Presentation Overview

• Explain the historical and pathophysiologic basis for TB disease.

• Describe clinical findings in patients with active TB

• Compare and contrast US and Mexican procedures for diagnosing TB
Robert Koch & World TB Day

- German Physician, Nobel Laureate
- Discovered etiology of tuberculosis 03/24/1882
- Yearly World TB day commemorates the discovery of *Mycobacterium tuberculosis*
- Tuberculosis, or Pthysis, is Greek for consumption

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Robert Koch’s Contribution

- Koch’s postulates and the germ theory of disease: Isolate germ from victim and transmit to host to reproduce disease
- Scientific approach towards TB diagnosis and treatment
- Tuberculosis vaccine development efforts
- Development of Purified Protein Derivative (PPD) as a treatment and diagnostic aid
Uniform Germ Theory of Disease

- Same Pathogen: *M. tuberculosis*
- Common host: *Homo sapiens*
- Common clinical findings
- Same diagnostic and treatment approaches in US and Mexico
- Management depends on disease prevalence and resources

*Mycobacterium tuberculosis*

- *M. tuberculosis* complex comprises closely related species, including *M. hominis*, *M. bovis*, and *M. africanum*
- Slow reproduction, doubling time in days versus hours
- Prolonged latent life phase
- Thick lipid cell coat, survives inside macrophage for prolonged time
Immunologic Basis for Tuberculosis Disease

- Role of humoral immune system, limited
- Active cell-mediated defenses, T lymphocytes, macrophages, CD4 cells
- Explains pathophysiologic basis for latent and active disease and infection
- Treatment implications: extended treatment with multiple drugs

Pathogenesis
Common Sites of TB Disease

- Lungs – 80%
- Extrapulmonary – 20%
  - Lymphatic – 40%
  - Pleural – 20%
  - Bones and joints -10%
  - Meningeal – 5%
  - Genitourinary - 5%
  - Other – 12%

Persons at Higher Risk for Developing TB Disease Once Infected

- Special Medical Conditions:
  - HIV 150X risk.
  - Chronic renal failure, 25X risk.
  - Old TB on CXR, 14X risk.
  - Diabetes, 4X risk.
- Recently infected, 50% lifetime risk.
- Persons who inject illicit drugs
- History of inadequately treated TB
- Persons with other immune suppressing conditions
- Persons with <105% ideal wt
Evaluation for Active TB

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

Medical History

- Symptoms of disease
- History of TB exposure, infection, or disease
- Past TB treatment
- Demographic risk factors for TB (e.g., foreign born)
- Medical conditions that increase risk (e.g., diabetes, HIV)
Tuberculosis
Symptomatology/Findings

- Depend on site of disease
- Pulmonary, respiratory symptoms
- Constitutional symptoms
- Extra Pulmonary, site specific
- Pleural, pleurisy
- Bone/joint, lesion/fracture
- Meningeal, neurologic
- Urogenital, mass / sterile pyuria

Respiratory Symptoms of Disease

- **Prolonged cough** in 80% of patients, mucoid to purulent
- **Hemoptysis** – usually indicates extreme invasive disease – but not always
- **Pleuritic pain** – dull, aching, gripping to sharp, inspiratory
- **Dyspnea** – rare, unless extreme lung involvement or co-existing cardiovascular disease
- **Acute - onset “bronchitis”** - may precede clinical TB symptoms
Constitutional Symptoms of Disease

- **Extreme fatigue** – insidious, with rapid deterioration, irregular menses, emotional stress
- **Weight loss** – Usually profound, related to disease process and diminished caloric intake
- **Fever** – 60%-80% of patients. May be acute to chronic-indolent-fever of unknown etiology
- **Night Sweats** – noticeable at bedtime, mild perspiration may happen; more commonly, soaking perspiration occurs

Physical Examination

- Examination is usually unremarkable, except in advanced cases
- Nonspecific respiratory findings
- Fever, unhealthy appearance in adults
- Children may be deceptively well appearing despite advanced stage of disease
- Emaciation, chachexia are late findings
- Organ-specific findings
Radiographic Examination

- In US, standard P-A views should be ordered for suspect cases. In Mexico, radiographs are ordered when available. A must in pediatric cases, with P-A and Lateral
- Apical lordotic views aid in visualizing lesions obscured by bony prominences
- Special CT imaging may provide further detail (mostly US)
  Imaging studies establish the presence of lesions in the lungs

Common Radiographic Presentation

- Primary: Hilar adenopathy, atelectasis, may be normal
- Secondary: nodular infiltrates of varying sizes, located especially in apical posterior segment of upper lobe and superior segments of lower lobes
- Cavitation is common in advanced cases
- Miliary TB characterized by uniform millet-like seeds throughout lung fields.
- Deceptively normal CXR in Immunocompromised patients.
Primary Tuberculosis

Secondary Tuberculosis
Pediatric Tuberculosis
Primary Complex

Pediatric Tuberculosis
Miliary Tuberculosis

Testing for *M. tuberculosis* Infection
Role of PPD according to Norma Oficial Mexicana

- Contact investigation
- Differential diagnosis
- Epidemiologic Studies
- Determine need for chemoprophylaxis
- Interpretation: Significant induration of ≥10mm in healthy individuals, ≥5 mm in immunocompromised

AFB Smear

AFB (shown in red) are tubercle bacilli “red snappers”
Sputum Collection

- Collect in approved containers. Seal properly
- At least 3 single early AM specimens will pick up 90% of smear-positive case
- Inhaled aerosolized saline may help induce
- Gastric aspiration useful in children
- Sputum collection with all chronic coughers (cough for 2 or more weeks) in Mexico

Smear for Acid-Fast Bacilli

- At least $10^4$ bacilli / mL = smear positive
- 40%-60% of culture-positive cases will be smear positive
- Primary determinant of smear positivity is the extent of disease
- The predictive value of a positive smear will be reduced in populations with increased prevalence of nontuberculous mycobacterial infection
Bacteriology in Mexico

- Diagnosis based on AFB smears
- AFB smear analysis on chronic coughers in a primary-care setting
- Unconcentrated Ziel-Nielsen technique, except in specialized laboratories
- Effective diagnostic strategy in border areas
- Three consecutively collected specimens required for confirmation

AFB Culture & Susceptibility Testing; Mexican Norms

- Diagnosing suspicious cases in the setting of 6 negative AFB smears.
- Diagnosis of extrapulmonary cases (especially genitourinary)
- Diagnose children with suspected TB
- Patients on Directly Observed Therapy with positive AFB smears persisting >4 months
- Diagnosis of epi-linked cases of drug resistance
**Colonies of M. tuberculosis growing on solid media**

**AFB Cultures**

- Use to confirm diagnosis of TB in both US & MX
- Culture all specimens, even if smear negative (US). After 6 neg AFB in suspect case (MX)
- Results in 4 - 8 weeks with Egg-based media, Lowenstein-Jensen
- Results in 4 - 6 weeks in Agar-based media, Middlebrook 7H10
- Results in 2 - 4 weeks with BACTEC liquid medium.

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**Comparison of Diagnostic Procedures: US & Mexico**

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<td>Primary Care</td>
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<td>Laboratory</td>
<td>Emphasis on ID &amp; susceptibility study</td>
<td>Emphasis on rapid field lab diagnosis, AFB</td>
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<td>Radiology</td>
<td>Chest X ray, other radiologic imaging</td>
<td>Chest X ray when available a must for pediatric patients</td>
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<td>Screening</td>
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Management of Tuberculosis

- In Mexico – Diagnosis and treatment occur in primary health-care centers
- In US – Diagnosis and treatment are integrated into specialized TB clinics of State and local health departments.
- Management of multidrug-resistant tuberculosis occurs in limited specialized centers in US and MX.
- Recent formation of drug-resistant TB State Committees in Mexico
- Surgical treatment limited in both US & MX

Tuberculosis Case Definition

- **Confirmed Case** (US & Mexico) Patient in whom tuberculosis pathogenesis has been proven by the following:
  A) Sputum AFB smear (Mexico)
  B) Culture identification (US & Mexico)
  C) Histology (US & Mexico)
Tuberculosis Case Definition (cont.)

- **Unconfirmed Case** (Mexico) – Patients with clinical presentation consistent with tuberculosis disease, but bacteriologic results are negative (common occurrence in pediatric TB)
- **Probable case** (Mexico only) – patient with chronic productive cough or hemoptisis for 2 or more weeks.

Tuberculosis Case Definition (Cont.)

- **Clinical Case** (US) – Patients with clinical symptoms consistent with TB, negative TB bacteriologic results and the following:
  a. Favorable clinical response starting after initiating treatment
  b. Noticeable radiologic improvement by serial CXRs (if pulmonary TB)
  c. PPD skin test positivity helpful for pleural TB case
Binational Case Definition
• Meets the active case definition used in both Mexico and the US
• Requires communication/coordination between US and Mexico providers for optimum case management
• Case-patient is a contact of a binational TB case or is the TB source case-patient for contacts across the border

Thank you very much!
Are there any questions?