolated in pure culture with reflex susceptibility testing if indicated</p>	<p>Susceptibility testing may not be performed on all isolates (varies by species)</p>	

Antimicrobial Susceptibility - AFB/ Mycobacteria 0060217 Method: Varies with organism identification	Availability: a. <i>M. tuberculosis</i> primary and secondary panel b. <i>M. avium-intracellulare</i> complex (MAC) c. Rapid-growing mycobacteria d. Other slowly growing non-tuberculosis mycobacteria (NTM)		
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Additional Tests Available

Test Name and Number	Comments
AFB Stain Only 0060151 Method: Auramine O Stain	Monitor respiratory specimens on previously diagnosed patients Should not be ordered without culture in previously undiagnosed patients
AFB Identification 0060999 Method: Standard reference procedures for identification of AFB. DNA probes available for <i>M. tuberculosis</i> complex and <i>M. avium-intracellulare</i> complex. DNA sequencing and other molecular techniques are used for other mycobacteria species.	Identification of acid-fast organisms (AFB) isolated in pure culture
Blood Culture, AFB & Fungal 0060024 Method: Bactec® 9240, continuous monitoring systems. Standard reference procedures for identification of positive cultures.	
Adenosine Deaminase, Body Fluid 0098115 Method: Spectrophotometry	
Chylomicron Screen, Body Fluid 0098457 Method: Electrophoresis	

Additional Information

The laboratory should be notified when the presence of *Mycobacterium genavense* is suspected as this organism will not grow on media routinely used for Mycobacterial isolation.

Guidelines

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