

# Tuberculosis

Tuberculosis (TB) is a contagious bacterial infection caused by *Mycobacterium tuberculosis*, primarily affecting the lungs but capable of involving any organ system. This guide provides physician assistant (PA) students with a comprehensive framework to understand the presentations, diagnosis, pathophysiology, complications, treatment, and hospital management of TB, particularly in acutely ill patients, with case scenarios to apply the knowledge.

## Introduction and Pathophysiology

Tuberculosis is caused by *Mycobacterium tuberculosis*, a slow-growing, acid-fast bacillus transmitted via airborne droplets (e.g., coughing, sneezing). It is a major global health concern, with higher prevalence in immunocompromised populations (e.g., HIV, diabetes) and resource-limited settings.

### Pathophysiology:

**Inhalation and Infection:** Inhaled bacilli are phagocytosed by alveolar macrophages but survive within them due to inhibition of phagolysosomal fusion.

**Granuloma Formation:** Infected macrophages recruit T-cells, forming granulomas (caseating necrosis in the center) to contain the infection; this is the hallmark of latent TB infection (LTBI).

**Active Disease:** Reactivation occurs in 5-10% of LTBI cases, often due to immunosuppression (e.g., HIV, steroids); bacilli multiply, leading to tissue destruction, cavitation, and dissemination.

**Dissemination:** Hematogenous spread can cause extrapulmonary TB (e.g., miliary TB, TB meningitis).

TB can present as latent infection, primary disease, or reactivation, with varied manifestations depending on host immunity and disease extent.

## Different Ways TB Can Present

### Pulmonary TB (80-85% of Cases):

- Primary TB:
  - Often asymptomatic or mild; fever, cough, night sweats, weight loss.

- Ghon focus (subpleural lesion) with hilar lymphadenopathy (Ghon complex).
- Reactivation TB:
  - Chronic cough (productive, sometimes hemoptysis), fever, night sweats, weight loss, fatigue.
  - Symptoms may be insidious, progressing over weeks to months.

### Extrapulmonary TB (15-20%):

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- TB Lymphadenitis (Scrofula):
  - Painless cervical lymphadenopathy, often in children or HIV patients.
- Pleural TB:
  - Pleuritic chest pain, dyspnea, pleural effusion (exudative, lymphocytic).
- Miliary TB:
  - Disseminated disease; fever, weight loss, dyspnea, hepatosplenomegaly, miliary nodules on imaging.
- TB Meningitis:
  - Headache, fever, neck stiffness, altered mental status; common in children, HIV patients.
- Skeletal TB (Pott's Disease):
  - Back pain, spinal deformity, gibbus formation (vertebral collapse).
- Genitourinary TB:
  - Dysuria, hematuria, sterile pyuria; often involves kidneys or epididymis.
- Peritoneal TB:
  - Abdominal pain, ascites, fever; mimics malignancy or cirrhosis.

### TB in Immunocompromised (e.g., HIV):

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**Atypical presentations:** More extrapulmonary involvement, miliary TB, non-cavitary disease on imaging.

Symptoms may be subtle (e.g., fever, weight loss) due to impaired immune response.

## How to Confirm or Test for Diagnosis

### Screening for Latent TB Infection (LTBI):

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**Tuberculin Skin Test (TST):** Intradermal injection of purified protein derivative (PPD); induration  $\geq 5$  mm (HIV/immunocompromised),  $\geq 10$  mm (high-risk), or  $\geq 15$  mm (low-risk) is positive.

**Interferon-Gamma Release Assays (IGRAs):** Blood tests (e.g., QuantiFERON-TB Gold); more specific than TST, no cross-reactivity with BCG vaccine.

## Diagnosis of Active TB:

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- Sputum Analysis:
  - **Acid-fast bacilli (AFB) smear:** Ziehl-Neelsen stain; rapid but low sensitivity (50-60%).
  - **Nucleic acid amplification tests (NAAT, e.g., Xpert MTB/RIF):** Detects *M. tuberculosis* DNA and rifampin resistance; sensitivity 90-95%.
  - **Culture:** Gold standard; takes 2-6 weeks (liquid media faster); confirms diagnosis and allows drug susceptibility testing (DST).
- Extrapulmonary TB:
  - **Tissue biopsy/fluid analysis:** AFB smear, NAAT, culture (e.g., lymph node biopsy for scrofula, CSF for TB meningitis).
- CSF Findings (TB Meningitis):
  - Lymphocytic pleocytosis, low glucose (<40 mg/dL), high protein (>100 mg/dL).

## Diagnostic or Imaging Studies

### Chest X-Ray:

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**Primary TB:** Hilar lymphadenopathy, Ghon complex, pleural effusion.

**Reactivation TB:** Upper lobe infiltrates, cavitation, tree-in-bud pattern (endobronchial spread).

**Miliary TB:** Diffuse millet-seed nodules (1-3 mm).

### CT Chest:

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- More sensitive; shows cavitation, tree-in-bud, mediastinal lymphadenopathy, miliary nodules.
- Useful for extrapulmonary TB (e.g., pleural thickening, pericardial effusion).

### Other Imaging:

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**MRI Spine:** For Pott's disease; vertebral destruction, paravertebral abscess.

**CT Abdomen:** For peritoneal TB; ascites, omental thickening, lymphadenopathy.

## Other Tests:

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**HIV Testing:** Mandatory; TB-HIV co-infection alters presentation and treatment.

**Liver Function Tests (LFTs):** Baseline before starting anti-TB drugs (risk of hepatotoxicity).

## Isolation Protocols

### Airborne Isolation:

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**Indication:** Suspected or confirmed pulmonary/laryngeal TB until non-infectious.

### Criteria for Isolation:

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- Place in a negative-pressure airborne infection isolation room (AIIR).
- Use N95 respirators for healthcare workers; surgical masks for patients during transport.

### Duration:

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- Isolate until 3 consecutive AFB smears are negative (typically after 2 weeks of effective therapy) AND clinical improvement (e.g., reduced cough, fever).
- Extrapulmonary TB (e.g., meningitis, lymphadenitis) usually does not require isolation unless pulmonary involvement.

### Infection Control:

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**Patient Education:** Cover mouth when coughing, adhere to treatment to reduce transmission.

**Contact Tracing:** Screen close contacts for LTBI/active TB using TST/IGRA, chest X-ray.

## Complications

### Pulmonary:

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**Hemoptysis:** Erosion of pulmonary vessels (e.g., Rasmussen aneurysm); can be massive (>600 mL/24h).

**Pneumothorax:** Rupture of cavitory lesion into pleural space.

**Bronchiectasis:** Chronic endobronchial spread; causes recurrent infections, hemoptysis.

**Pulmonary Hypertension (PH):** Chronic lung destruction, hypoxia-induced vasoconstriction.

### Extrapulmonary:

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**CNS:** TB meningitis can cause hydrocephalus, cranial nerve palsies, stroke (basilar vasculitis).

**Skeletal:** Pott's disease leads to paraplegia if spinal cord compression occurs.

**Disseminated:** Miliary TB can cause ARDS, multi-organ failure (MOF).

### Treatment-Related:

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**Hepatotoxicity:** Rifampin, isoniazid, pyrazinamide; monitor LFTs, stop drugs if ALT >5x ULN.

**Drug Resistance:** Multidrug-resistant TB (MDR-TB, resistant to isoniazid and rifampin); extensively drug-resistant TB (XDR-TB, MDR plus resistance to fluoroquinolones and injectables).

## Medications

### First-Line Treatment (Active TB):

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- RIPE Regimen (2-month intensive phase, 4-month continuation phase):
  - Rifampin (RIF): 10 mg/kg/day PO (max 600 mg); bactericidal, inhibits RNA synthesis.
  - Isoniazid (INH): 5 mg/kg/day PO (max 300 mg); bactericidal, inhibits mycolic acid synthesis; give with pyridoxine (vitamin B6, 25 mg PO daily) to prevent neuropathy.
  - Pyrazinamide (PZA): 15-30 mg/kg/day PO (max 2 g); bactericidal in acidic environments (e.g., within macrophages); used in intensive phase only.
  - Ethambutol (EMB): 15-25 mg/kg/day PO (max 1.6 g); bacteriostatic, inhibits cell wall synthesis; dropped in continuation phase if susceptible.
- Duration:
  - **Pulmonary TB:** 6 months total (2 months RIPE, 4 months RIF/INH).
  - **Extrapulmonary TB (e.g., meningitis, skeletal):** 9-12 months.

- Monitoring:
  - Monthly LFTs (hepatotoxicity risk).
  - Visual acuity/color vision (ethambutol optic neuritis).
  - Sputum AFB smear/culture at 2 months to assess response.

## Latent TB Infection (LTBI):

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- Preferred Regimens:
  - **Isoniazid + Rifapentine (3HP):** Once weekly x 12 weeks (INH 15 mg/kg, rifapentine 900 mg).
  - **Rifampin:** 10 mg/kg/day PO x 4 months.
  - **Isoniazid:** 5 mg/kg/day PO x 9 months (with pyridoxine).
- Monitoring:
  - Monthly LFTs, adherence counseling.

## MDR-TB/XDR-TB:

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**Regimen:** Individualized based on DST; typically 5-7 drugs (e.g., bedaquiline, linezolid, fluoroquinolones, injectables like amikacin) for 18-24 months.

**Management:** Refer to TB specialist; often requires inpatient initiation due to toxicity.

## Hospital Management of Sick TB Patients

Sick TB patients, such as those with severe pulmonary TB, miliary TB, or TB meningitis, often present with respiratory failure, sepsis, or neurological complications, requiring aggressive hospital management.

## Supportive Care:

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- **Oxygen Therapy:** High-flow nasal cannula or non-invasive ventilation (NIV) for hypoxemia (SpO<sub>2</sub> <90%); intubate if respiratory failure (low tidal volumes to minimize barotrauma).
- **Fluid Resuscitation:** IV fluids for hypotension (e.g., 30 mL/kg crystalloid bolus); cautious in miliary TB with ARDS risk.
- **Nutrition:** Enteral feeding if possible; TB causes cachexia, and malnutrition worsens outcomes.

## Anti-TB Therapy:

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- Start RIPE immediately (adjust doses for renal/hepatic impairment).

- **TB Meningitis:** Extend intensive phase to 2 months, total duration 9-12 months; add adjunctive corticosteroids (dexamethasone 0.4 mg/kg/day IV, taper over 6-8 weeks) to reduce inflammation and mortality.
- **Miliary TB:** Monitor for IRIS (immune reconstitution inflammatory syndrome) in HIV patients starting ART; continue RIPE, consider steroids if severe (e.g., prednisone 1 mg/kg/day).

### Isolation:

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Airborne isolation in AIIR until 3 consecutive negative AFB smears; N95 for staff, surgical mask for patient during transport.

### Treat Complications:

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- **Hemoptysis:** Bronchial artery embolization for massive hemoptysis; avoid intubation if possible (risk of airway obstruction).
- **ARDS (Miliary TB):** Low tidal volume ventilation (6 mL/kg), PEEP titration; steroids (methylprednisolone 1 mg/kg/day IV) for severe inflammation.
- **TB Meningitis with Hydrocephalus:** Neurosurgical consult for ventriculoperitoneal shunt if obstructive hydrocephalus.
- **Sepsis:** Broad-spectrum antibiotics (e.g., cefepime 2 g IV q8h + vancomycin 15 mg/kg IV q12h) until secondary infection ruled out.

### HIV Co-Infection:

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- Start ART within 2 weeks if CD4 >50 cells/ $\mu$ L, within 8 weeks if CD4 <50 cells/ $\mu$ L (e.g., dolutegravir-based regimen).
  - Monitor for IRIS (worsening symptoms post-ART); treat with steroids if severe (e.g., prednisone 1 mg/kg/day).
- Monitoring:
  - Daily sputum AFB smears until negative.
  - Serial lactate, renal/hepatic function, neurological status (TB meningitis).
  - Chest X-ray/CT for worsening infiltrates, ARDS, or pneumothorax.

## Key Pearls

**Presentations:** Pulmonary (cough, hemoptysis), extrapulmonary (lymphadenitis, meningitis, miliary), atypical in HIV (non-cavitary, disseminated).

**Diagnosis:** Sputum AFB, NAAT, culture; HRCT (cavitation, tree-in-bud, miliary nodules); extrapulmonary (biopsy, CSF analysis).

**Isolation:** Airborne until 3 negative AFB smears; AIIR, N95 for staff.

**Pathophysiology:** Granuloma formation, reactivation in immunosuppression, dissemination to extrapulmonary sites.

**Complications:** Hemoptysis, pneumothorax, PH (pulmonary); meningitis complications, paraplegia (skeletal).

**Treatment:** RIPE x 6 months (pulmonary), 9-12 months (extrapulmonary); steroids in meningitis/miliary TB.

**Hospital Management:** Oxygen, RIPE, treat complications (ARDS, hemoptysis), isolation, HIV co-management.

## References

**UpToDate:** "Tuberculosis: Diagnosis and Management" (2025). UpToDate TB

**CDC:** "Guidelines for the Treatment of Tuberculosis" (2024). CDC TB Guidelines

**WHO:** "Global Tuberculosis Report" (2023). WHO TB Report

**NEJM:** "Management of Multidrug-Resistant Tuberculosis" (2024). NEJM MDR-TB

## Case Scenarios

### Case 1: A 35-Year-Old Male with Chronic Cough

- Presentation: A 35-year-old male presents with a 2-month history of productive cough, night sweats, and 10-pound weight loss. Exam shows T 38°C, fine crackles in right upper lobe, no lymphadenopathy.
- Labs/Imaging: HIV negative, sputum AFB smear positive, NAAT confirms M. tuberculosis. Chest X-ray shows right upper lobe cavitation.
- Diagnosis: Pulmonary TB (Reactivation) → Chronic cough, weight loss, cavitation.
- Management: Admit to AIIR. Start RIPE (rifampin 600 mg, isoniazid 300 mg, pyrazinamide 1500 mg, ethambutol 1200 mg PO daily). Pyridoxine 25 mg PO daily. Isolate until 3 negative AFB smears (achieved at 2 weeks). Monitor LFTs monthly (normal). Continue RIPE x 2 months, then rifampin/isoniazid x 4 months. Discharge with public health follow-up.



## Case 2: A 28-Year-Old Female with Headache and Fever

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- Presentation: A 28-year-old female with HIV (CD4 40 cells/ $\mu$ L, not on ART) presents with 1 week of headache, fever, and confusion. Exam shows T 38.5°C, neck stiffness, altered mental status (GCS 13).
- Labs/Imaging: **CSF**: WBC 200/ $\mu$ L (lymphocytic), glucose 30 mg/dL, protein 150 mg/dL, AFB smear positive. CT head shows basilar enhancement, no hydrocephalus.
- Diagnosis: TB Meningitis → Headache, fever, HIV, CSF findings.
- Management: Admit to ICU, AIIR. Start RIPE (adjust doses for meningitis: isoniazid 5 mg/kg IV, rifampin 10 mg/kg IV). Dexamethasone 0.4 mg/kg/day IV x 2 weeks, taper over 6 weeks. Start ART (dolutegravir-based) at 2 weeks. Monitor for IRIS (worsening symptoms post-ART; manage with prednisone 1 mg/kg/day if severe). Total RIPE duration 12 months. Discharge with neurology follow-up.

## Case 3: A 45-Year-Old Male with Severe Dyspnea

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- Presentation: A 45-year-old male with untreated pulmonary TB presents with acute dyspnea, fever, and hypoxia. Exam shows T 39°C, RR 30/min, SpO<sub>2</sub> 85% on room air, diffuse crackles.
- Labs/Imaging: Lactate 3.0 mmol/L, HIV negative. Chest CT shows miliary nodules, bilateral GGO (ARDS). Sputum AFB smear positive.
- Diagnosis: Miliary TB with ARDS → Acute dyspnea, miliary pattern, ARDS.
- Management: Admit to ICU, AIIR. High-flow oxygen to SpO<sub>2</sub> >90%; intubate if needed (low tidal volume 6 mL/kg). Start RIPE (rifampin 600 mg, isoniazid 300 mg, pyrazinamide 1500 mg, ethambutol 1200 mg PO daily). Methylprednisolone 1 mg/kg/day IV x 5 days for ARDS. Broad-spectrum antibiotics (cefepime 2 g IV q8h + vancomycin 15 mg/kg IV q12h) until secondary infection ruled out. Monitor lactate, ABG, LFTs. Continue RIPE x 6 months. Discharge with pulmonology follow-up.

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