TB Nurse Case Management
San Antonio, Texas
July 18 – 20, 2012

Pediatric TB
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Kim Smith, MD, MPH has the following disclosures to make:

• No conflict of interests
• No relevant financial relationships with any commercial companies pertaining to this educational activity
Childhood Tuberculosis

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MD, MPH

OUTLINE
- Stages of tuberculosis
- Differences of disease in children and adults
- Diagnostic challenges of pediatric TB
- Treatment of TB in children
- Clinical cases
Stages of Tuberculosis

Exposure to Contagious Adult with Pulmonary Disease

Household contacts 20-30%

Latent TB Infection LTBI

5-10%

Risk varies by age 5-50%

Adult Active TB Disease

Child Active TB Disease
## Percent Risk of Disease by Age

<table>
<thead>
<tr>
<th>Age at Infection</th>
<th>Risk of Active TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth – 1 year*</td>
<td>43%</td>
</tr>
<tr>
<td>1 – 5 years*</td>
<td>24%</td>
</tr>
<tr>
<td>6 – 10 years*</td>
<td>2%</td>
</tr>
<tr>
<td>11 – 15 years*</td>
<td>16%</td>
</tr>
<tr>
<td>Healthy Adults</td>
<td>5-10% lifetime risk</td>
</tr>
<tr>
<td>HIV Infected Adults+</td>
<td>30-50% lifetime</td>
</tr>
</tbody>
</table>

*Miller, Tuberculosis in Children Little Brown, Boston, 1963
+WHO, 2004

## Risk of Progression to TB Disease by Age

| Age @ primary infection | Risk of Disease | |
|-------------------------|-----------------|
| **Birth-12months**      | **Risk of Disease** |
| Disease                 | 50%             |
| Pulmonary Dis           | 30-40%          |
| Miliary or TBM          | 10-20%          |
| **1-2 years**           | **Risk of Disease** |
| Disease                 | 20-25%          |
| Pulmonary Dis           | 75%             |
| Miliary or TBM          | 2-5%            |

Marais BJ. *Int J Tuberc Lung Dis* 2004;8:392-402
TREATMENT OF TUBERCULOSIS IN CHILDREN

Stages of TB Skin Test or IGRA CXR SXs Treatment

**Exposure**
- Child < 4 years of age
- Household contact with adult with active pulmonary disease

<table>
<thead>
<tr>
<th>Skin Test or IGRA</th>
<th>CXR</th>
<th>SXs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Normal</td>
<td>None</td>
<td>INH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duration: 8-10 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repeat skin test: 8-10 wks after exp if positive ≥ 5mm, see LTBI</td>
</tr>
</tbody>
</table>

**Latent TB infection (LTBI)**
- Positive

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<tbody>
<tr>
<td>Positive</td>
<td>Normal</td>
<td>None</td>
<td>INH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duration: INH 9 mo or for INH resistant LTBI, RIF 6 mo</td>
</tr>
</tbody>
</table>

**Disease**
- Pulmonary and extrapulmonary (except disseminated disease and meningitis, see below)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Skin Test or IGRA</th>
<th>CXR</th>
<th>SXs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary and extrapulmonary</td>
<td>90% positive</td>
<td>Abnormal</td>
<td>+/-</td>
<td>INH, RIF, PZA (consider EMB or an aminoglycoside)</td>
</tr>
<tr>
<td>Duration: 6 mo total, Stop PZA after 2 mo, continue INH &amp; RIF for susceptible disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disease**
- Disseminated including miliary, bone/joint and multi-site disease

<table>
<thead>
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<th>Disease</th>
<th>Skin Test or IGRA</th>
<th>CXR</th>
<th>SXs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disseminated including miliary, bone/joint and multi-site disease</td>
<td>TST may be negative early in disseminated TB, most positive by end of treatment</td>
<td>+/-</td>
<td>Yes</td>
<td>INH, RIF, PZA and EMB or an aminoglycoside or Ethionamide daily for 2 mo, then INH and RIF for 7-10 mo</td>
</tr>
<tr>
<td>Duration: 9-12 mo total for drug susceptible disease</td>
<td></td>
<td></td>
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</tbody>
</table>

**Disease**
- Meningitis

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<thead>
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<th>Disease</th>
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<th>CXR</th>
<th>SXs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>Often negative early in meningitis and miliary disease</td>
<td>+/-</td>
<td>Yes</td>
<td>INH, RIF, PZA and an aminoglycoside or EMB or Ethionamide daily for 2 mo, then INH and RIF for 7-10 mo</td>
</tr>
<tr>
<td>Duration: 9-12 mo total for drug susceptible disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids recommended for first 1-2 mo for meningitis</td>
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<td></td>
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</tr>
</tbody>
</table>

**Pediatric Tuberculosis Treatment Table**

**Daycare Exposure**

- Child < 4 years of age
- Household contact with adult with active pulmonary disease
Daycare Exposure

- Index case, teacher assistant with AFB smear positive pulmonary disease and cough for 6 weeks

- 135 children < 4 years of age, plus adult staff members exposed

Smith, KC. *Southern Medical Journal* 93(9):877-880, 2000

Daycare Exposure Management

- Who is at risk?
  - Children and staff

- Who needs TST?
  - Everyone with significant contact with source case

- Who needs CXR?
  - All children less than 4 years of age even if TST negative
  - Any contacts with positive TST (≥ 5mm)

- Who needs treatment?
  - LTBI (positive TST >5mm and normal CXR) INH for 9 months
  - Exposed children less than 4 years of age need INH window prophylaxis for 8-10 weeks

- Follow up?
  - Repeat TST 8-10 weeks after exposure
  - If negative and contact broken, stop INH prophylaxis
TB Prevention After Exposure

- Household contact with contagious person
  - Teen or adult with pulmonary TB disease
  - Usually ≥ 4 hours of contact
- Initial TST negative
  - Window period for TST conversion (8-10 weeks)
- CXR and physical exam normal
- **INH prophylaxis recommended:**
  - For children <4 yrs of age
  - Immunosuppressed patients
  - May prevent progression to disease during window period
- Repeat TST 8-10 wks after exposure
- May stop INH if 2nd TST negative <5mm in immunocompetent patients

Preventable Case
Pediatric TB Case a Missed Opportunity

15 mo old
- 10 days fussiness & decreased appetite
- 3 days inability to walk or sit up
- CSF: 96 WBC (NL <7), 72% Lymphs,
  198 Protein (NL <45), Glucose 8
- Source case: mother of child
- Diagnosis: TB Meningitis

Family history
- Mom with pulmonary TB diagnosed 5 mo earlier on appropriate treatment
- Dad diagnosed with LTBI on INH
- Baby initial TST 0mm @ 10 months of age
  - no CXR
  - no treatment
  - lost to follow up

TB Meningitis
Treatment and Clinical Course

- 12 months RIPE therapy
- Steroids for 1-2 month with 2-3 week taper
  - decreases CNS inflammation
- Fever common for first month, symptoms may initially worsen followed by gradual improvement

Possible complications
- Seizures
- Hydrocephalus
- CNS tuberculosis, stroke, MR, CP
- Mortality usually 100% if not diagnosed and treated

This case was potentially preventable if treated with window prophylaxis when parent diagnosed
Differences In Adult and Pediatric TB

- Occurs years after primary infection
- Typical of adult disease
- Occasionally seen in teens
- Often cavitary disease
- High numbers of organisms (AFB +)
- Usually symptomatic and contagious
Primary Disease

- Typical of childhood TB
- Usually not cavitary
- Classic x-ray:
  - **Hilar lymphadenopathy** with or without pulmonary infiltrates
  - Miliary infiltrates
- Low numbers of organisms
  - AFB smears negative in 95% of pedi cases
  - Culture negative in 60% of cases
- Most children <12 yrs not contagious
- Often asymptomatic (50%)
Adult TB Disease

- **Pulmonary**: 85%
- **Extrapulmonary**: 15%

CDC
Adult Extrapulmonary TB Disease (15%)

- Lymphatic: 25%
- Pleural: 23%
- GU: 16%
- Other: 13%
- Bone/Joint: 9%
- Miliary: 4%
- Meningeal: 4%

Pediatric TB Disease

- Pulmonary: 75%
- Extrapulmonary: 25%
Extrapulmonary TB Disease in Children (25%)

- lymphatic: 67%
- pleural: 6%
- miliary: 14%
- meningeval: 14%
- bone/joint: 5%
- other: 4%

*Feigin & Cherry, Text of Pedi ID
Common symptoms of TB disease in children

- Cough and/or respiratory distress
- Pulmonary findings on examination
- Lymphadenopathy or lymphadenitis
- S/Sx of meningitis including seizures
- Persistent fever (FUO)
- Weight loss or failure to thrive
- Unlike adults, up to 50% of children with TB disease have no symptoms

Unique Challenges of TB in Children

- More difficult diagnosis
- Nonspecific signs and symptoms
- Fewer mycobacteria
- Fewer positive bacteriologic tests
- Increases risk of progression to disease
- Higher risk of extrapulmonary and TB meningitis
Diagnosis for TB in Children

- **Gold Standard** –
  Positive TB Culture

OR,

- **Clinical Diagnosis**: Abnormal CXR, laboratory, or physical examination consistent with TB **AND**

  1 or more of the following:
  - Positive tuberculin skin test
  - Contagious adult source case identified
  - Clinical course consistent with TB disease, or
  - Improvement on TB therapy

---

**Diagnostic Triad**
for TB Disease in Children

- Abnormal CXR and/or physical exam
- Positive TST or IGRA
- Infectious adult source case identified
### Clinical Disease Examples

#### 3 Year Old
- Contact to AFB smear + source case (parent)
- TST 7 mm
- No symptoms
- Normal physical exam
- CXR hilar LAN

**Clinical Diagnosis:**
- Abnormal CXR, laboratory, or physical examination consistent with TB **AND**
- 1 or more of the following:
  - Positive tuberculin skin test
  - Contagious adult source case identified
  - Clinical course consistent with TB disease, or
  - Improvement on TB therapy

#### 2 Year Old
- Normal physical
- TST 10 mm
- CXR hilar adenopathy
- TB cultures negative

**Clinical Diagnosis:**
- Abnormal CXR, laboratory, or physical examination consistent with TB **AND**
- 1 or more of the following:
  - Positive tuberculin skin test
  - Contagious adult source case identified
  - Clinical course consistent with TB disease, or
  - Improvement on TB therapy
AFB smears and Cultures in Children

- AFB smear usually negative
  - In 95% of patients <12 years of age

- Low yield on TB culture
  - Only 40% positive in children 1-12 yrs of age with pulm TB

- Obtaining cultures from children with pulmonary TB
  - Early morning gastric aspirates (x3)
  - Broncho alveolar lavage (BAL)
  - Induced sputum
  - Adult source case important

IGRA Tests in Kids

- Good sensitivity
  - Variable 70-90%

- Highly specific
  - Does not cross react with BCG vaccine or most other mycobacteria
  - Specificity is 90-95%

- Single visit required

- Helpful (preferred) in BCG vaccinated patients

- Children <5 yrs
  - Not FDA approved in this age, limited data
  - Consider either test (IGRA or TST) positive in this vulnerable age

- May save costs by reducing false positives
Expected Clinical Course for TB Disease in Children

- **Pulmonary**
  - CXR takes months to improve
- **Hilar lymphadenopathy**
  - May take a year or more to regress on x-ray
- **Cervical lymphadenitis**
  - Gets worse before improvement over months to years
- **Meningitis**
  - Inflammation increases initially with treatment

Monitoring Children on TB Treatment

- Risk of drug toxicity very low
- Monitor clinical signs
  - regular clinical visits (4-6 wks)
  - patient education
- Routine blood work not necessary unless
  - symptoms
  - risk factors for toxicity
- Monitor and reinforce adherence
- When to follow up CXR’s for pulmonary TB
  - Beginning and end of therapy
  - If clinical change
- Completion of therapy certificate
Management of TB Medication Reactions

- Hepatotoxicity
- Medication refusal in children
  - Crush tablets, medication sandwich
- Vitamin B6
  - Breastfed infants, teens & picky eaters
- Going back to school
  - Children <12 yrs of age are not contagious

Prevention of TB Disease in Children

- Contact Investigation
- INH Window Prophylaxis
- Treatment of LTBI
Questions
Pediatric TB Cases

Kim Connelly Smith, MD, MPH

Lymphadenopathy
Clinical Case
Cervical Lymphadenopathy

- 8 yr old with cervical lymphadenopathy

History:
- LAN for 3 months
- PMHx: Healthy
  - BCG vaccine at birth
  - TB skin test 10 mm

Physical Exam:
- 3 cm anterior cervical LAN
- 1.5 cm supraclavicular lymphadenopathy

CXR:
- Hilar LAN, no infiltrates

Is this TB disease?
What else could it be?

Hilar & Cervical Lymphadenopathy

- Differential Dx
  - Tuberculosis
  - Non TB mycobacteria (NTM)
  - Lymphoma/Leukemia
  - HIV
  - Other causes

- Diagnostic tests
  - Biopsy (FNA or surgical for culture and path)
  - Interferon γ Blood test for TB infection
Results

- **Fine needle aspirate of node:**
  - Pathology: lymphoma, no TB by culture or microscopy

- **Interferon γ Blood test for TB**
  - Positive
  - Diagnostic for latent TB infection or disease

- **Diagnoses:**
  - LTBI
  - AND
  - Hodgkin’s Lymphoma

- **Treatment:**
  - Chemotherapy for lymphoma AND
  - INH daily for 9 months for LTBI
    - consider prolonged treatment during immunosuppression

Primary TB Disease
Primary TB Disease

- Father with pulmonary, smear positive, pansusceptible tuberculosis
- 9 year old son with 5 mm TST
  - Otherwise healthy kid with no symptoms
  - Initial CXR with small pleural effusion
  - No treatment started

- What was diagnosis at this point?
Treatment and Follow up

- 6 weeks later child with fever and respiratory difficulty
- See follow up CXR
Questions

- What went wrong?
- What treatment would you recommended?

Skin Test in Foreign Born
Skin Test in Foreign Born

- 5 year old with positive TST for school entry
- Born in Asia
- BCG documented on vaccination records at birth and BCG scar present
- TST measures 12mm

CXR normal

- How do you interpret the skin test?
- Is this BCG effect or LTBI?
- Are there any other tests that may help?
Algorithm for TB Testing in Children

TB Risk Questionnaire positive?
  Yes
  No

Age < 5 years?
  Yes
  No

BCG Vaccinated?
  Yes
  No

Initial TST Done?
  Yes
  No

TST Result?
  Positive
  Negative

Concern for TB disease?*
  Yes
  No

Concern for TB disease?*
  Yes
  No

TST Preferred*

Likely to return for TST reading?
  Yes
  No

TST or IGRA Acceptable

IGRA Preferred

Indeterminate

Repeat IGRA

Indeterminate

Consider TST if not done

Negative, testing complete

Algorithm for TB Testing in Children

*If clinical suspicion of TB disease consider doing both tests and either positive TST or IGRA may be significant.

TB in Newborn Nursery
New Mother with Positive TST

- Newborn infant in hospital nursery
- Mother with 15 mm TST
- CXR: calcified granuloma no active disease
- Not on treatment
  - What is mother’s diagnosis?
  - Do mother or baby need isolation?
  - May baby breast feed and room with mother?

New Mother with Positive TST

- What if mother had cavitary disease on CXR with AFB + pulmonary disease?
- How should baby be treated?
Fig 1  Mother or Household Contact with Latent TB Infection (+ skin test, normal CXR) Not Contagious

No treatment needed for infant (may breastfeed & room in)

Refer infant for MDR/HRM screens, usually started 3 months after delivery

No treatment necessary for infant

PPD Negative

Skin test result before baby goes home

PPD Positive

Refer contact for chest X-ray

Normal CXR: Latent TB Infection (noncontagious)

No treatment needed for infant

No treatment necessary

Refer mother for INH chemoprophylaxis; usually started 3 months after delivery

Screen household contacts for symptoms of TB

Infant needs INH prophylaxis

Abnormal CXR: TB Disease (contagious)

Was mother previously diagnosed?

Yes

Continue INH for duration of 9 months

Consult TB specialist for drug therapy

May be sensitive to all drugs

Stop INH

Obtain CXR

Normal CXR: Latent TB infection

Continue INH for duration of 9 months

Refer to TB Specialist. Admission required for full work-up includes gastric aspirates, LP, and management by TB specialist

PPD Positive from birth

Skin test result at 3 months of age

PPD Negative

Skin test result at 6 months of age* 

Normal CXR: Latent TB infection

Continue INH for duration of 9 months

Consult TB specialist for drug therapy

May be sensitive to all drugs

Stop INH

Obtain CXR

Abnormal CXR: TB Disease (contagious)

Was mother on treatment?

Yes

Refer to TB Specialist. Admission required for full work-up includes gastric aspirates, LP, and management by TB specialist

Was mother's AFB culture negative for 3 mos.?

Yes

Mother is not contagious. No treatment needed for infant

No

Verify that mother's sputum specimens sent for AFB smear, Culture & Sensitivity

Health Department will skin test infant at 3 months of age*

Skin test result at 6 months of age*

PPD Positive

Obtain CXR

Abnormal CXR: TB Disease (contagious)

PPD Negative

Obtain CXR

Normal CXR: Latent TB infection

Stop INH

No treatment needed for infant

*Negative skin test may be unreliable in infants < 6 months of age

Fig 2  Mother or Household Contact with Pulmonary TB Disease (abnormal CXR) Possibly Contagious

Was mother previously diagnosed?

No

Continue INH for baby

Sensitve

Was mother on treatment?

Yes

Continue INH for duration of 9 months

Consult TB specialist for drug therapy

PPD Positive

Obtain CXR

Normal CXR: Latent TB infection

Stop INH

Obtain CXR

Abnormal CXR: TB Disease (contagious)

Was mother's AFB culture sensitive to all drugs?

Yes

Mother is not contagious. No treatment needed for infant

No

Verify that mother's sputum specimens sent for AFB smear, Culture & Sensitivity

Health Department will skin test infant at 3 months of age*

Skin test result at 6 months of age*

PPD Positive

Obtain CXR

Abnormal CXR: TB Disease (contagious)

PPD Negative

Obtain CXR

Normal CXR: Latent TB infection

Stop INH

No treatment needed for infant

*Negative skin test may be unreliable in infants < 6 months of age

Developed by Pediatric Tuberculosis Team, University of Texas - Houston Medical School
Prevention of TB in Children

- **Contact Investigation**
  - EARLY evaluation critical to prevent disease in infants

- **Window Prophylaxis for TB Exposure**
  - If TST and CXR negative: INH x 8-10 weeks for children < 4 yrs

- **Treatment of LTBI**
  - INH x 9 months

Treatment of TB Disease in Children

- **Pulmonary or lymphadenopathy**
  - Standard RIPE therapy for 6 months

- **TB Meningitis or Miliary TB**
  - Standard RIPE therapy for 9-12 months
  - Steroids for first 1-2 months for meningitis
  - Consultation with Pediatric TB expert available through HNTC