Tuberculosis
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Outline
• History
• Epidemiology
• Transmission and pathophysiology
• Latent TB Infection (LTBI)
• TB disease
• Diagnosis
• Treatment

Famous Persons with TB

Epidemiology

World TB, 1995
WHO data, 1996

HIV and TB
Double Trouble
Adults and children estimated to be living with HIV/AIDS as of end 1999

Leading causes of death in Africa, 1999

HIV prevalence among pregnant women in South Africa, 1990 to 1999

Tuberculosis Prevalence in South Africa
Reported TB Cases
United States, 1981-2001
TB Morbidity
United States, 1997-2001
TB Case Rates, United States, 2001
TB Case Rates by Age Group and Sex, United States, 2001
TB Case Rates by Race/Ethnicity
United States, 1991-2001
Reported TB Cases by Race/Ethnicity
United States, 2001
Number of TB Cases in U.S.-born vs. Foreign-born Persons
United States, 1991-2001

Percentage of TB Cases Among Foreign-born Persons
United States


Countries of Birth for Foreign-born Persons Reported with TB
United States, 2001

Completeness of HIV Test Results in Persons with TB by Age Group
United States, 1993-2000

Estimated HIV Coinfection in Persons Reported with TB
United States, 1993-2000

Transmission and Pathophysiology

Transmission
• Humans are the principal reservoir of TB in nature
• Infected persons generate droplet nuclei (5um) containing mycobacteria when they cough, speak, or sing
• Susceptible persons inhale the droplet nuclei and become infected

Three Transmission Factors
• The transmitter
• The environment
• The receiver

The Transmitter
• Number of organisms in the sputum
• Viability of the organisms
• Virulence of the organisms
• Presence of cough or other mechanisms to produce droplet nuclei

The Environment
• Factors discouraging transmission of M. tuberculosis
  – Good ventilation
  – Dilution effect–large volume of air containing droplet nuclei
  – Dry air (lack of humidity)
  – Exposure to sunlight or ultraviolet light

The Receiver
• Amount of time spent sharing air with transmitter
• Resistance to infection
  – Previous TB infection or disease
  – Other mycobacterial diseases, BCG
  – Illnesses known to impair resistance

PPD Status and Risk of TB after Exposure
<table>
<thead>
<tr>
<th>TB cases</th>
<th>PPD pos</th>
<th>PPD neg</th>
</tr>
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<tbody>
<tr>
<td>5 outbreaks before 1960</td>
<td>5/330 (1.5)</td>
<td>167/456 (37)</td>
</tr>
<tr>
<td>6 outbreaks since 1980</td>
<td>0/76 (0)</td>
<td>19/98 (19)</td>
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W.W. Stead, AIM, 1995

Two Forms of Clinical TB

- **Latent TB infection (LTBI)**
  - Tuberculin skin test positive
  - Needs preventive therapy
- **TB Disease (active TB)**
  - Requires therapy with multiple agents

Latent TB Infection (LTBI)

A Tuberculin Reaction of

- 5mm is positive in:
  - HIV-positive persons
  - Recent contacts of TB cases
  - Patients with fibrotic changes on chest radiograph consistent with old healed TB

A Tuberculin Reaction of

- \( \geq 10 \) mm is positive in:
  - Recent arrivals (<5yr) from high-prevalence countries
  - Injection drug users
  - Residents and employees of high-risk congregate settings
  - Mycobacteriology laboratory personnel

A Tuberculin Reaction of \( \geq 15 \) mm is positive in:

A negative PPD does not exclude TB

Especially in HIV infected persons with a CD4 count \( \leq 200 \)

- Place other antigens (tetanus, mumps, trichophyton, Candida) on other arm
- Any reaction is considered positive
- Generally no longer done
- Boosting
  - In older persons, the first PPD may be negative
  - A second test, 2-3 weeks later may be positive
  - Two-step testing is especially important, the first time, in persons who will be tested annually.

Interpretation of Two-Step Testing

- If the first and second test are negative, the person is not infected
- If the first test is positive, the person is infected
- If the first test is negative, but the second test is positive, the person is infected

Risk of Developing TB Disease

- Recent converter = 5% first 1-2 years then 5% remainder of lifetime
- HIV infected = 10% per year

Preventive Therapy

- INH for 9 months
- Rifampin for 4 months
- Therapy for resistant bacteria??
- TB Disease (active TB)
- TB History
  - Exposure to a known, active case
  - Past history of TB infection or disease
  - Inadequate or incomplete therapy
  - Other risk factors for TB (HIV, immunosuppression, etc.)

TB Signs and Symptoms

- Persistent cough \( \geq 3 \) weeks in duration
- Plus one or more of the following:
  - Hemoptysis
  - Night sweats
  - Weight loss \( \geq 10\% \) body weight over six months
  - Fever \( \geq 101^\circ F \) or 38.5\(^\circ C \) on more than one occasion during the past 3 weeks

Clinical Forms of TB

- "Primary" Pulmonary Disease
  - Often lower lobe infiltrate, with hilar lymphadenopathy
  - Relatively small numbers of bacteria, so may not be very contagious

- May resolve spontaneously (leaving LTBI), cause a pleural effusion, or become widespread (especially in children)
“Reactivation” TB
• Apical infiltrates (due to higher oxygen tension, or less lymphatic clearance?)
• Often cavitary, but may not be “classic” with AIDS
• High numbers of bacteria—very contagious
• Can become widespread
Extrapulmonary TB
• Pleural—may be long standing
• Miliary—spread throughout the body is poorly controlled by the immune system
• Lymphadenopathy—a manifestation of widespread disease
• Genitourinary—sterile pyuria
• Bone—Pott’s disease
Diagnosis of TB
Making the Diagnosis
• Get an organism!
  ~ Confirms the diagnosis
  ~ Allows sensitivity testing
• Obtain sputum specimens X 3
  ~ Spontaneous cough
  ~ Induced cough
  ~ Bronchoscopy
  ~ Gastric aspirate (children)
Treatment of TB
Basic Principles of Treatment
• Use the safest, most effective therapy in the shortest time
• Use multiple drugs to which the organism is sensitive
• Never add one drug to a failing regimen
• Ensure compliance with therapy
Initial 4-drug Regimen for All Kentucky Patients with TB
Directly Observed Therapy (DOT)
• Noncompliance is the major reason for treatment failure and the emergence of MDR-TB
• Consider DOT for all patients
• In DOT, the health care worker watches the patient swallow each dose of medication
Monitoring Response to Therapy
• Follow the patient at least monthly in the clinic
• Ask about drug side effects
• Obtain laboratory data as required
• Obtain specimens to ensure bacteriologic cure
Expected Success of TB Therapy
Most Common Reasons for Failure

• Problems with drug regimens
  ~ Too few drugs given too long
  ~ Failure to anticipate/manage side effects
• No directly observed therapy (DOT)
• Poor patient compliance/adherence

WHO data, 1994-1997
• Among patients treated < 1 month:
  ~ 36% had isolates resistant to at least one of the 4 primary drugs
  ~ 13% had multidrug resistant isolates
• Isolates from 9.9% of patients with no prior treatment had resistance to at least one drug
  ~ 7.3% INH
  ~ 6.5% streptomycin
  ~ 1.8% rifampin
  ~ 1.0% ethambutol
  ~ 0.4% multidrug

Primary Anti-TB Drug Resistance
United States, 1993-2001
Primary Isoniazid Resistance in U.S.-born vs. Foreign-born Persons
United States, 1993-2001
Mode of Treatment Administration in Persons Reported with TB United States, 1993-1999
Completion of TB Therapy
United States, 1993-1999
Resistant TB - Initial Isolates Kentucky 1996-2000
Take-Home Messages for All Clinicians!
• Think TB!!
• Get an isolate and do susceptibility testing
• Start with 4-drug, short course, therapy
• Ensure compliance with directly observed therapy (DOT)