Pediatric TB Update

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Objectives

• To describe the global and local epidemiology of TB
• To list at least five risk factors for progression from LTBI to TB disease
• To describe the role of Public Health in TB care
• To list at least three differences between the clinical presentation of TB in adults versus young children
• To describe appropriate cultural and linguistic interventions for foreign-born patients

TB of the Famous

• John Keats
• Louis XIII
• Rene Laennec
• Frederic Chopin
• Ralph Waldo Emerson

• Percy Bysshe Shelley
• King Lunalilo
• Emily Bronte
• Eleanor Roosevelt
• Christian Dior
Estimated TB incidence rate, 2005

<table>
<thead>
<tr>
<th>Estimated new TB cases per 100,000 population</th>
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<tbody>
<tr>
<td>0-24</td>
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<tr>
<td>25-49</td>
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<tr>
<td>50-99</td>
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<tr>
<td>100-299</td>
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<td>300 or more</td>
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Global TB Morbidity, 2000

- Estimated 8.3 million new cases
- 884,019 (11%) were children
- TB & pneumonia are major causes of pediatric death from respiratory diseases in endemic areas

TB Data in Los Angeles County, 1990-2007 - Cases and Rates

Year of Report vs. Number of Cases and Cases per 100,000 population

*Provisional
Data exclude Pasadena and Long Beach TB cases
TB cases in LAC, 1990-2007
US and Foreign Born

Year of Report

Percent of Total Cases

<table>
<thead>
<tr>
<th>Year</th>
<th>US Born</th>
<th>Foreign Born</th>
<th>Unknown</th>
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<tbody>
<tr>
<td>'90</td>
<td>90%</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td>'91</td>
<td>90%</td>
<td>0%</td>
<td>10%</td>
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<td>'93</td>
<td>90%</td>
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<td>'06</td>
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<td>10%</td>
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<tr>
<td>'07</td>
<td>90%</td>
<td>0%</td>
<td>10%</td>
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</tbody>
</table>

Tuberculosis Cases by Country of Birth
Los Angeles County, 2007 (n=816) *

- Mexico 24.1%
- Philippines 15.4%
- U.S. 20.5%
- Vietnam 7.0%
- China 4.7%
- El Salvador 4.4%
- Guatemala 4.2%
- Other 19.7%

*Provisional
Data Excludes Long Beach Cases

Patient 1
- A 30-year-old Thai man c/o productive cough for 3-6 months and weight loss
- Ht: 6 feet  Wt: 96 lbs
- Exam: Thin man, NAD. Coughing.
Patient 1 (cont.)

- Lungs: bilateral rhonchi, L > R
- TST: 20 mm (positive)
- CXR (next slide)

Patient 1: Follow-Up

- Sputa: 3-4+ AFB on smear;
culture grew Mtb complex,
sensitive to INH, RIF, SM, PZA,
EMB
- Pending culture/suscep. results, patient
was started on INH, RIF, PZA, EMB given
by DOT
- PZA & EMB d/c’ed after 2 mo., patient
completed at least 6 mo. of TB tx
Patient 2

• A 25-year-old Thai woman, partner of Patient 1 (the index case), found during contact investigation

• c/o Cough and lump above her right collar bone

• Worked-up at LAC-USC Med Center

Patient 2 (cont.)

• Exam: Enlarged R supraclavicular LN
  Lungs: CTAP

• TST: 15 mm (positive)

• CXR: (next slide)
Patient 2 (cont.)

• Working diagnosis: Pulmonary TB with 2<sup>o</sup> TB lymphadenitis

• FNA of R supraclavicular LN: caseating granulomata; AFB smear & cult. neg

• Sputum: AFB smear negative; Culture Mtb complex, Sensitive to INH, RIF, SM, PZA, EMB

• Pending culture/suscep. results, patient was started on INH, RIF, PZA, EMB, given by DOT

• PZA & EMB d/c'ed after 2 mo., patient completed at least 6 mo. of TB tx.
Patient 3 (Pediatric)

- 13-month-old girl born in the U.S. (child of Patients 1 & 2, found during Contact Investigation)
- No symptoms
- TST: 15 mm (positive)

Patient 3 (cont.)

- Exam: Active, well-developed child
- CXR: (next slide)
- Referred to Children’s Hospital for work-up
Patient 3 (cont.)

• Dx: Pulmonary TB with 2° hilar lymphadenitis

• GI aspirate: smear-negative, culture positive for Mtb complex

• Patient was started on: INH, RIF, PZA, EMB (given by DOT) pending susceptibility results

• Discharged after a written D/C plan was faxed to and approved by TBC

Lessons to Be Learned:

1. Case 1 = Index Case (first identified)

2. Health care providers in California must report TB suspects and cases to Public Health (TBC) within 24 hours

3. Case reports trigger Contact Investigation

Lessons to Be Learned (cont.):

4. Cases 2 & 3 = Secondary Cases found during contact investigation done by the DPHN

5. TB usually causes pulmonary disease but can disseminate to other organs (e.g., lymph nodes)
Lessons to Be Learned (cont.):

6. TB suspects and cases cannot be discharged from health facilities unless a written treatment plan is approved by the local health officer (TBC)

7. DOT is the standard of care for TB

What is TB?
An infectious disease caused by Mtb complex:
- *M. tuberculosis*
- *M. bovis*
- *M. africanum*
- *M. canettii*
- *M. microti*
- *M. caprae*
- *M. pinnipedii*

Transmission
Factors That Determine Likelihood of Transmission

- Number of organisms expelled into the air
- Concentration of organisms in the air
- Duration of exposure to contaminated air
- Virulence of the organism
- Immunity of the host*

Conditions That Increase the Risk of Progression from LTBI to TB Disease

- HIV infection
- Substance abuse
- Recent infection
- CXR findings suggestive of previous TB
- Diabetes mellitus
- Silicosis
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy

Conditions That Increase the Risk of Progression from LTBI to TB Disease (cont.)

- Cancer of the head and neck
- Hematologic and reticuloendothelial diseases
- End-stage renal disease
- Intestinal bypass or gastrectomy
- Chronic malabsorption syndromes
- Low body weight (10% or more below the ideal)
Risk Stratification of Pediatric TB

• In immunocompetent children, age is the most important factor predicting risk of disease after primary infection

Am J Respir Crit Care Med 2006;173:1078-1090

Age-Specific Risk of TB Disease Progression after Infection in Immunocompetent Children

<table>
<thead>
<tr>
<th>Age @ Primary Infection (yr)</th>
<th>Risk for Disease Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>50% no disease</td>
</tr>
<tr>
<td></td>
<td>30-40% pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>10-20% dissem./TB meningitis</td>
</tr>
<tr>
<td>5-10</td>
<td>98% no disease</td>
</tr>
<tr>
<td></td>
<td>2% pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>&lt;0.5% dissem./TB meningitis</td>
</tr>
<tr>
<td>&gt;10</td>
<td>80-90% no disease</td>
</tr>
<tr>
<td></td>
<td>10-20% pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>&lt;0.5% dissem./TB meningitis</td>
</tr>
</tbody>
</table>

Am J Respir Crit Care Med 2006;173:1078-1090

Symptoms & Signs of Pediatric Pulmonary TB

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Infants &amp; Young Children</th>
<th>Older children &amp; Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Night Sweats</td>
<td>Rare</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Cough</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Productive Cough</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>Never</td>
<td>Common</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Sign</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Rales</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Wheezing</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Dullness</td>
<td>Rare</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Breath Sounds</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>

Implications of Pediatric TB Disease

- The occurrence of TB among infants & young children indicates recent transmission
- Average of 50% of household contacts to pediatric TB cases have LTBI or TB disease
- Incubation period of severe TB (e.g., miliary, meningeal) in young children can be only 4-6 weeks

Possible Disease Manifestations of Pediatric TB Disease

- Lymphadenitis - e.g., cervical, hilar (may cause airway impingement, hyperinflation, lobar collapse)
- Pulmonary - primary lesions or aspiration of caseous material
- Other extrapulmonary (e.g., psoas abscess, Pott’s)
- Disseminated or miliary - including TB meningitis
Miliary TB

Gibbus due to Spinal TB
Possible Disease Manifestations of Pediatric TB Disease (cont.)

- Very young TB cases often have paucibacillary disease and are noninfectious
- Children entering or past puberty often have adult-type disease (e.g., smear-positive pulmonary TB) and may be infectious

Making the Diagnosis

- Medical & family-social history
- Physical examination
- Mantoux tuberculin skin test
- Chest radiograph
- Bacteriologic or histologic exam
What is PPD or Tuberculin?

• PPD = Purified Protein Derivative

• The TB skin test (TST) using PPD is a very imperfect test.

• Children < 6 months old may have false negative TST reactions.

Reading the Tuberculin Skin Test

• Read reaction 48-72 hours after injection

• Measure only induration

• Record reaction in millimeters
TST Positive

> 5 mm:
  • HIV-infected (known or suspected)
  • Recent contacts to infectious TB case
  • TB suspects
  • Immunosuppressed persons

> 10 mm:
  • All others

Blood assay for LTBI

• FDA-approved blood assay for M. tuberculosis – Quanti-FERON®-TB Gold IT

• Quantifies amount of gamma-interferon released by lymphocytes in response to in vitro challenge with 3 Mtb antigens: CFP-10, ESAT-6, TB 7.7 (P4)

• Does not cross-react with BCG

• Does cross-react with: M. kansasii, M. marinum, M. szulgai

Blood assay for LTBI

• Requires a minimum of 0.8 ml into each of 3 tubes: nil control, TB antigens, mitogen control (optional but desirable)

• If butterfly needle is used, requires a “purge” tube

• The amount of blood required is significant for young children

• Tubes must be shaken well and incubated within 18 hours
Diagnostic Classes of TB

- Class 0: No exposure, no infection
- Class 1: Exposure to TB, no infection (TST neg.)
- Class 2: Latent TB infection (TST pos.)
- Class 3: Active TB disease
- Class 4: Old, inactive TB disease
- Class 5: Suspect active TB disease

LTBI = Latent TB Infection

- Patient has no sx & physical exam is WNL
- TST is (+)*
- CXR is negative

How Do You Treat LTBI?
LTBI Treatment

• Preferred:
  • Isoniazid (INH) 10-15 mg/kg daily for 9 months

• Alternate:
  • Rifampin (RIF) 10-20 mg/kg daily for 4-6 months

Monitoring Patients on LTBI Tx

• Patients must be seen monthly in clinic

• Assess for s/sx of adverse drug reactions (e.g., nausea, vomiting, jaundice)

• Routine baseline and follow-up labs are indicated in certain groups (e.g., HIV+, pregnant/postpartum women, chronic liver disease, alcoholics)

Diagnosing Pediatric TB Suspects and Cases
Pediatric TB: Diagnostic Principles

- Up to 50% of pediatric TB cases in the U.S. with abnormal CXRs have few or no S/Sx, but are found during contact investigations of adult suspects and cases.
- Infants are more likely than older children to have S/Sx.
- Those < 5 y.o. are at risk for disseminated TB.

Starke JR, Correa AG. Pediatr Infect Dis J 1995;14:455-470

Pediatric TB: Diagnostic Principles

- Positive TST + S/Sx => TB Disease
- Hx of TB Exposure + S/SX => TB Disease
- Positive TST alone = LTBI

Starke JR, Correa AG. Pediatr Infect Dis J 1995;14:455-470

Clinical Presentation: Children vs. Adults

- May have false (-) TST, esp. < 6 mo.
- S/Sx are often absent or nonspecific.
- Extrapulmonary disease common, esp. hilar LN.
- CXR findings: hilar LN, lower lobe lesions.
- Unable to produce sputum for dx.
- Clinical presentation of older children is similar to adults.

L.A. County TB Control Program
Bacteriologic Confirmation

• Collect early morning sputa (preferably by induction) for AFB smear & culture if possible

• If not, base treatment on source case’s susceptibility results

Starke JR, Correa AG. Pediatr Infect Dis J 1995;14:455-470

Bacteriologic Confirmation

Do early morning GI aspiration if:
  • Child cannot produce sputum
  • Source case is unknown
  • There are several possible source cases
  • The likely source has drug-resistant TB
  • The child has extrapulmonary TB (may also need sampling of extrapulmonary site)

Starke JR, Correa AG. Pediatr Infect Dis J 1995;14:455-470

Basic Principles of Treatment

If the patient has or may have active TB disease (i.e., TB case or suspect),

Do Not Treat With Only One TB Drug
Basic Principles of Treatment

Standard Empiric Regimen:

• INH 15-20 mg/kg daily
• RIF 10-20 mg/kg daily
• Pyrazinamide (PZA) 15-30 mg/kg daily
• Ethambutol (EMB) 15 mg/kg daily

Each drug plays a unique role

Is EMB Safe to Use in the Very Young?

- Older children and adults should receive monthly monitoring (red & green color discrimination, Snellen exam)
- Toxicity is related to cumulative dose
- “…Should be used with caution in children in whom visual acuity cannot be monitored (generally less than 5 years of age)…In younger children EMB can be used if there is concern with resistance to INH or RIF.”

Am J Respir Crit Care Med 2003;167:603–62

Is EMB Safe to Use in the Very Young?

“The effect is dose related, with minimal risk at a daily dose of 15 mg/kg.”

“No difference was found in the prevalence of decreased visual acuity between regimens that contained EMB at 15 mg/kg and those not containing the drug.”

Am J Respir Crit Care Med 2003;167:603–62
**Treatment Tips**

- Dosing for all anti-TB meds is in mg/kg
- Liquid susp. (esp. RIF) has short shelf life
- Liquid susp. often causes diarrhea
- Powder meds & mix with something sweet or peanut butter

**Pediatric TB**

- Treatment of active TB disease requires multiple drugs to which the organism is sensitive
- DOT ensures treatment completion
- Public Health oversees management of all TB suspects and cases

**Remember:**

All health care providers must be aware of patients' cultural needs (e.g., desire to be addressed formally by surname, misunderstanding of certain gestures)
Remember:

All health care providers must be aware of patients’ linguistic needs (use linguistically-competent staff or language lines)

L.A. County TB Control Program

Paraplegia due to Spinal TB

PROTECT

them from TUBERCULOSIS

Keep them away from sick people
Health screening and tests
Teach them in healthy habits
Consult the doctor regularly