Pediatric Tuberculosis

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A Deeper Dive into TB Nurse Case Management

October 25th-27th, 2022

San Antonio, TX

Epidemiology of Pediatric TB

Percent Risk of Disease by Age

Age at Infection	Risk of Active TB
Birth – 1 year*	43%
1 – 5 years*	24%
6 – 10 years*	2%
11 – 15 years*	16%
Healthy Adults	5-10% lifetime risk
HIV Infected Adults+	30-50% lifetime

*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 – 12 months	Disease	50%
	Pulmonary Dis	30-40%
	Miliary or TBM	10-20%
• 1 - 2 years	Disease	20-25%
	Pulmonary Dis	75%
	Miliary or TBM	2-5%

Marais BJ. *Int J Tuberc Lung Dis* 2004;8:392-402

Risk of Progression from TB Infection to Disease by Age

Age at Primary Infection (yr)	No Disease (%)	Pulmonary Disease (%)	Miliary or Central Nervous System TB (%)
<1	50	30 to 40	10 to 20
1 to 2	75 to 80	10 to 20	2.5
2 to 5	95	5	0.5
5 to 10	98	2	<0.5
>10	80 to 90	10 to 20	<0.5

Adapted from Marais, et al. Childhood pulmonary tuberculosis: old wisdom and new challenges. *Am J Resp Crit Care Med*. 2006;173:1078–1090.

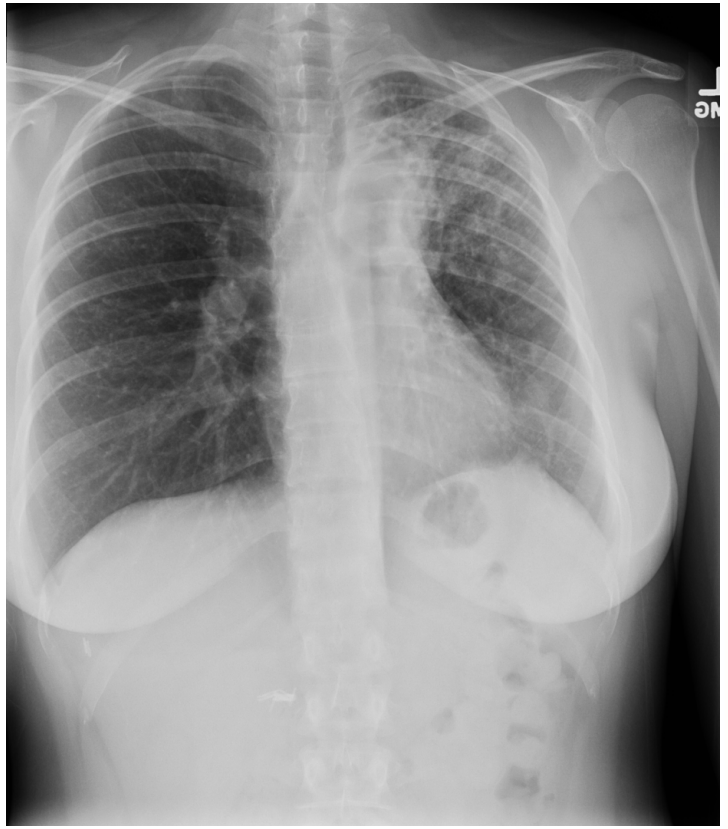
Peds in Review 2010;31:13

Differences in Adult and Pediatric TB

Reactivation Disease

Adults and older children

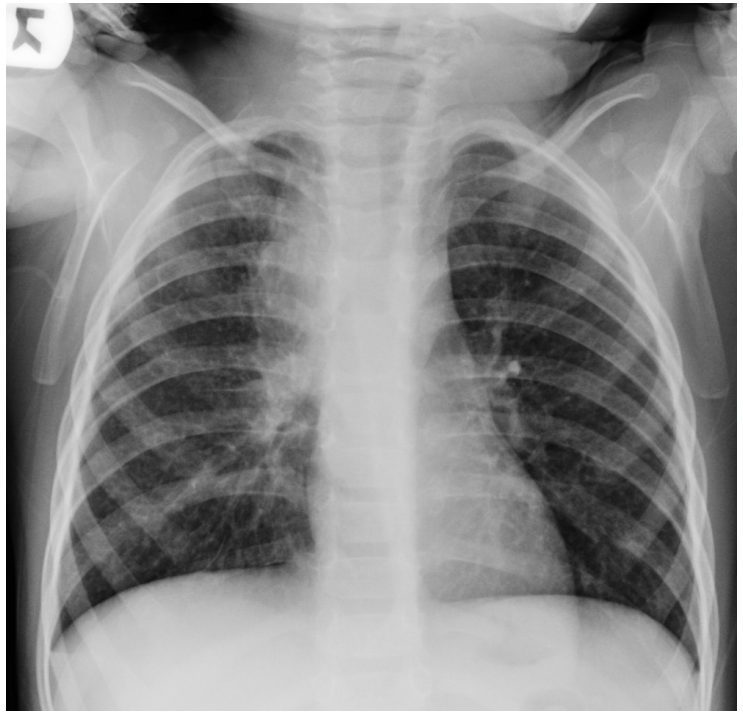
- Occurs years after infection
- Occasionally seen in teens
- Often cavitary disease
- High numbers of organisms (AFB+)
- Usually symptomatic and contagious



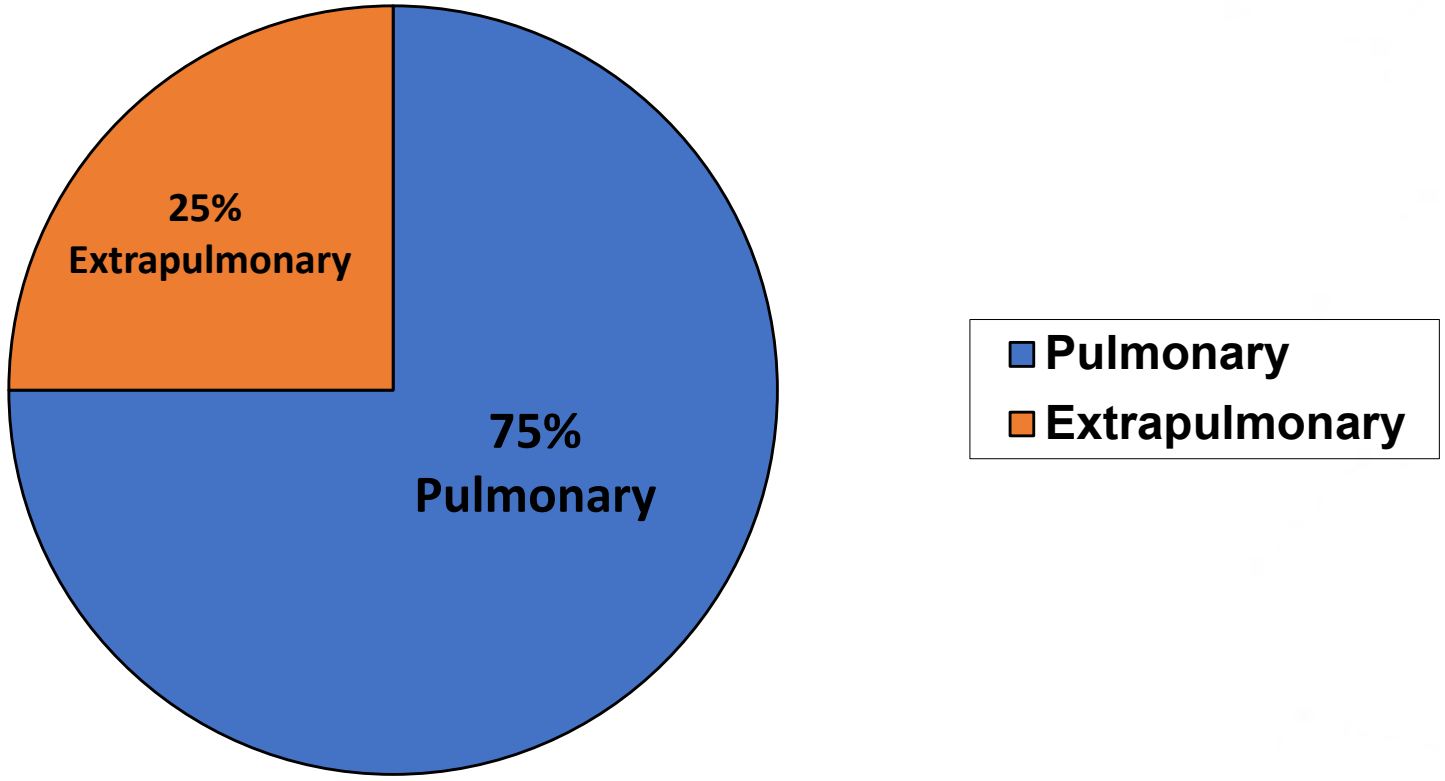
Primary Disease

Small children and immunosuppressed

- Typical of childhood TB
- Usually not cavitary
- Classic x-ray:
  - Lobar pulmonary infiltrates
  - **Hilar lymphadenopathy or**
  - 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%)

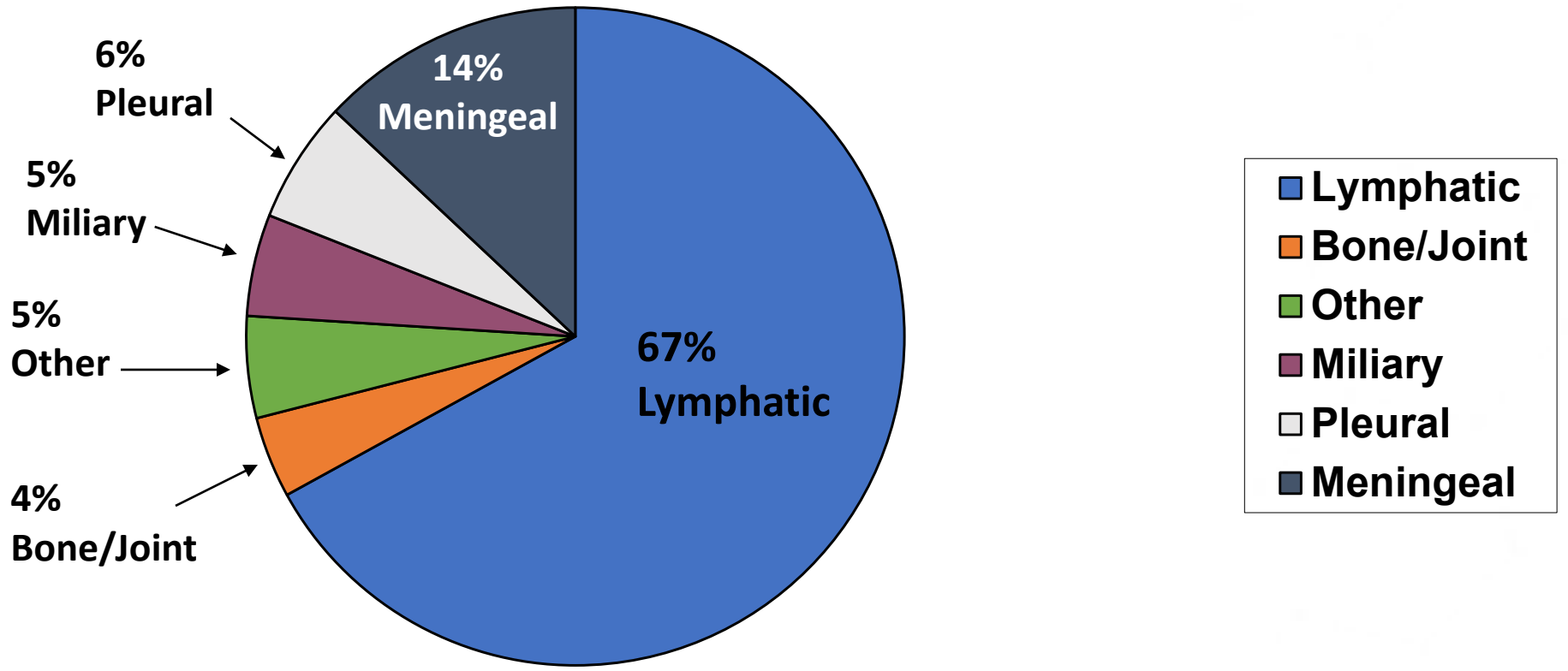


Pediatric TB Disease



CDC

Extrapulmonary TB Disease in Children (25%)



CDC

Diagnosing Tuberculosis in Children

How is tuberculosis diagnosed?

Adults – Mycobacterial-based diagnosis

- positive sputum AFB smear — 60% - 75%
- positive sputum culture — 90%
- positive tuberculin skin test — 80% [HIV < 50%]

Children

- positive sputum/gastric AFB smear — 10%
- positive sputum/gastric culture — 10% - 40%
- positive tuberculin skin test — 50% - 80%

Gastric Aspirates

- Inpatient procedure
- Overnight fasting
- Lavage with NS if volume < 20cc

- Generally done qAM x3
- Inpatient costs
- AFB smear yield: minimal
- AFB Culture yield: 20-30%

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 TST/IGRA
  - Contagious adult source case identified
  - Clinical course consistent with TB disease, or
  - Improvement on TB therapy

IGRAs and the 2018 AAP "RED BOOK"

- Can use IGRAs in immunocompetent children 2 y/o and older in all situations when a TST would be used
- Preferred test for children 2 years and older who have received a BCG vaccination
- Data shows IGRAs perform consistent well in children 2 years and older, some experts use down to 1 y/o
- Neither IGRAs nor the TST are perfect; always need clinical judgment!

Clinical Presentation of TB in Children

Signs and Symptoms of Pulmonary TB

Clinical Feature or Disease Type	Infants	Children	Adolescents
Symptom			
Fever	Common	Uncommon	Common
Night sweats	Rare	Rare	Uncommon
Cough	Common	Common	Common
Productive cough	Rare	Rare	Common
Hemoptysis	Never	Rare	Rare
Dyspnea	Common	Rare	Rare
Sign			
Rales	Common	Uncommon	Rare
Wheezing	Common	Uncommon	Uncommon
Decreased breath sounds	Common	Rare	Uncommon
Location of Disease			
Pulmonary	Common	Common	Common
Pulmonary + Extrapulmonary	Common	Uncommon	Uncommon

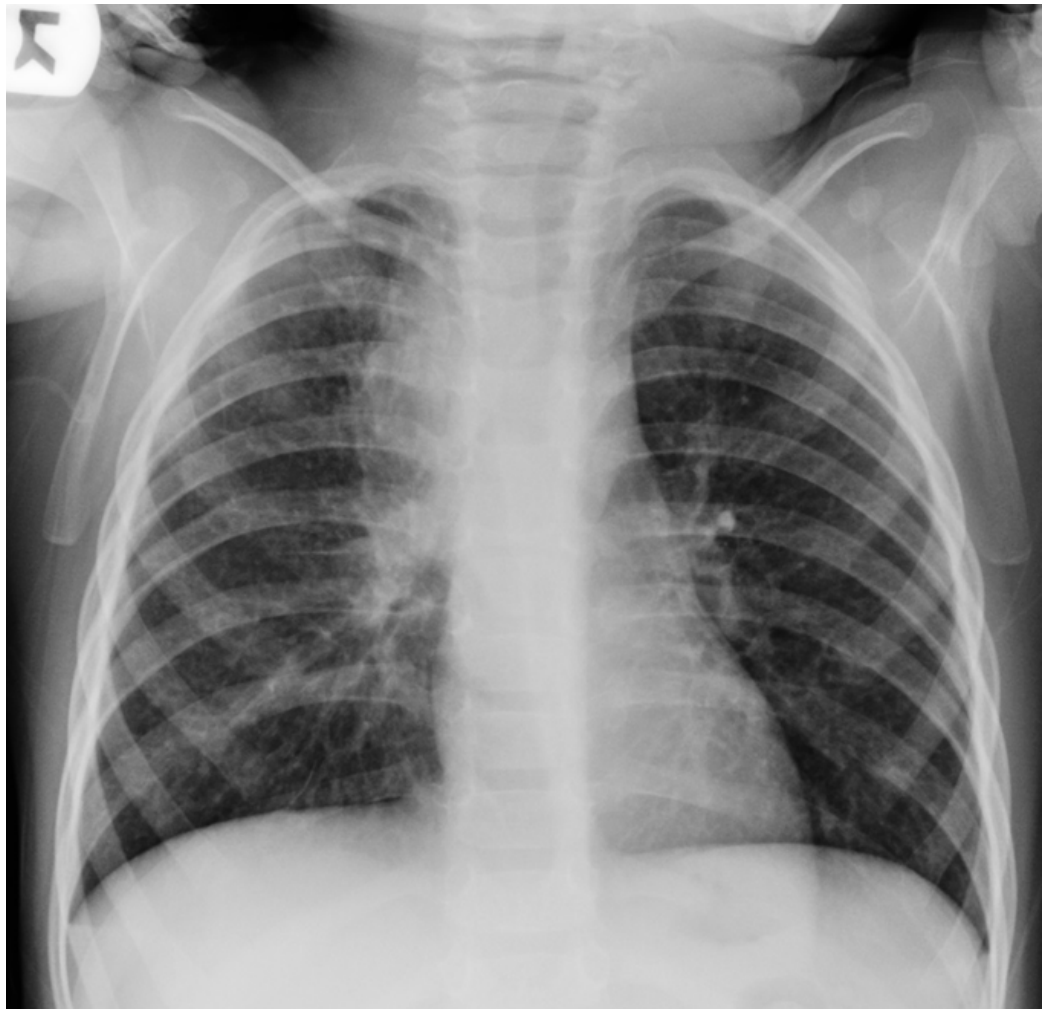
Peds in Review 2010;31:13

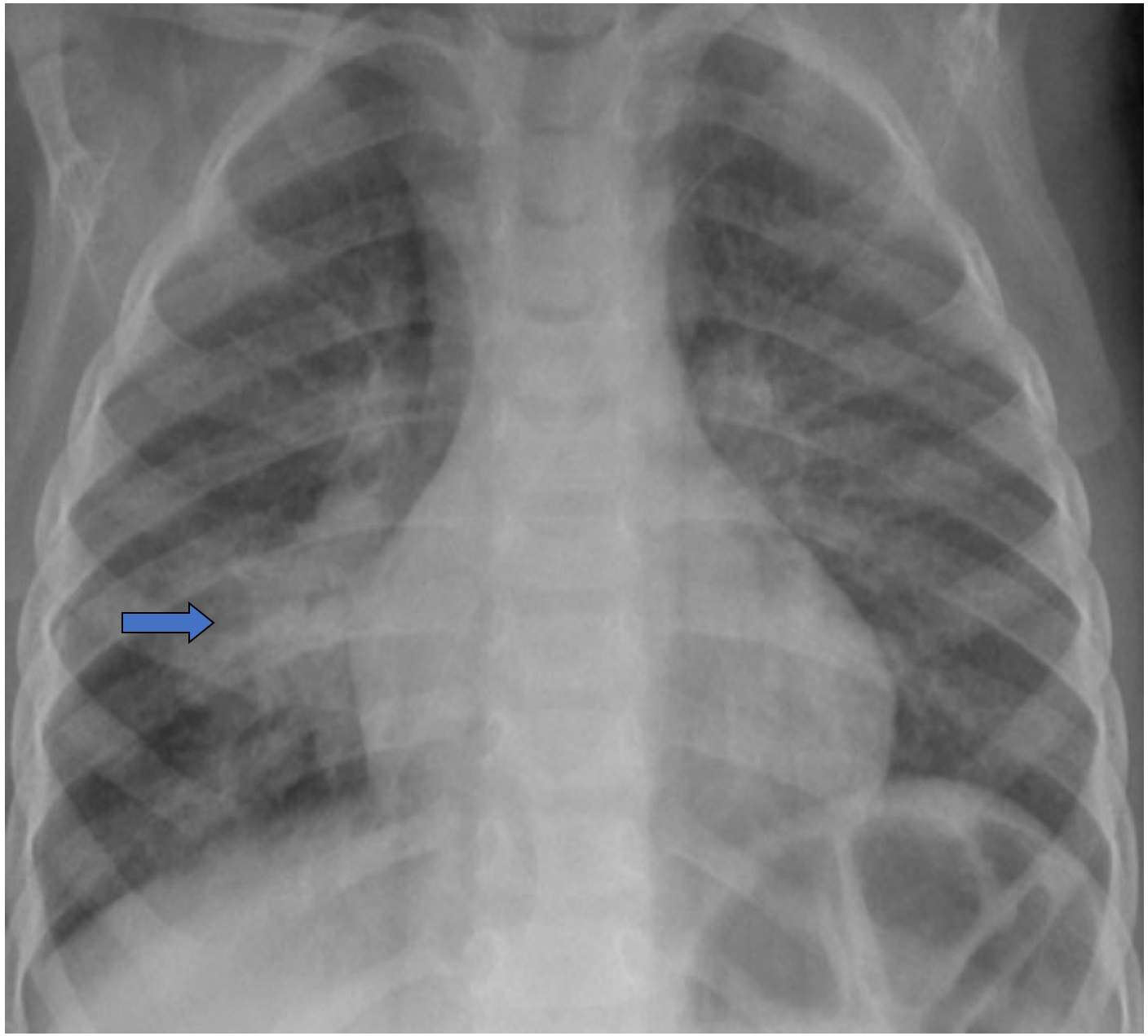
CXR Findings in Pediatric TB

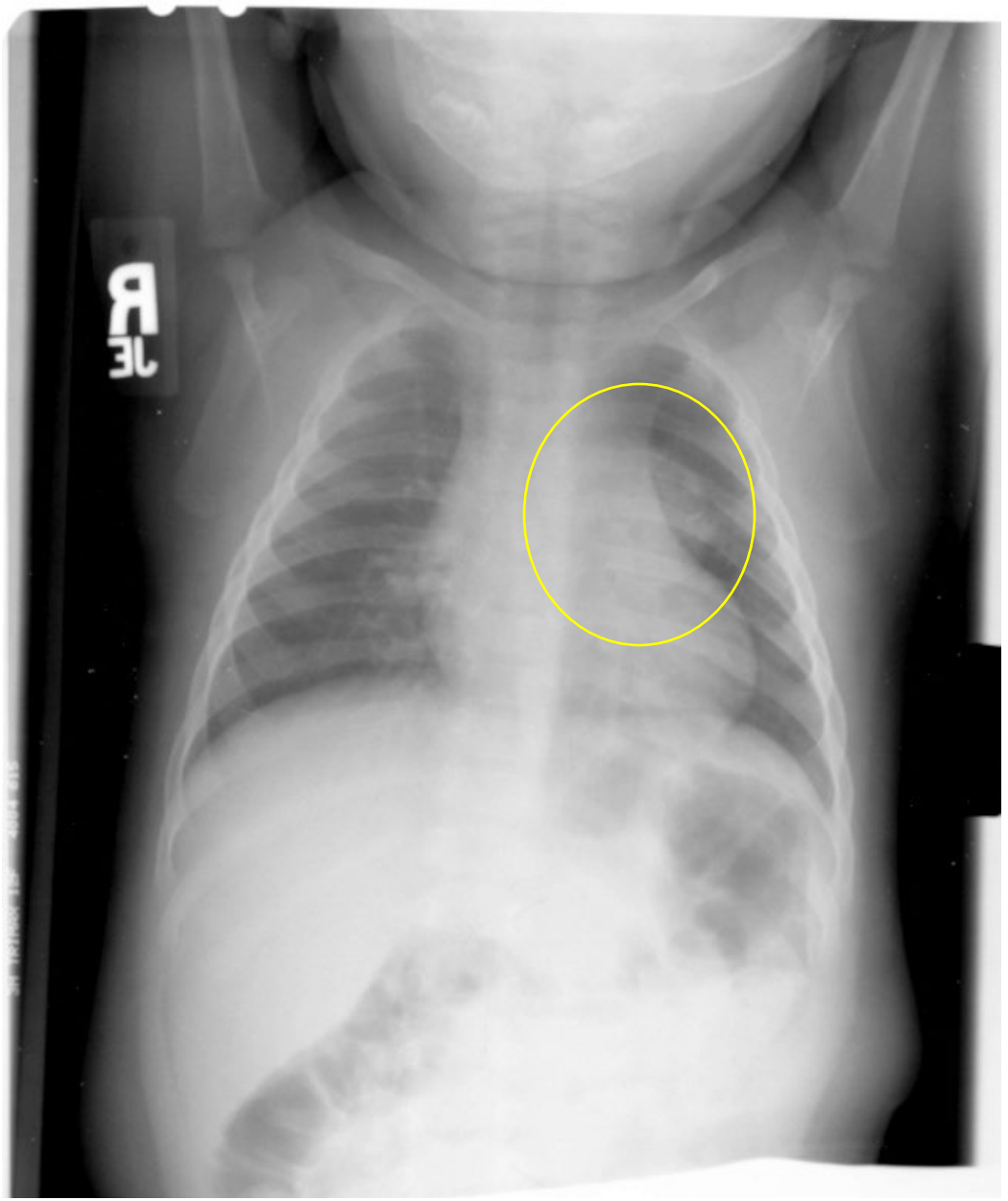
- Hilar or mediastinal adenopathy
- Segmental/lobar infiltrates
- Calcifications (seen in 75-80% of children with pulmonary TB)
- Miliary disease
- Pleural effusions

15% of patients with TB disease will have normal CXRs

Intrathoracic Lymphadenopathy





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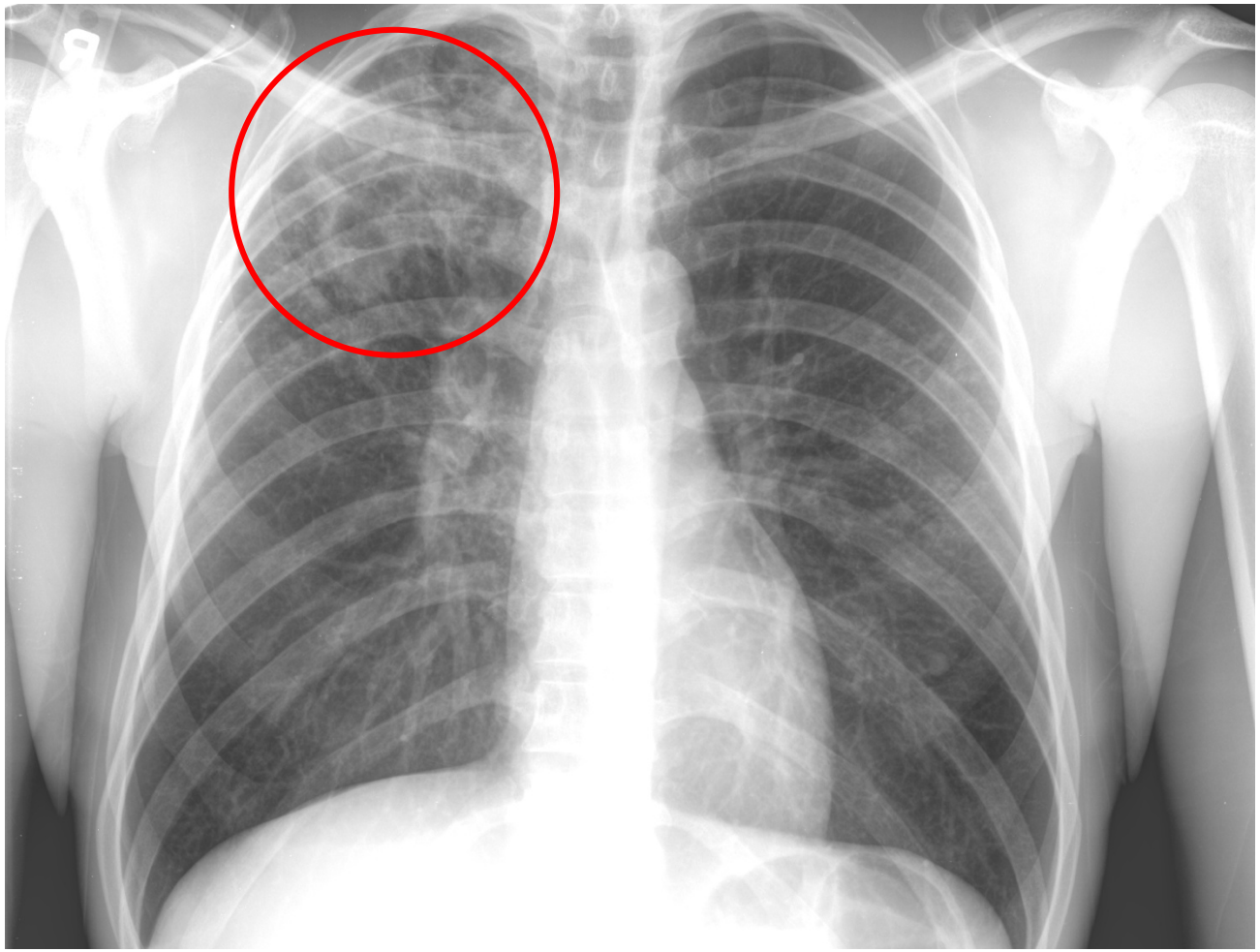
Cavitary Lesions



W.C. 2005

Unique Diagnostic 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

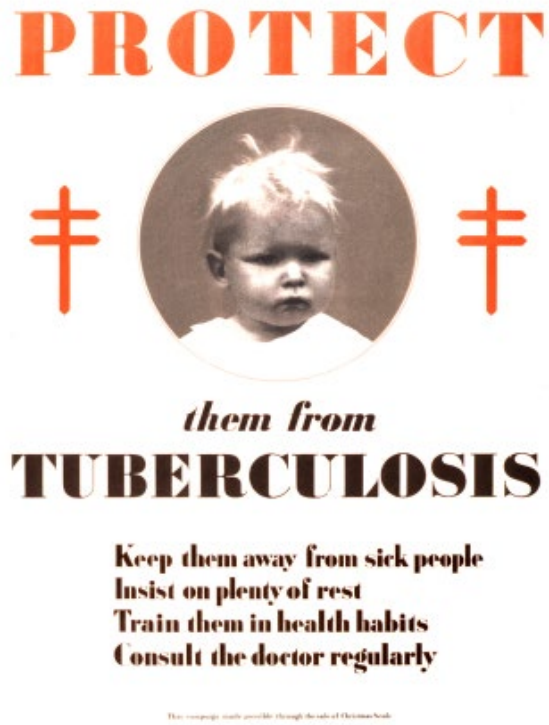
Treating Tuberculosis in Children

Why treat exposed children?

- Very high rate of infection
- Takes up to 3 months for the skin test to turn positive
- U.S. studies – 10% to 20% of childhood TB cases can be prevented if children exposed in a household receive isoniazid
- WHO standards – children <5 years old in a TB household should be treated

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
- **Window prophylaxis recommended:**
  - For children < 5 yrs of age
  - Immunosuppressed patients
  - Patients on tumor necrosis factor-alpha blockers or other biologic
  - May prevent progression to disease during window period
- Repeat TST 8-10 wks after exposure
- May stop medication if 2nd TST negative < 5mm in immunocompetent patients



Treating TB infection

- 3HP (approved for children ≥ 2 years old:

  INH:

  15 mg/kg rounded up to the nearest 50 or 100 mg
  20-30 mg/kg rounded up **ages 2-11 y/o** maximum 900 mg

  RPT:

  10.0–14.0 kg 300 mg
  14.1–25.0 kg 450 mg
  25.1–32.0 kg 600 mg
  32.1–49.9 kg 750 mg
  ≥ 50.0 kg 900 mg maximum

- Rifampin x 4 months [4R]
  - 10-20 mg/kg daily dose ages 2 years and older (max 600 mg)
  - 20-30 mg/kg daily
    - Infants and toddlers
    - Immunosuppressed
    - Disseminated disease, ESPECIALLY meningitis

- Isoniazid (INH) x 6-9 months [6H/9H]
  - 10-15 mg/kg single daily dose
  - 20-30 mg/kg twice weekly given by DOT
  - Duration: 9 months

- INH + rifampin [3HR] x 3 months

Pearls of Wisdom for Treating TB Infection in children

- Use INH suspension only in children ≤ 5 kg
- Compliance with 9 months of INH averages 50% - be vigilant and skeptical, consider shorter course treatments
- Use DOPT for: recent contacts, infants, immune compromised
- When children aren't tolerating treatment, the problem is more often with the parent than the child
- Routine LFTs only for: other liver toxic drugs, liver disease, signs or symptoms of hepatitis

Directly Observed Therapy for Tuberculosis

- means a dispassionate 3rd party is actually present when medications are taken with every dose
- “standard of care” in U.S. for treating tuberculosis disease
- desirable for high-risk infections - newborns and infants, household contacts, HIV - infected or immune compromised

INCREASING ADHERENCE FOR LATENT TUBERCULOSIS INFECTION THERAPY WITH HEALTH DEPARTMENT–ADMINISTERED THERAPY

Andrea T. Cruz, MD, MPH,† and Jeffrey R. Starke, MD**

Abstract: Therapy is almost universally recommended for children with latent tuberculosis infection, but long courses of therapy can decrease adherence to drug therapy. The only variable positively associated with adherence to latent tuberculosis infection therapy in our population was health department–assisted administration of drugs (odds ratio, 7.2; 95% confidence interval, 3.8–13.8).

The Pediatric Infectious Disease Journal 2012 31: 2

TABLE 1. Characteristics of the Study Population

Variable	Subcategory	All Patients N (%)*†	Completed N (%)*‡	Defaulted N (%)*‡
Total		248	186 (75%)	62 (25%)
How medications administered	Self-medicated	99 (40%)	49 (49%)	50 (51%)
	ESAT	20 (8%)	17 (85%)	3 (15%)
	DOPT	129 (52%)	120 (93%)	9 (7%)
	ESAT or DOPT	149 (60%)	137 (92%)	12 (8%)

Therapy for TB Disease

- Start 4-drug therapy (a change from 2006 Red Book)
  - INH, rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB); INH/RIF are the backbone of therapy
- Use PZA only during 1st 2 months for susceptible TB
  - This is your 'shortening agent': consolidate from 9 to 6 months of therapy
- Stop EMB once culture results known, if have pan-susceptible TB
  - This is your insurance in case you have drug-resistant TB
- Anticipate minimum 6-month therapy, may need to extend it to longer periods, especially for extensive, CNS or bone disease
- Can dose BIW or TIW after first 2 weeks of daily dosing
- ***Always*** administered by directly observed therapy (DOT)

2018 Red Book

Monitoring Children on TB Treatment

- Risk of drug toxicity very low
- Monitor clinical signs
  - regular clinical visits (4-6 wks)
  - patient education
  - Weigh at least monthly and increase dose as needed
- Routine blood work not necessary unless
  - symptoms
  - risk factors for toxicity
- Monitor and reinforce adherence

Monitoring Children on TB Treatment
(cont.)

- When to follow up CXR's for pulmonary TB
  - Beginning and end of therapy
  - If clinical change
- Adequate nutrition
- Routine vitamin B_6 not necessary except breast-feeding, pregnant adolescents, poor diet
  - Vitamin B_6 doses 1-2 mg/kg
- Completion of therapy certificate

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
  - Can get worse before improvement over months to years
- Meningitis
  - Inflammation increases initially with treatment
  - Steroids crucial for 1st month
  - Hospitalization recommended until clinically stable or improving

When do we worry about contagiousness?

- Older adolescents
- Children with certain findings on CXR
- Producing sputum
- Any draining skin lesions

Children with tuberculosis are rarely contagious, but their caregivers may be. Only 7 (12%) of 59 children were potentially contagious, and 10 (17%) were accompanied by contagious adults. Screening caregivers was more cost-effective than performing employee contact investigations, with one-sixteenth the cost ($5,470 vs $88,323) and requiring screening of 35 times fewer persons.

Infect Control Hosp Epidemiol 2011;32(2):188-190

Infect Control Hosp Epidemiol 2011;32:188

Questions?

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