

Diagnosis of TB Disease

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Objectives

- Describe the classification system for TB
- Identify populations most likely to have been recently infected with *M. tb*
- List four of the most common symptoms of pulmonary TB disease
- Describe the primary diagnostic tools and procedures used to diagnose TB disease
- Explain the purpose and significance of the acid-fast bacilli (AFB) smear
- Explain the purpose and significance of drug susceptibility testing

Outline

- Clinical suspicion in the diagnosis of TB
- Groups at risk for TB
- Symptoms and signs of TB
- Radiographic findings of TB
- Laboratory diagnosis of TB

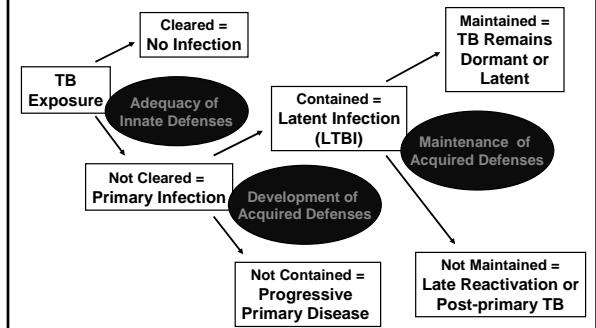
Key Points about the Diagnosis of TB

- Rapid, accurate diagnosis of TB is essential for both individual and public health
- Diagnosis of TB depends on clinical and radiographic features that heighten suspicion and trigger the appropriate evaluation
- Confirmation of TB usually requires specific diagnostic testing

Clinical Suspicion in the Diagnosis of TB

- Epidemiologic and Clinical Risk Factors
- Individual Susceptibility
- Clinical Features
- Imaging Findings

Latent TB Infection (LTBI) vs. Active TB Disease



TB Definitions (CDC & ATS, 2000)

- Class 0 = “No TB exposure; not infected”
- Class 1 = “TB exposure; not infected”
- Class 2 = “LTBI; no disease”
- Class 3 = “TB; clinically active”
- Class 4 = “TB; not clinically active”
- Class 5 = “TB suspect; diagnosis pending”

Who Gets TB?

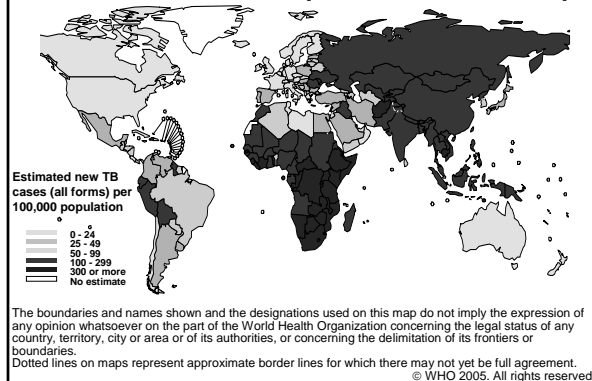
- People with an increased risk of being infected with *M. tuberculosis* (LTBI)
- People with an increased risk of progressing from LTBI to active TB disease

Persons at High Risk for Having TB Infection

Risks of Exposure and Infection

- Foreign-born in countries where TB endemic
- Close contacts of active TB cases
- Homeless and “medically underserved”
- Elderly
- Residents of congregate and long term care facilities
- Injection drug users
- Healthcare workers with occupational TB exposures
- Locally-identified high risk groups

Global TB Burden (Incidence Rates)



Who Gets TB?

- People with an increased risk of being infected with *M. tuberculosis* (LTBI)
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Persons at High Risk for Developing TB Disease

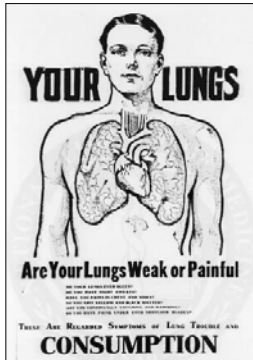
- Risk of progression, if infected
- HIV infection
 - Immunosuppression
 - Recently infected with TB
 - Injection drug and substance abuse
 - History of inadequate TB treatment
 - Underlying medical conditions
 - Malnutrition
 - Renal failure, diabetes mellitus, silicosis, head and neck cancer, x-ray c/w with old TB, others

Risks of TB Quantified

Risk Factor	Estimated Increased Risk (Compared with Persons with no Risk Factors)
AIDS	170
HIV Infection	113
Kidney transplant	37
Silicosis	30
Chronic renal failure	10-25
Immunocompromised	4-16
Infection within past 2 years	15
Chest x-ray c/w prior TB	2-14
Age <5 and >60	2-5
Diabetes mellitus	2-4

MMWR 1992; 41(RR-11)1-8

Symptoms and Signs of TB



TB: Classic Clinical Presentation

- Insidious onset and chronic course
- Chest symptoms
 - Cough (usually productive)
 - Hemoptysis
 - Chest pain (usually pleuritic)
- Nonspecific constitutional symptoms
- Extrapulmonary symptoms

Typical Systemic Symptoms

- Fever
- Chills/sweats
- Fatigue/malaise
- Anorexia
- Weight loss

Be Aware...

- TB symptoms and severity can range from none (in 10-20%) to overwhelming
- Tempo of illness can range from indolent to fulminant
- Symptoms/findings may be both local and systemic
- TB can involve any organ or tissue

TB Presentation in HIV-infected Patients May be Atypical

	HIV+	HIV-
Fever >4 weeks	30-90	15-30 (%)
Cough	50	50-75
Hemoptysis	15	20
Weight loss (>20%)	30-85	11-55
Lymphadenopathy	11-80	3-44
Oral thrush	5-11	<1
History of herpes zoster	8-15	<1
Diarrhea	10-51	1-23

Radiographic Findings of TB

Classic Radiographic Presentations of TB

	Primary	Reactivation
Infiltrates	Any lobe	85% Upper
Cavitation	Rare	Often present
Adenopathy	Adults ~30% Children-common	Rare
Effusion	Seen	Seen

Radiographic Features of TB in HIV

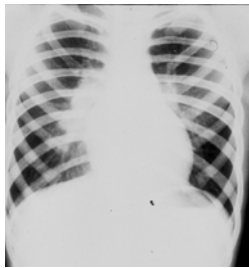
	Early HIV	Late HIV
Pattern	"Reactivation"	"Primary"
Infiltrates	Upper	Lower
Cavitation	Common	Rare
Adenopathy	Uncommon	Common
Effusion	Uncommon	Uncommon

Primary TB

- Middle and lower lobe infiltrates
- Ipsilateral adenopathy
- Pleural effusion



Primary TB (2)

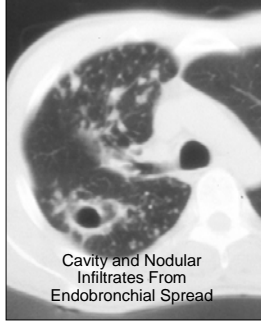


Reactivation TB

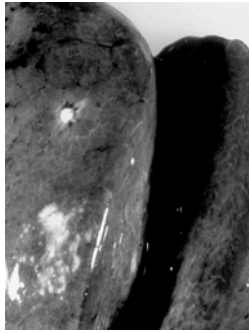
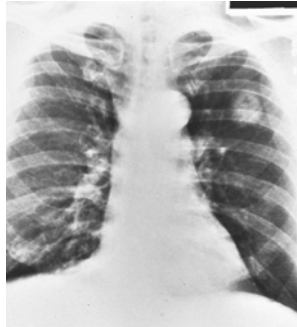
- Apical Infiltrates
- Cavitation
- Scarring and volume loss



Reactivation TB (2)

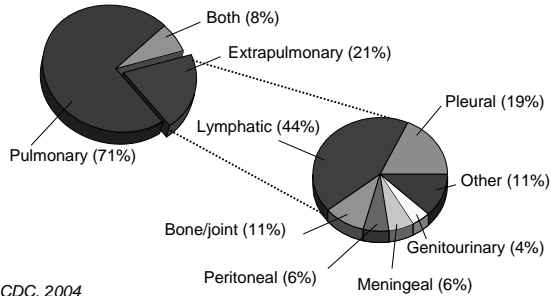


Tuberculoma



Extrapulmonary TB

TB Presentation by Site of Disease



TB Lymphadenitis



- Usually, painless swelling of the lymph nodes
- Most often involves the cervical and supraclavicular sites (scrofula)
- Usually discrete in early stage, but may become inflamed and develop a fistulous tract

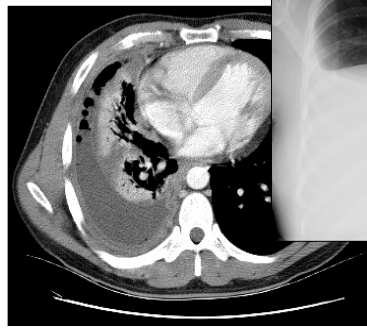
TB Lymphadenitis (2)

- Lymphadenitis is usually a "paucibacillary" form of TB
- Fine needle aspiration:
 - Smear positive 40%, culture 60-65%
 - PCR sensitivity >90%
- Excisional biopsy:
 - Culture positive 70-75%, granulomas 85-90%
 - Excision without TB Rx → 83% relapse rate

TB Pleurisy Clinical Manifestations

- Acute illness (pleuritic CP, cough, fever) often mistaken for bacterial pneumonia or pleurisy
- Usually 6-12 weeks after primary TB infection but can occur during reactivation
- Pleural effusion usually unilateral and small or moderate in size
- Parenchymal lung involvement evident in 1/3

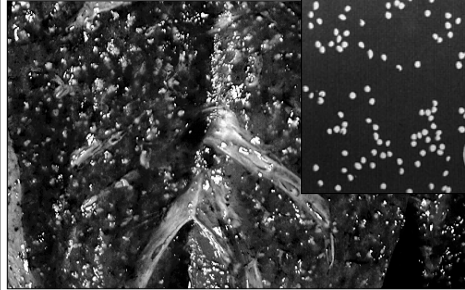
Pleural TB



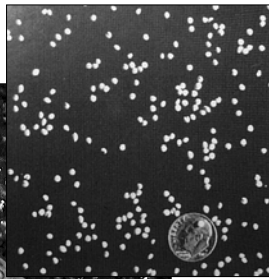
Disseminated (Miliary) TB

- Either primary or post-primary
- Symptoms: primarily systemic (fever, weight loss, night sweats)
- Multiple organ involvement
- Miliary chest x-ray (CXR) pattern
- Pathology: grossly, 1-2 mm yellowish nodules that resemble millet seeds (histologically, granulomas)

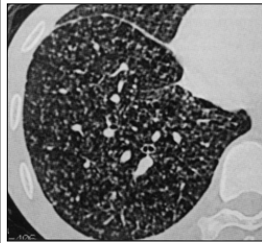
Miliary TB



Millet Seeds



Miliary TB (2)



Diagnosis of Disseminated TB

- Sputum (positive smear 30%, culture 60%)
- Morning urine (positive culture 30%)
- Biopsy and culture of new skin lesions or superficial lymph nodes
- Lumbar puncture if (+) meningeal signs
- Consider bronchoscopy, liver biopsy, bone marrow biopsy

Summary of Factors Leading to Clinical Suspicion of TB

- Epidemiological and clinical risk factors
- Individual susceptibility
- Clinical features
- Imaging findings

Diagnosis of TB: The Tuberculin Skin Test (TST)

- TST is standardized screening test for detecting LTBI in high risk groups
- False positives due to other mycobacteria or BCG vaccination
- False negatives due to anergy, or overwhelming TB...

A negative TST never excludes TB

Routine Laboratory Findings in TB

All are nonspecific

- Leukocytosis, leukopenia, pancytopenia
- Hyponatremia (SIADH)
- Elevated ESR
- Elevated transaminases, alkaline phosphatase

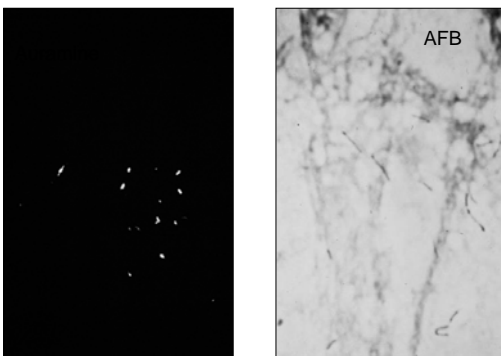
Diagnosis of TB Disease

- TB is a clinical, radiographic, and (usually) laboratory diagnosis
- Suitable laboratory specimens
 - Sputum or bronchoscopic sample
 - Gastric aspirate
 - Pleural fluid, stool, urine, csf, other
 - Tissue (lung, pleura, lymph node, other)

Sputum Examination

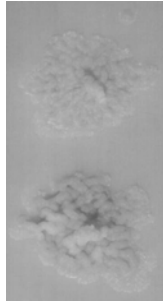
- AFB Smears
 - Ziehl-Nielsen, auramine-rhodamine
 - Rapid, ~50-70% sensitive, nonspecific (NTM)
- Culture
 - Sensitive and specific, but slow
 - Beware “culture negative” TB
- Molecular methods
 - AMTD and PCR

Sputum Examination (2)



Mycobacterial Culture in the Diagnosis of TB

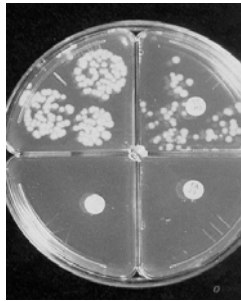
- Culture is the “Gold Standard” test for the diagnosis of TB
- Culture all specimens, even if smear negative
- Up to 20% of TB cases may be culture negative
- Culture results are not available immediately (2-6 weeks depending on culture techniques)
- Culture permits susceptibility testing



Colonies of *M. tuberculosis* growing on solid media

TB Drug Susceptibility Testing

- Always request drug susceptibility testing when TB is isolated
- Results usually available 2-4 weeks after culture is reported positive
- Drug resistance influences treatment decisions



Drug susceptibility testing on solid media. Upper left quadrant contains no drug.

Collection of Respiratory Specimens for TB Diagnosis

- Sputum Expectoration:
 - 3 specimens (at least 8 hours apart)
 - Spontaneous morning specimens best
- Sputum Induction: if non-productive
- Bronchoscopy: if alternative diagnoses are a substantial concern
 - Collect post-bronchoscopy sputum too

Sensitivities of Sputum AFB Smear and Culture Tests

- Smear (+) threshold: At least 5,000-10,000 organisms per mL of sputum
(ARRD 1966;95:998)
- Culture (+) threshold: At least 10 (liquid media) - 100 (solid media) per mL
- Only 50 to 60% of *pulmonary TB* cases are *smear-positive*

Negative sputum AFB smears never exclude TB

Nucleic Acid Amplification Tests (NAAT) MMWR 2000/49(26);593-4.

- FDA-approved for use with sputum specimens
 - Gen-Probe "Amplified *M. tb* Direct" Test (AMTD)
 - Roche *M. tb* "Amplicor" Test (PCR)
- Sensitivity of AMTD
 - >95% for AFB smear-positive TB patients (and high specificity confirms TB diagnosis)
 - 70-90% of AFB smear-negative, culture-positive TB patients
 - "If sputum is smear (-) and MTD (-) x2, the patient can be presumed not to be infectious"

Summary of Laboratory Diagnosis of TB

- AFB Smears: rapid, inexpensive, and readily available, but insensitive and nonspecific
- TB Cultures: sensitive and specific, but slow
- NAAT: rapid, more sensitive than smear, and highly specific, but complex and not readily available

Approach to the Patient with Suspected TB

Maintaining a High Index of Clinical Suspicion

- If a patient has *risk factors for TB...*
- And, they have a clinical illness, exam finding, and/or radiographic image *compatible with TB...*
- Then, they may have active TB, and they should be *evaluated for TB disease*

When there is a High Index of Suspicion for TB...

- Obtain a chest radiograph
- Perform sputum examination (AFB smear and culture)
- Evaluate any non-pulmonary symptoms and signs

Diagnosis of TB: Summary

- Think TB if “high-risk” profile
- Although lungs are primary site of infection, TB can involve any organ
- Positive smears correlate with contagiousness and the extent of disease, but are negative in half of all TB cases
- New TB diagnostic tests can improve on the sensitivity and specificity of AFB smear results
- Clinical suspicion remains key to TB diagnosis
