

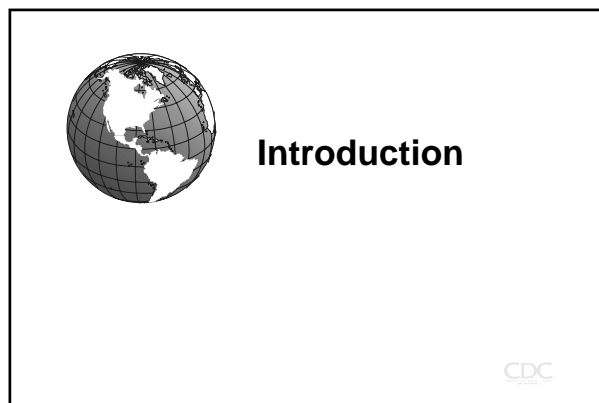

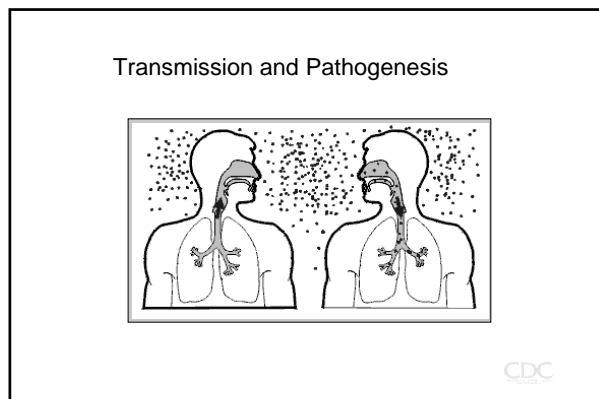



- ### Core Curriculum Contents
- Introduction
 - Transmission and Pathogenesis
 - Epidemiology of TB in the U.S.
 - Testing for TB Disease and Infection
 - Diagnosis of TB
 - Treatment of Latent TB Infection (LTBI)
 - Treatment of TB Disease
 - Infection Control in Health Care Settings
 - BCG Vaccination
 - Community TB Control
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- ### Areas of Concern
- TB cases continue to be reported in every state
 - Drug-resistant cases reported in almost every state
 - Estimated 10-15 million persons in U.S. infected with *M. tuberculosis*
 - Without intervention, about 10% will develop TB disease at some point in life
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- ### Transmission of *M. tuberculosis*
- Spread by droplet nuclei
 - Expelled when person with infectious TB coughs, sneezes, speaks, or sings
 - Close contacts at highest risk of becoming infected
 - Transmission occurs from person with infectious TB disease (not latent TB infection)
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Probability TB Will Be Transmitted

- Infectiousness of person with TB
- Environment in which exposure occurred
- Duration of exposure
- Virulence of the organism



Pathogenesis

- 10% of infected persons with normal immune systems develop TB at some point in life
- HIV strongest risk factor for development of TB if infected
 - Risk of developing TB disease 7% to 10% each year
- Certain medical conditions increase risk that TB infection will progress to TB disease



Common Sites of TB Disease

- Lungs
- Pleura
- Central nervous system
- Lymphatic system
- Genitourinary systems
- Bones and joints
- Disseminated (miliary TB)



Drug-Resistant TB

- Drug-resistant TB transmitted same way as drug-susceptible TB
- Drug resistance is divided into two types:
 - Primary resistance develops in persons initially infected with resistant organisms
 - Secondary resistance (acquired resistance) develops during TB therapy



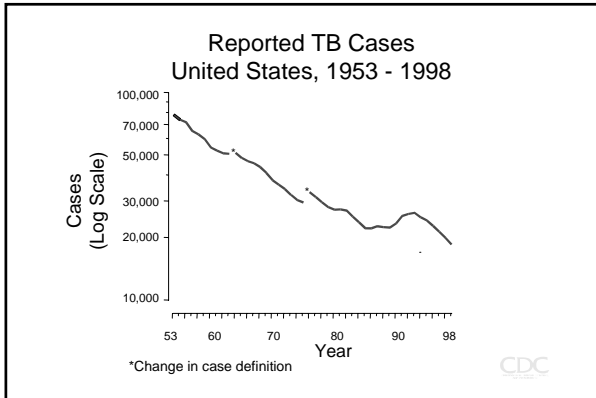
Epidemiology of TB in the United States



TB Morbidity Trends in the United States

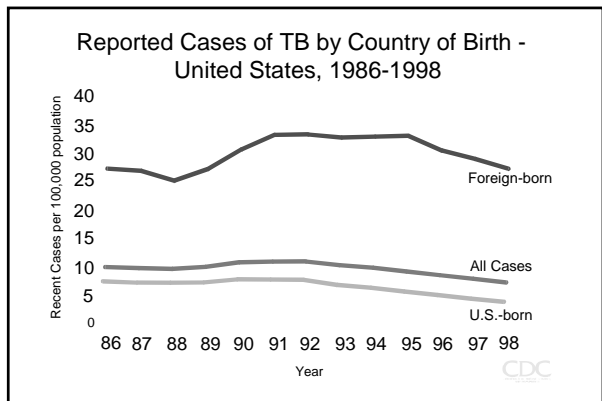
- From 1953 to 1984, reported cases decreased by an average of 5.6% per year
- From 1985 to 1992, reported TB cases increased by 20%
- Since 1993, reported TB cases have been declining again
- 18,361 cases reported in 1998



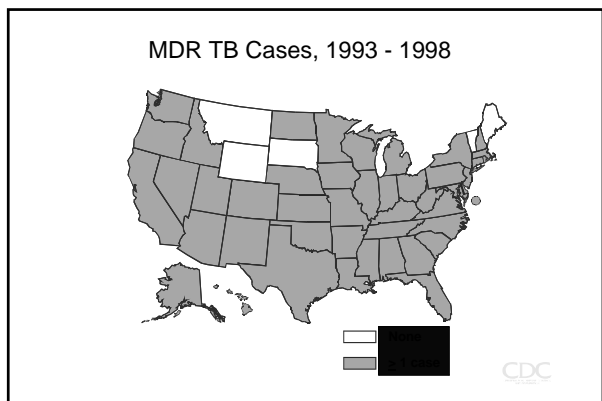


- ### Factors Contributing to the Increase in TB Morbidity: 1985-1992
- Deterioration of the TB public health infrastructure
 - HIV/AIDS epidemic
 - Immigration from countries where TB is common
 - Transmission of TB in congregate settings
- CDC

- ### Factors Contributing to the Decrease in TB Morbidity Since 1993
- Increased efforts to strengthen TB control programs that
- Promptly identify persons with TB
 - Initiate appropriate treatment
 - Ensure completion of therapy
- CDC



- ### Multidrug-Resistant TB (MDR TB) Remains a Serious Public Health Concern
- Resistance to INH 4% in 46 states and District of Columbia (DC) during 1993-1998
 - 45 states and DC reported at least one MDR TB case during 1993-1998
- CDC



Testing for TB Disease and Infection



CDC

Purpose of Targeted Testing

- Find persons with LTBI who would benefit from treatment
- Find persons with TB disease who would benefit from treatment
- Groups that are not high risk for TB should not be tested routinely

CDC

All testing activities should be accompanied by a plan for follow-up care.



CDC

Groups That Should Be Tested for LTBI Persons at higher risk for exposure to or infection with TB

- Close contacts of a person known or suspected to have TB
- Foreign-born persons from areas where TB is common
- Residents and employees of high-risk congregate settings
- Health care workers (HCWs) who serve high-risk clients

CDC

Groups That Should Be Tested for LTBI (cont.)

Persons at higher risk for exposure to or infection with TB

- Medically underserved, low-income populations
- High-risk racial or ethnic minority populations
- Children exposed to adults in high-risk categories
- Persons who inject illicit drugs

CDC

Groups That Should Be Tested for LTBI (Cont.)

Persons at higher risk for TB disease once infected

- Persons with HIV infection
- Persons recently infected with *M. tuberculosis*
- Persons with certain medical conditions
- Persons who inject illicit drugs
- Persons with a history of inadequately treated TB

CDC

Administering the Tuberculin Skin Test

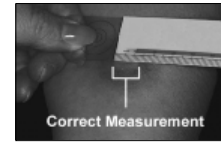
- Inject intradermally 0.1 ml of 5 TU PPD tuberculin
- Produce wheal 6 mm to 10 mm in diameter
- Do not recap, bend, or break needles, or remove needles from syringes
- Follow universal precautions for infection control



CDC

Reading the Tuberculin Skin Test

- Read reaction 48-72 hours after injection
- Measure only induration
- Record reaction in millimeters



CDC

Classifying the Tuberculin Reaction

\$5 mm is classified as positive in

- HIV-positive persons
- Recent contacts of TB case
- Persons with fibrotic changes on chest radiograph consistent with old healed TB
- Patients with organ transplants and other immunosuppressed patients

CDC

Classifying the Tuberculin Reaction (cont.)

\$10 mm is classified as positive in

- Recent arrivals from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children <4 years of age, or children and adolescents exposed to adults in high-risk categories

CDC

Classifying the Tuberculin Reaction (cont.)

\$15 mm is classified as positive in

- Persons with no known risk factors for TB
- Targeted skin testing programs should only be conducted among high-risk groups

CDC

Occupational Exposure to TB, Appropriate Cutoff Depends on

- Individual risk factors for TB
- Prevalence of TB in the facility

CDC

Factors that May Affect the Skin Test Reaction

Type of Reaction	Possible Cause
False-positive	Nontuberculous mycobacteria BCG vaccination
False-negative	Anergy Recent TB infection Very young age (< 6 months old) Live-virus vaccination Overwhelming TB disease

CDC

Anergy

- Do not rule out diagnosis based on negative skin test result
- Consider anergy in persons with no reaction if
 - HIV infected
 - Overwhelming TB disease
 - Severe or febrile illness
 - Viral infections
 - Live-virus vaccinations
 - Immunosuppressive therapy.
- Anergy skin testing no longer routinely recommended

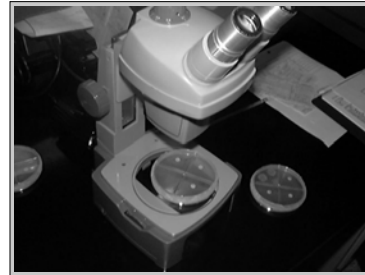
CDC

Boosting

- Some people with LTBI may have negative skin test reaction when tested years after infection
- Initial skin test may stimulate (boost) ability to react to tuberculin
- Positive reactions to subsequent tests may be misinterpreted as a new infection

CDC

Diagnosis of TB



CDC

Evaluation for TB

- Medical history
- Physical examination
- Mantoux tuberculin skin test
- Chest radiograph
- Bacteriologic or histologic exam

CDC

Symptoms of Pulmonary TB

- Productive, prolonged cough (duration of ≥ 3 weeks)
- Chest pain
- Hemoptysis

CDC

Systemic Symptoms of TB

- Fever
- Chills
- Night sweats
- Appetite loss
- Weight loss
- Easy fatigability



Medical History

- Symptoms of disease
- History of TB exposure, infection, or disease
- Past TB treatment
- Demographic risk factors for TB
- Medical conditions that increase risk for TB disease



Mantoux Tuberculin Skin Test

- Preferred method of testing for TB infection in adults and children
- Tuberculin skin testing useful for
 - Examining person who is not ill but may be infected
 - Determining how many people in group are infected
 - Examining person who has symptoms of TB



Chest Radiograph

- Abnormalities often seen in apical or posterior segments of upper lobe or superior segments of lower lobe
- May have unusual appearance in HIV-positive persons
- Cannot confirm diagnosis of TB



Arrow points to cavity in patient's right upper lobe.



Specimen Collection

- Obtain 3 sputum specimens for smear examination and culture
- Persons unable to cough up sputum, induce sputum, bronchoscopy or gastric aspiration
- Follow infection control precautions during specimen collection

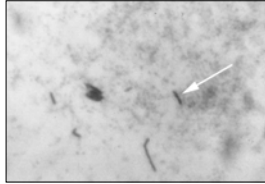


Smear Examination

- Strongly consider TB in patients with smears containing acid-fast bacilli (AFB)
- Results should be available within 24 hours of specimen collection
- Presumptive diagnosis of TB



AFB smear

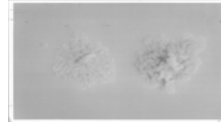


AFB (shown in red) are tubercle bacilli



Cultures

- Use to confirm diagnosis of TB
- Culture all specimens, even if smear negative
- Results in 4 to 14 days when liquid medium systems used



Colonies of *M. tuberculosis* growing on media



Drug Susceptibility Testing

- Drug susceptibility testing on initial *M. tuberculosis* isolate
- Repeat for patients who
 - Do not respond to therapy
 - Have positive cultures despite 2 months of therapy
- Promptly forward results to the health department

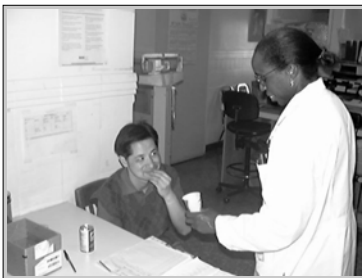


Persons at Increased Risk for Drug Resistance

- History of treatment with TB drugs
- Contacts of persons with drug-resistant TB
- Foreign-born persons from high prevalent drug resistant areas
- Smears or cultures remain positive despite 2 months of TB treatment
- Received inadequate treatment regimens for >2 weeks



Treatment of Latent TB Infection (LTBI)



Treatment of LTBI with Isoniazid (INH)

- 9-month regimen considered optimal
- Children should receive 9 months of therapy
- Can be given twice-weekly if directly observed



Treatment of LTBI with a Rifamycin and Pyrazinamide (PZA)

HIV-Positive Persons

- A rifamycin and PZA daily for 2 months
- May be given twice weekly
- Administration of rifampin (RIF) contraindicated with some protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs)

HIV-Negative Persons

- Clinical trials have not been conducted
- Daily RIF and PZA for 2 months
- May be given twice weekly



Contacts of INH-Resistant TB

- Treatment with a rifamycin and PZA
- If unable to tolerate PZA, 4-month regimen of daily RIF
- HIV-positive persons: 2 month regimen with a rifamycin and PZA

Contacts of Multidrug-Resistant TB

- Use 2 drugs to which the infecting organism has demonstrated susceptibility
- Treat for 6 months or observe without treatment (HIV-negative)
- Treat HIV-positive persons for 12 months
- Follow for 2 years regardless of treatment



Monitoring Patients

Before treatment for LTBI is started, clinicians should

- Rule out possibility of TB disease
- Determine history of treatment for LTBI or disease
- Determine contraindications to treatment
- Obtain information about current and previous drug therapy
- Recommend HIV testing if risk factors are present



Monitoring Patients (cont.)

Establish rapport with patient and emphasize

- Benefits of treatment
- Importance of adherence to treatment regimen
- Possible adverse side effects of regimen
- Establishment of optimal follow-up plan



Monitoring Patients (cont.)

Baseline laboratory testing

- Not routinely indicated
- Baseline hepatic measurements for
 - Patients whose initial evaluation suggests a liver disorder
 - Patients with HIV infection
 - Pregnant women and those in immediate postpartum period
 - Patients with history of chronic liver disorder



Monitoring Patients (cont.)

At least monthly, evaluate for

- Adherence to prescribed regimen
- Signs and symptoms of active TB disease
- Signs and symptoms of hepatitis (if receiving isoniazid alone, and at 2, 4, and 8 weeks if receiving RIF and PZA)



Treatment of TB Disease



CDC

Basic Principles of Treatment

- Provide safest, most effective therapy in shortest time
- Multiple drugs to which the organisms are susceptible
- Never add single drug to failing regimen
- Ensure adherence to therapy

CDC

Adherence

- Nonadherence is a major problem in TB control
- Use case management and directly observed therapy (DOT) to ensure patients complete treatment

CDC

Case Management

- Assignment of responsibility
- Systematic regular review
- Plans to address barriers to adherence

CDC

Directly Observed Therapy (DOT)

- Health care worker watches patient swallow each dose of medication
- Consider DOT for all patients
- DOT should be used with all intermittent regimens
- DOT can lead to reductions in relapse and acquired drug resistance
- Use DOT with other measures to promote adherence

CDC

Treatment of TB for HIV-Negative Persons

- Include four drugs in initial regimen
 - Isoniazid (INH)
 - Rifampin (RIF)
 - Pyrazinamide (PZA)
 - Ethambutol (EMB) or streptomycin (SM)
- Adjust regimen when drug susceptibility results are known

CDC

Treatment of TB for HIV-Positive Persons

- Management of HIV-related TB is complex
- Care for HIV-related TB should be provided by or in consultation with experts in management of both HIV and TB



Extrapulmonary TB

- In most cases, treat with same regimens used for pulmonary TB

Bone and Joint TB, Miliary TB, or TB Meningitis in Children

- Treat for a minimum of 12 months



Pregnant women

- Consult with specialist

Children

- Consult with specialist

Infants

- Consult with specialist



Treatment Regimens for TB Resistant Only to INH

HIV-Negative Persons

- Carefully supervise and manage treatment to avoid development of MDR TB
- Discontinue INH and continue RIF, PZA, and EMB or SM for the entire 6 months
- Or, treat with RIF and EMB for 12 months

HIV-Positive Persons

- Regimen should consist of a rifamycin, PZA, and EMB



Multidrug-Resistant TB (MDR TB)

- Presents difficult treatment problems
- Treatment must be individualized
- Clinicians unfamiliar with treatment of MDR TB should seek expert consultation
- Always use DOT to ensure adherence



Monitoring for Adverse Reactions

- Baseline measurements
- Monitor patients at least monthly
- Monitoring for adverse reactions must be individualized
- Instruct patients to immediately report adverse reactions

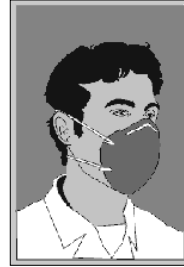


Monitoring Response to Treatment

- Monitor patients bacteriologically monthly until cultures convert to negative
- After 3 months of therapy, if cultures are positive or symptoms do not resolve, reevaluate for
 - Potential drug-resistant disease
 - Nonadherence to drug regimen
- If cultures do not convert to negative despite 3 months of therapy, consider initiating DOT



Infection Control in Health Care Settings



Infectiousness

Patients should be considered infectious if they

- Are coughing
- Are undergoing cough-inducing or aerosol-generating procedures, or
- Have sputum smears positive for acid-fast bacilli and they
- Are not receiving therapy
- Have just started therapy, or
- Have poor clinical response to therapy



Infectiousness (cont.)

Patients no longer considered infectious if they meet **all** of these criteria:

- Are on adequate therapy
- Have had a significant clinical response to therapy, and
- Have had 3 consecutive negative sputum smear results



Infection Control Measures

- Administrative controls to reduce risk of exposure
- Engineering controls to prevent spread and reduce concentration of droplet nuclei
- Personal respiratory protection in areas where increased risk of exposure



Administrative Controls

Reduce risk of exposing uninfected persons to infectious disease:

- Develop and implement written policies and protocols to ensure
 - Rapid identification
 - Isolation
 - Diagnostic evaluation
 - Treatment
- Implement effective work practices among HCWs
- Educate, train, and counsel HCWs about TB
- Test HCWs for TB infection and disease



Administrative Controls (cont.)

Perform risk assessment and classification of facility based on

- Profile of TB in community
- Number of infectious TB patients admitted
- Analysis of HCW skin test conversions



Engineering Controls

To prevent spread and reduce concentration of infectious droplet nuclei

- Use ventilation systems in TB isolation rooms
- Use HEPA filtration and ultraviolet irradiation with other infection control measures



Personal Respiratory Protection

Use in areas where increased risk of exposure:

- TB isolation rooms
- Rooms where cough-inducing procedures are done
- Homes of infectious TB patients



BCG Vaccination



Recommendations for BCG Vaccination

- Not recommended in immunization programs or TB control programs in the U.S.
- BCG vaccination undertaken after consultation with health department



Recommendations for BCG Vaccination (cont.)

Considered for an infant or child with negative skin-test result who

- Is continually exposed to untreated or ineffectively treated patient
- Will be continually exposed to multidrug-resistant TB



Recommendations for BCG Vaccination (cont.)

HCWs considered on individual basis in settings in which

- High percentage of MDR TB patients has been found
- Transmission of drug-resistant TB strains and subsequent infection are likely, and
- Comprehensive TB infection-control precautions implemented and not successful



BCG Vaccination and Tuberculin Skin Testing

- Tuberculin skin testing not contraindicated for BCG-vaccinated persons
- LTBI diagnosis and treatment for LTBI considered for any BCG-vaccinated person whose skin test reaction is ≥ 10 mm, if any of these circumstances are present:
 - Was contact of another person with infectious TB
 - Was born or has resided in a high TB prevalence country
 - Is continually exposed to populations where TB prevalence is high



Community TB Control



Preventing and Controlling TB

Three priority strategies:

- Identify and treat all persons with TB disease
- Identify contacts to persons with infectious TB; evaluate and offer therapy
- Test high-risk groups for LTBI; offer therapy as appropriate



Health care providers should work with health department in the following areas:

- Overall planning and policy development
- Identification of persons with clinically active TB
- Management of persons with disease or TB suspects
- Identification and management of persons with LTBI
- Laboratory and diagnostic services
- Data collection and analysis
- Training and education



Overall Planning and Policy

- Develop overall TB control strategy
- Review local laws, regulations, and policies
- Guide and oversee TB control efforts of local institutions and practitioners
- Provide consultations in TB treatment, contact investigations, and infection control practices
- Seek out necessary funding and resources
- Educate policymakers



Identification of Persons Who Have Clinically Active TB

Health department has ultimate responsibility for ensuring TB patients do not transmit TB

Contact Investigation

Purpose of a contact investigation is to find persons who

- Have TB disease so treatment can be given, and further transmission stopped
- Have LTBI so treatment can be given
- Are at high risk of developing TB disease and require treatment until LTBI excluded



Management of Persons Who Have TB Disease or TB Suspects

Management involves range of services, which include

- Developing a treatment plan
- Promoting and ensuring adherence
- Providing a referral system for other medical problems
- Providing clinical consultation services
- Providing inpatient care when necessary
- Providing appropriate facilities to isolate and treat patients with infectious TB
- Maintaining an infection control program



Identification and Management of Persons with LTBI

- Establish working relationships with other health care providers
- Target testing to well-defined high-risk groups
- Flexibility needed in defining high-priority groups



Laboratory and Diagnostic Services

- Readily accessible
- AFB results within 24 hours of specimen collection
- Clinicians promptly report all TB cases and suspected cases
- All TB smear and culture results reported by laboratories



Data Collection and Analysis

- TB reporting required in every state
- All new cases and suspected cases promptly reported to health department
- All drug susceptibility results sent to health department



Training and Education

TB control programs should

- Provide training for program staff
- Provide leadership in TB education to the community
- Ensure community leaders, clinicians, and policymakers are knowledgeable about TB
- Educate the public

