# Fundamentals of Tuberculosis (TB)

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## TB in the United States

- From 1953 to 1984, reported cases decreased by approximately 5.6% each year
- From 1985 to 1992, reported cases increased by 20%
- 25,313 cases reported in 1993
- Since 1993, cases are steadily declining

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## Factors Contributing to the Increase in TB Cases

- HIV epidemic
- Increased immigration from high-prevalence countries
- Transmission of TB in congregate settings (e.g., correctional facilities, long term care)
- Deterioration of the public health care infrastructure

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## Transmission and Pathogenesis of TB

- Caused by *Mycobacterium tuberculosis (M. tuberculosis)*
- Spread person to person through airborne particles that contain *M. tuberculosis*, called droplet nuclei
- Transmission occurs when an infectious person coughs, sneezes, laughs, or sings
- Prolonged contact needed for transmission
- 10% of infected persons will develop TB disease at some point in their lives

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## Sites of TB Disease

- Pulmonary TB occurs in the lungs
  - 85% of all TB cases are pulmonary
- Extrapulmonary TB occurs in places other than the lungs, including the:
  - Larynx
  - Lymph nodes
  - Brain and spine
  - Kidneys
  - Bones and joints
- Miliary TB occurs when tubercle bacilli enter the bloodstream and are carried to all parts of the body

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## Not Everyone Exposed Becomes Infected

- Probability of transmission depends on:
  - Infectiousness
  - Type of environment
  - Length of exposure
- 10% of infected persons will develop TB disease at some point in their lives
  - 5% within 1-2 years
  - 5% at some point in their lives

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## Persons at Risk for Developing TB Disease

- Persons at high risk for developing TB disease fall into 2 categories
  - Those who have been recently infected
  - Those with clinical conditions that increase their risk of progressing from LTBI to TB disease

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## Recent Infection as a Risk Factor

Persons more likely to have been recently infected include

- Close contacts to persons with infectious TB
- Skin test converters (within past 2 years)
- Recent immigrants from TB-endemic areas (within 5 years of arrival to the U.S.)
- Children ≤ 5 years with a positive TST
- Residents and employees of high-risk congregate settings (e.g. correctional facilities, homeless shelters, healthcare facilities)

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## Increased Risk for Progression to TB Disease

Persons more likely to progress from LTBI to TB disease include

- HIV infected persons
- Those with history of prior, untreated TB
- Underweight or malnourished persons
- Injection drug use
- Those receiving TNF-α antagonists for treatment of rheumatoid arthritis or Crohn's disease
- Certain medical conditions

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## Latent TB Infection (LTBI)

- Occurs when person breathes in bacteria and it reaches the air sacs (alveoli) of lung
- Immune system keeps bacilli contained and under control
- Person is not infectious and has no symptoms

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## TB Disease

- Occurs when immune system cannot keep bacilli contained
- Bacilli begin to multiply rapidly
- Person develops TB symptoms

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## LTBI vs. TB Disease

| LTBI | TB Disease |
|---|---|
| Tubercle bacilli in the body | |
| TST or QFT-Gold® result usually positive | |
| Chest x-ray usually normal | Chest x-ray usually abnormal |
| Sputum smears and cultures negative | Symptoms smears and cultures positive |
| No symptoms | Symptoms such as cough, fever, weight, loss |
| Not infectious | Often infectious before treatment |
| Not a case of TB | A case of TB |

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## Targeted Testing

- Detects persons with LTBI who would benefit from treatment
- De-emphasize testing of groups of people who are not at risk (mass screening)
- Consider using a risk assessment tool
- Testing should be done only if there is an intent to treat
- Can help reduce the waste of resources and prevent unnecessary treatment

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## Groups to Target with the Tuberculin Skin Test

- Persons with or at risk for HIV infection
- Close contacts of persons with infectious TB
- Persons with certain medical conditions
- Injection drug users
- Foreign-born persons from areas where TB is common
- Medically underserved, low-income populations
- Residents of high-risk congregate settings
- Locally identified high-prevalence groups

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## Administering the TST

- Use Mantoux tuberculin skin test
- 0.1 mL of 5-TU of purified protein derivative (PPD) solution injected intradermally
- Use a 27 gauge needle
- Produce a wheal that is 6-10mm in diameter

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## Reading the TST

- Read within 48-72 hours
- Measure induration, not erythema
- Positive reactions can be measured accurately for up to 7 days
- Negative reactions can be read accurately for only 72 hours

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## TST Interpretation - 1

**5 mm of induration is positive in:**

- HIV-infected persons
- Close contacts to an infectious TB case
- Persons who have chest x-ray findings consistent with prior untreated TB
- Organ transplant recipients
- Persons who are immunosuppressed (e.g., those taking the equivalent of >15 mg/d of prednisone for 1 month or those taking TNF-α antagonists)

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## TST Interpretation - 2

**10 mm induration is positive in:**

- Recent immigrants (within last 5 years) from a high-prevalence country
- Injection drug users
- Persons with other high-risk medical conditions
- Residents or employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Children < 4 years of age; infants, children, and adolescents exposed to adults at high risk

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## TST Interpretation - 3

**15 mm induration is positive in:**

- Persons with no known risk factors for TB

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## Recording TST Results

- Record results in millimeters of induration, not “negative” or “positive”
- Only trained healthcare professionals should read and interpret TST results

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## False Positive TST Reactions

- Nontuberculous mycobacteria
  - Reactions are usually ≤10mm of induration
- BCG vaccination
  - Reactivity in BCG vaccine recipients generally wanes over time
  - Positive TST results is likely due to TB infection if risk factors are present
  - BCG-vaccinated persons with positive TST result should be evaluated for treatment of LTBI
  - QFT is able to distinguish *M.tb* from other mycobacteria and BCG vaccine

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## False Negative TST Reactions

- Anergy, or inability to react to TST because of weakened immune system
- Recent TB infection (2-10 weeks after exposure)
- Very young age (newborns)
- Recent live-virus vaccination can temporarily suppress TST reactivity
- Poor TST administration technique (too shallow or too deep, or wheal is too small)

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## Boosting

- Some people with history of LTBI lose their ability to react to tuberculin (immune system "forgets" how to react to TB-like substance, i.e., PPD)
- Initial TST may stimulate (boost) the ability to react to tuberculin
- Positive reactions to subsequent tests may be misinterpreted as new infections rather than "boosted" reactions

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## Two-Step Testing - 1

- A strategy for differentiating between boosted reactions and reactions caused by recent TB infection
- Use two-step testing for initial (baseline) skin testing of adults who will be re-tested periodically
- 2$^{nd}$ skin test given 1-3 weeks after baseline

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## Two-Step Testing - 2

- If the 1st TST is positive, consider the person infected
- If the 1st TST is negative, administer 2nd TST in 1-3 weeks
- If the 2nd TST is positive, consider the person infected
- If the 2nd TST is negative, consider the person uninfected at baseline

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## Infectiousness - 1

- Patients should be considered infectious if they:
  - Are undergoing cough-inducing procedures
  - Have sputum smears positive for acid-fast bacilli (AFB) and:
    - Are not receiving treatment
    - Have just started treatment, or
    - Have a poor clinical or bacterial response to treatment
  - Have cavitary disease
- Extrapulmonary TB patients are not infectious

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## Infectiousness - 2

- Patients are not considered infectious if they meet all these criteria:
  - Received adequate treatment for 2-3 weeks
  - Favorable clinical response to treatment
  - 3 consecutive negative sputum smears results from sputum collected on different days

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## Techniques to Decrease TB Transmission

- Instruct patient to:
  - Cover mouth when coughing or sneezing
  - Wear mask as instructed
  - Open windows to assure proper ventilation
  - Do not go to work or school until instructed by physician
  - Avoid public places
  - Limit visitors
  - Maintain home or hospital isolation as ordered

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## Evaluation for TB

- Medical history
- Physical examination
- Mantoux tuberculin skin test
- Chest x-ray
- Bacteriologic exam (smear and culture)

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## Symptoms of TB

- Productive prolonged cough*
- Chest pain*
- Hemoptysis*
- Fever and chills
- Night sweats
- Fatigue
- Loss of appetite
- Weight loss

*Commonly seen in cases of pulmonary TB

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## Chest x-Ray

- Obtain chest x-ray for patients with positive TST results or with symptoms suggestive of TB
- Abnormal chest x-ray, by itself, cannot confirm the diagnosis of TB but can be used in conjunction with other diagnostic indicators

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## Sputum Collection

- Sputum specimens are essential to confirm TB
  - Specimens should be from lung secretions, not saliva
- Collect 3 specimens on 3 different days
- Spontaneous morning sputum more desirable than induced specimens
- Collect sputum before treatment is initiated

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## Smear Examination

- Strongly consider TB in patients with smears containing acid-fast bacilli (AFB)
- Use subsequent smear examinations to assess patient's infectiousness and response to treatment

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## Culture

- Used to confirm diagnosis of TB
- Culture all specimens, even if smear is negative
- Initial drug isolate should be used to determine drug susceptibility

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## Treatment of Latent TB Infection

- Daily Isoniazid therapy for 9 months
  - Monitor patients for signs and symptoms of hepatitis and peripheral neuropathy
- Alternate regimen – Rifampin for 4 months

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## Treatment of TB Disease

- Include four 1st-line drugs in initial regimen
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)
- Adjust regimen when drug susceptibility results become available or if patient has difficulty with any of the medications
- Never add a single drug to a failing regimen
- Promote adherence and ensure treatment completion

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## Directly Observed Therapy (DOT)

- Health care worker watches patient swallow each dose of medication
- DOT is the best way to ensure adherence
- Should be used with all intermittent regimens
- Reduces relapse of TB disease and acquired drug resistance

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## Clinical Monitoring

Instruct patients taking TB medications to immediately report the following:

- Rash
- Nausea, loss of appetite, vomiting, abdominal pain
- Persistently dark urine
- Fatigue or weakness
- Persistent numbness in hands or feet

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## Drug Resistance

- Primary - infection with a strain of *M. tuberculosis* that is already resistant to one or more drugs
- Acquired - infection with a strain of *M. tuberculosis* that becomes drug resistant due to inappropriate or inadequate treatment

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## Barriers to Adherence

- Stigma
- Extensive duration of treatment
- Adverse reactions to medications
- Concerns of toxicity
- Lack of knowledge about TB and its treatment

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## Improving Adherence

- Adherence is the responsibility of the provider, not the patient and can be ensured by:
  - Patient education
  - Directly observed therapy (DOT)
  - Case management
  - Incentives/enablers

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## Measures to Promote Adherence

- Develop an individualized treatment plan for each patient
- Provide culturally and linguistically appropriate care to patient
- Educate patient about TB, medication dosage, and possible adverse reactions
- Use incentives and enablers to address barriers
- Facilitate access to health and social services

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## Completion of Therapy

- Based on total number of doses administered, not duration of treatment
- Extend or re-start if there were frequent or prolonged interruptions

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## Meeting the Challenge

- Prevent TB by assessing risk factors
- If risk is present, perform TST
- If TST is positive, rule out active disease
- If active disease is ruled out, initiate treatment for LTBI
- If treatment is initiated, ensure completion

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## Remember

"A decision to test is a decision to treat."

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