

# **Tuberculosis in Children and Adolescents 2011- Part I**

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NJMS Global Tuberculosis Institute**

**TB Intensive Workshop  
April 12-14, 2011**





# **Tuberculosis in Children and Adolescents 2011**

- **Classification system for tuberculosis**
- **Transmission of tuberculosis to children and its significance**
- **Epidemiology: Global, national, and local**
- **Public Health Aspects of Tuberculosis Control**
  - Targeted Tuberculin Skin Testing: Use of a Risk Assessment Questionnaire
  - Contact Investigations
- **Management of the TB-exposed child**
- **Latent TB Infection: Diagnosis and treatment**
  - Interferon-gamma release assays (IGRAs)
  - BCG vaccine
- **TB disease: Diagnosis and treatment**
- **Special considerations in immigrant and adopted children**



# Classification System for TB

Class	Type	Description
0	No TB exposure Not infected	No history of exposure Negative reaction to tuberculin skin test
1	TB exposure No evidence of infection	History of exposure Negative reaction to tuberculin skin test
2	TB infection No disease	Positive reaction to tuberculin skin test Negative bacteriologic studies (if done) No clinical, bacteriological, or radiographic evidence of active TB
3	TB, clinically active	<i>M. tuberculosis</i> cultured (if done) Clinical, bacteriological, or radiographic evidence of current disease
4	TB Not clinically active	History of episode(s) of TB <b>or</b> Abnormal but stable radiographic findings Positive reaction to the tuberculin skin test Negative bacteriologic studies (if done) <b>and</b> No clinical or radiographic evidence of current disease
5	TB suspected	Diagnosis pending

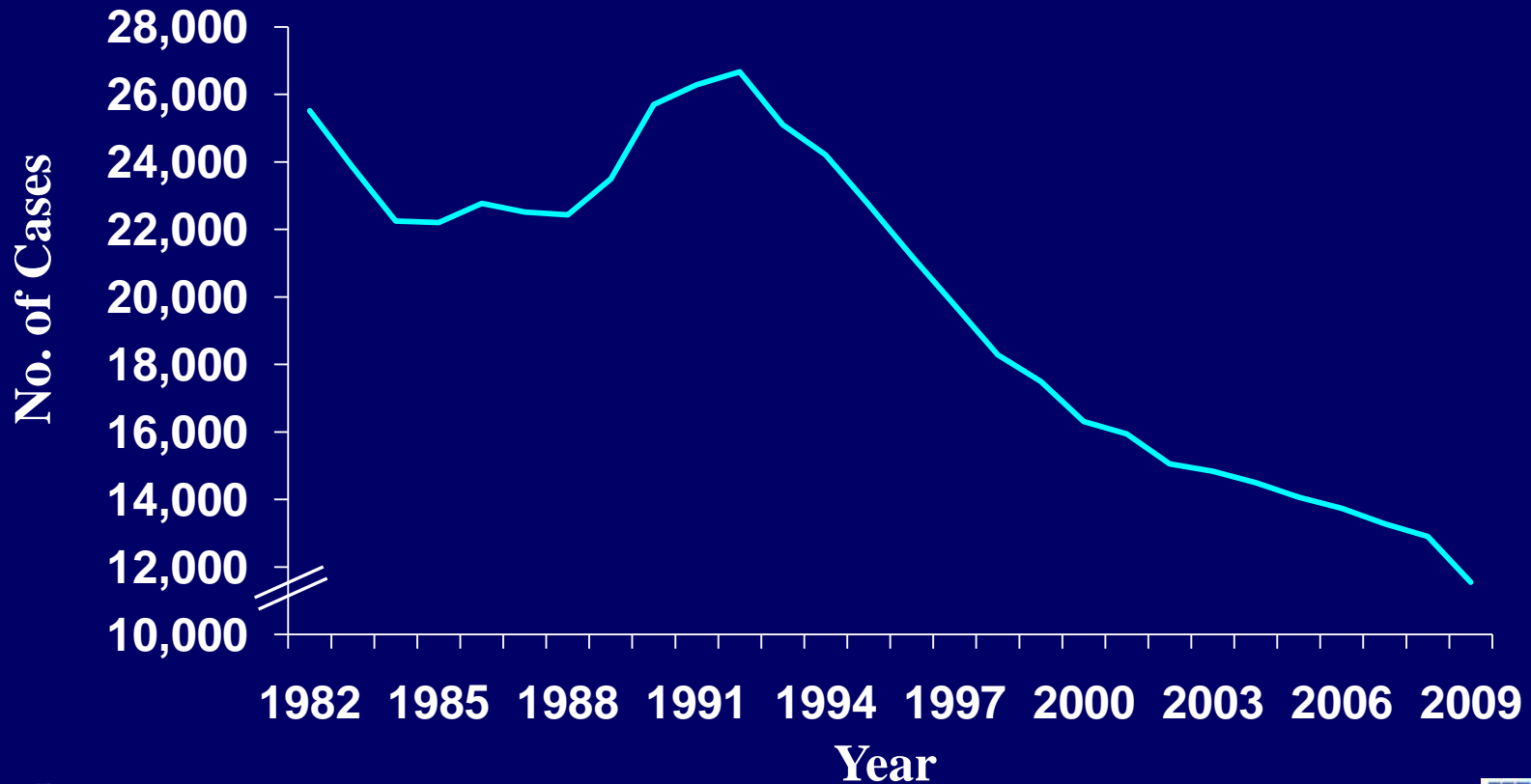


# Epidemiology

- **Tuberculosis remains the leading infectious disease in the world**
  - Approximately 1/3 of the world's population (>1.9 billion people) is infected with *M. tuberculosis*
  - In the 1990s:
    - 90 million new cases
    - 30 million deaths
  - Among children <15 years of age:
    - Approximately 13 million cases
    - 5 million deaths

Dye C, et al. JAMA 1999;282:677

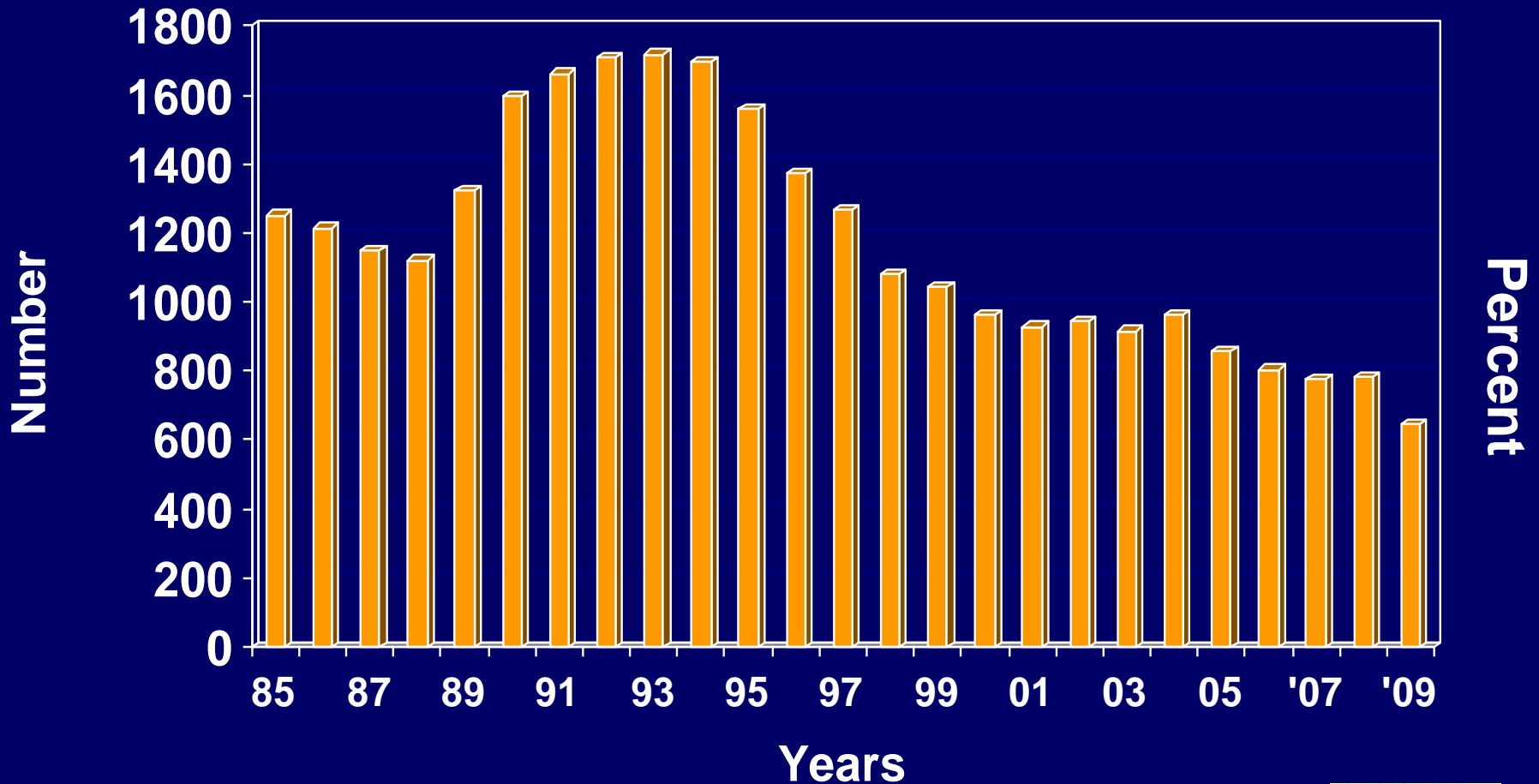
# Reported TB Cases\* United States, 1982–2009



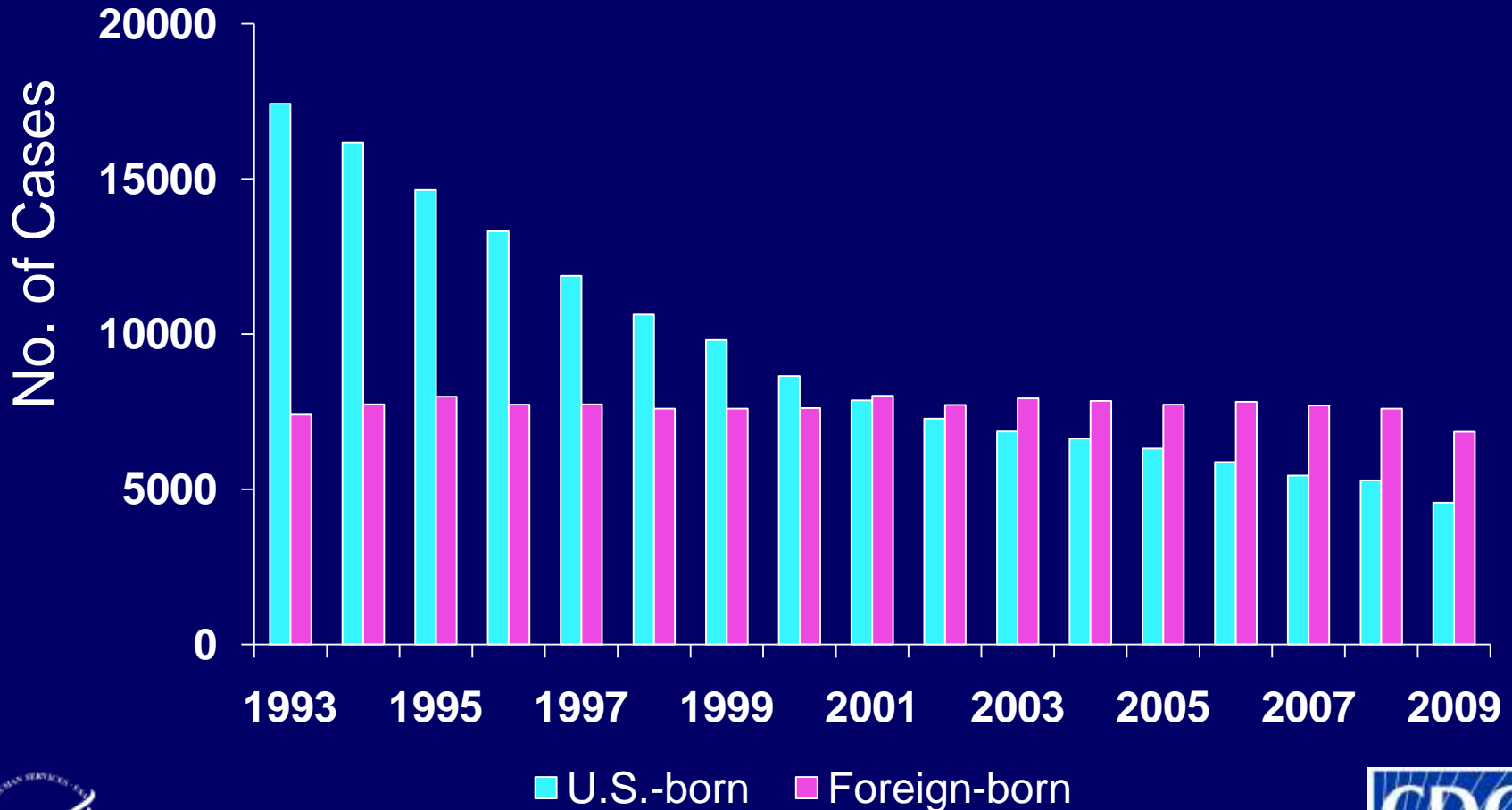
\*Updated as of July 1, 2010.



# Number and Percent of All TB Cases Occurring Among Children <15 Years



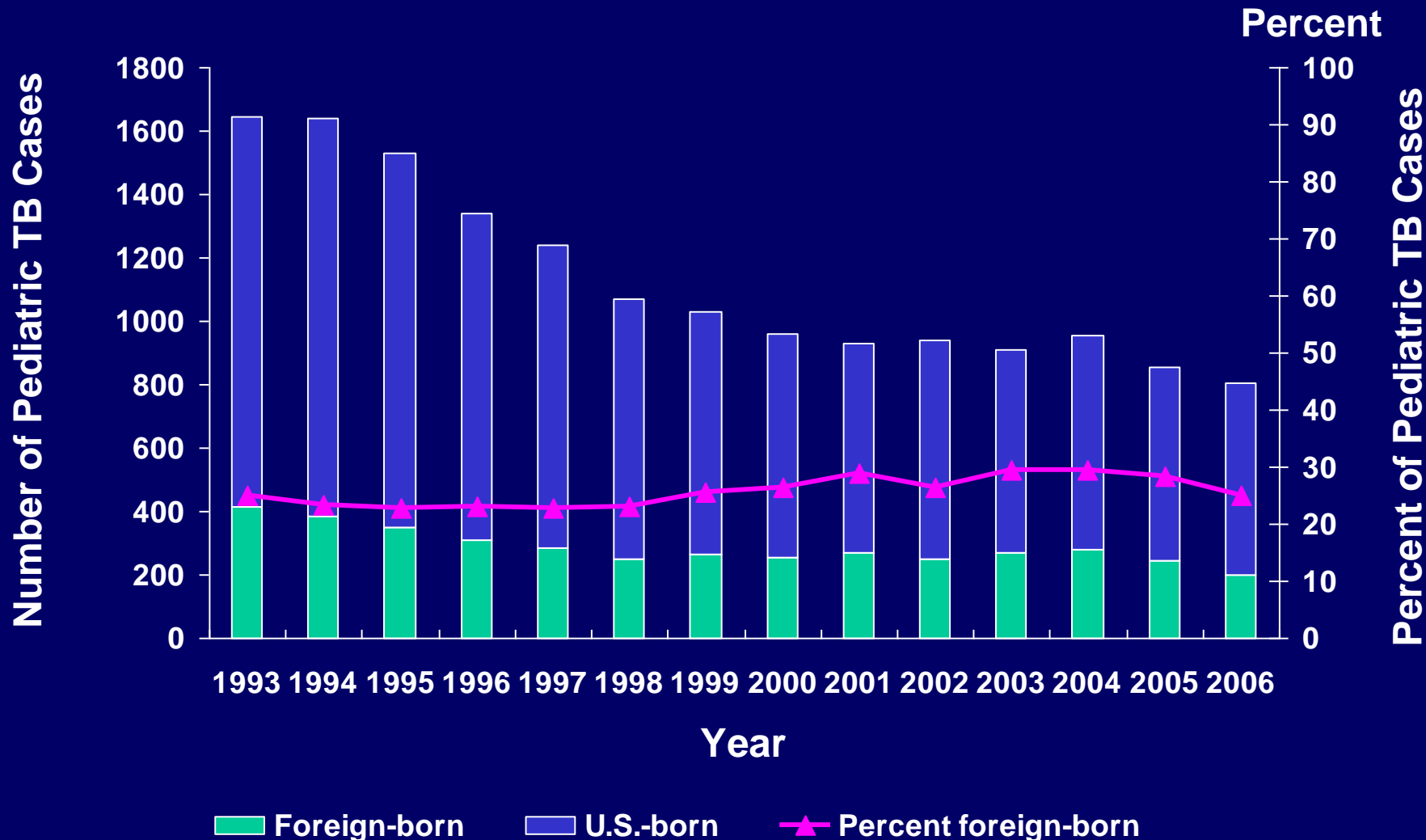
# Number of TB Cases in U.S.-born vs. Foreign-born Persons United States, 1993–2009\*



\*Updated as of July 1, 2010.



# Number and Percent Foreign-born Pediatric TB Cases, 1993–2006







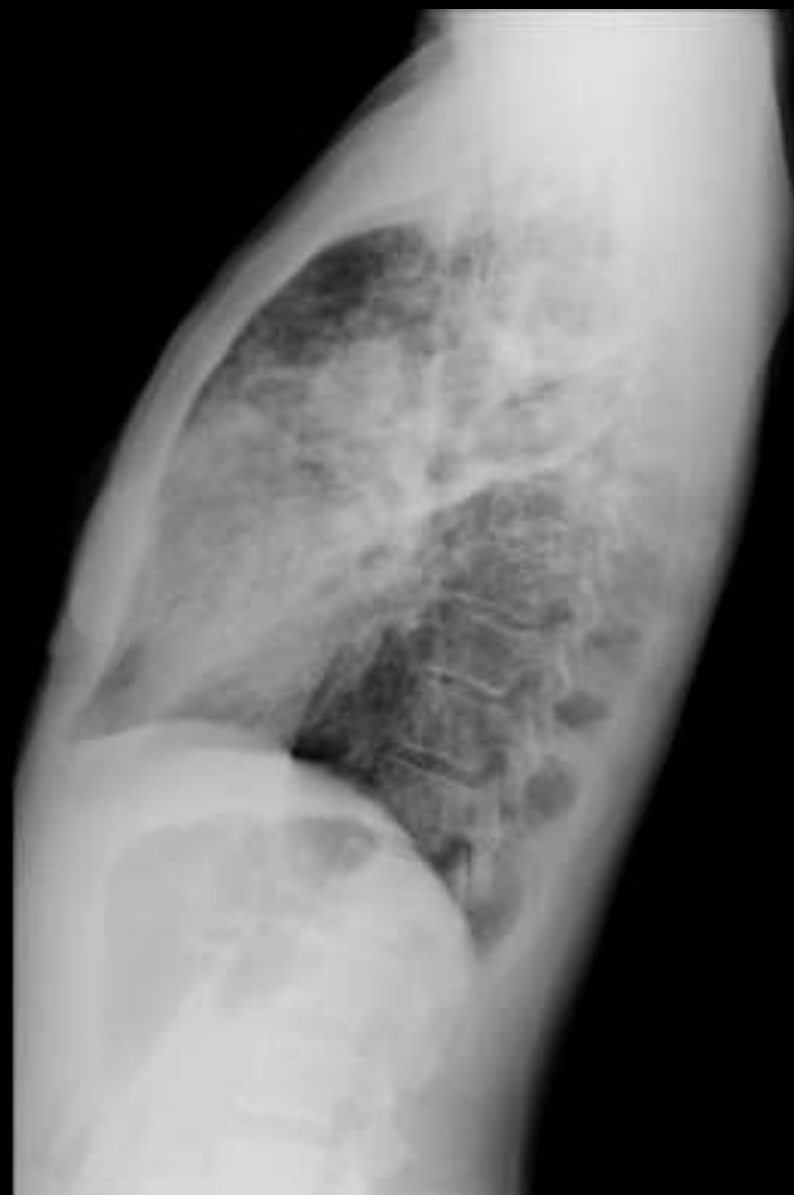
# **Epidemiology: United States**

- **Case rates for all ages are higher in urban, low-income areas, and in nonwhite racial and ethnic minorities**
- **Specific groups with high LTBI and TB disease rates:**
  - Immigrants and refugees from high-prevalence regions (Asia, Africa, Latin America, countries of the former Soviet Union)
  - International adoptees
  - Travelers to countries with high-prevalence
  - Homeless people
  - Residents of correctional facilities

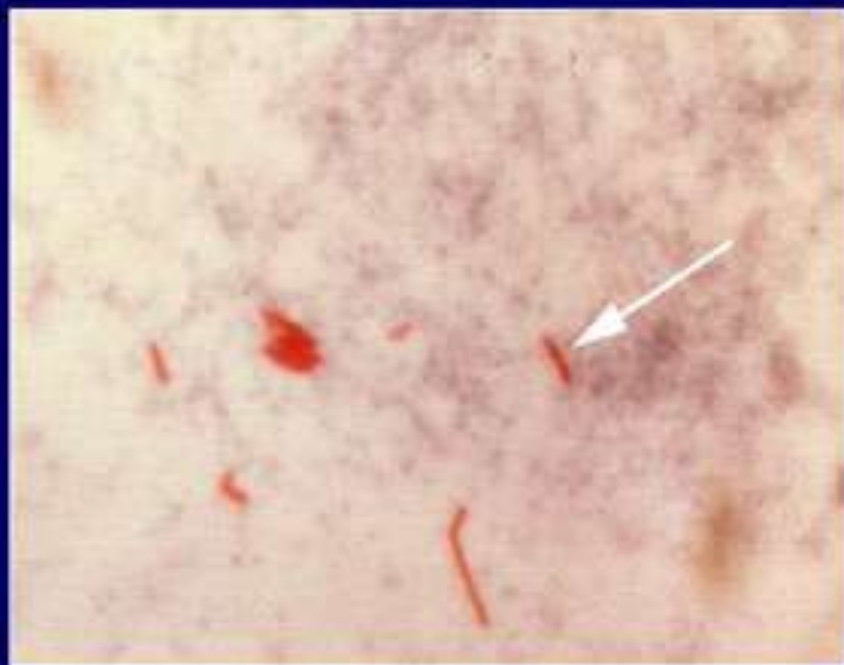


# **Transmission of *M. tuberculosis* to Children**

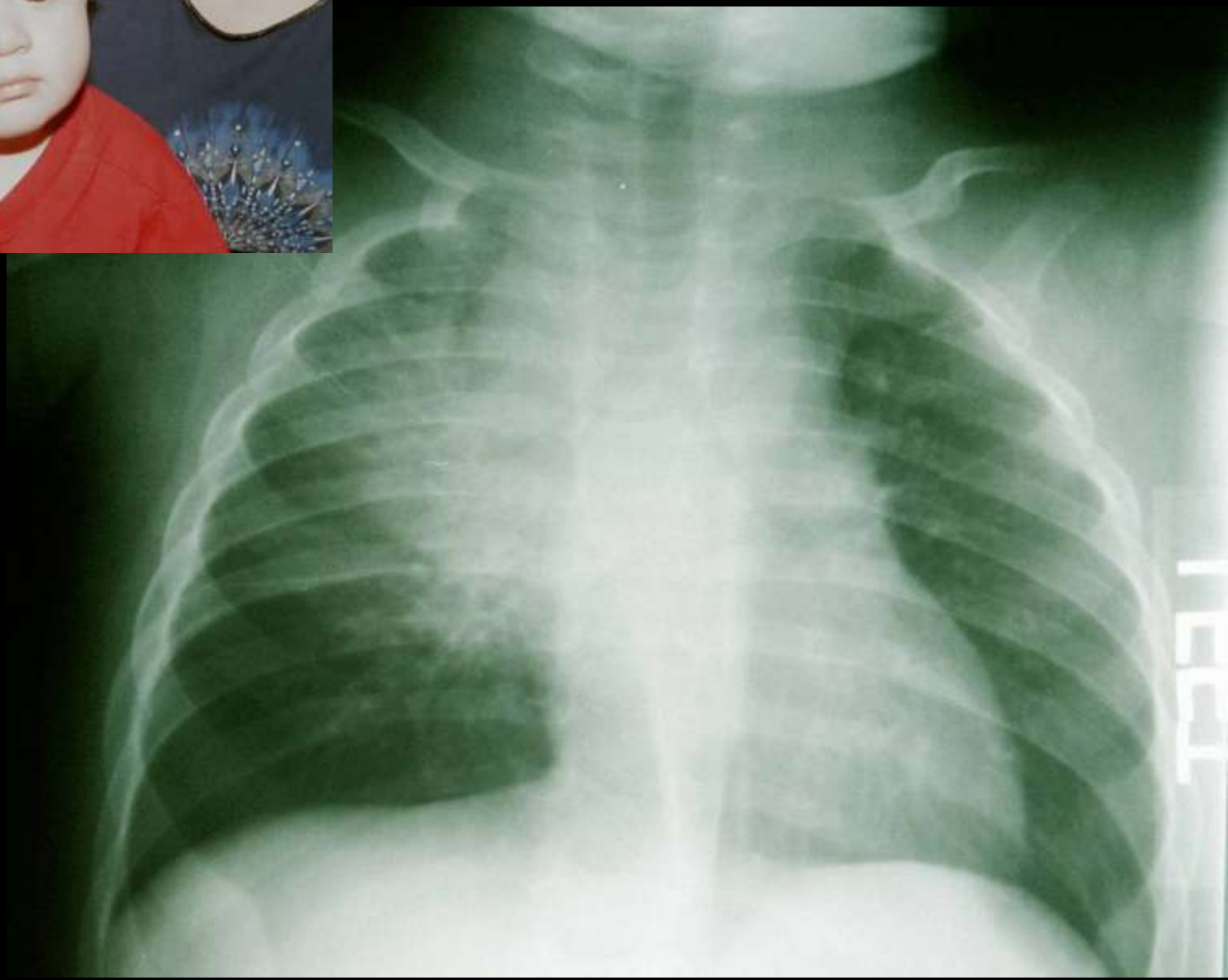
- **Children are usually infected by an adult or adolescent in the immediate household**
- **Casual extra-familial contact is less often the source of infection**
- **Children rarely infect other children or adults:**
  - Tubercle bacilli are relatively sparse in secretions
  - Children with pulmonary TB rarely cough
  - Cough, when present, lacks the force needed to aerosolize bacilli



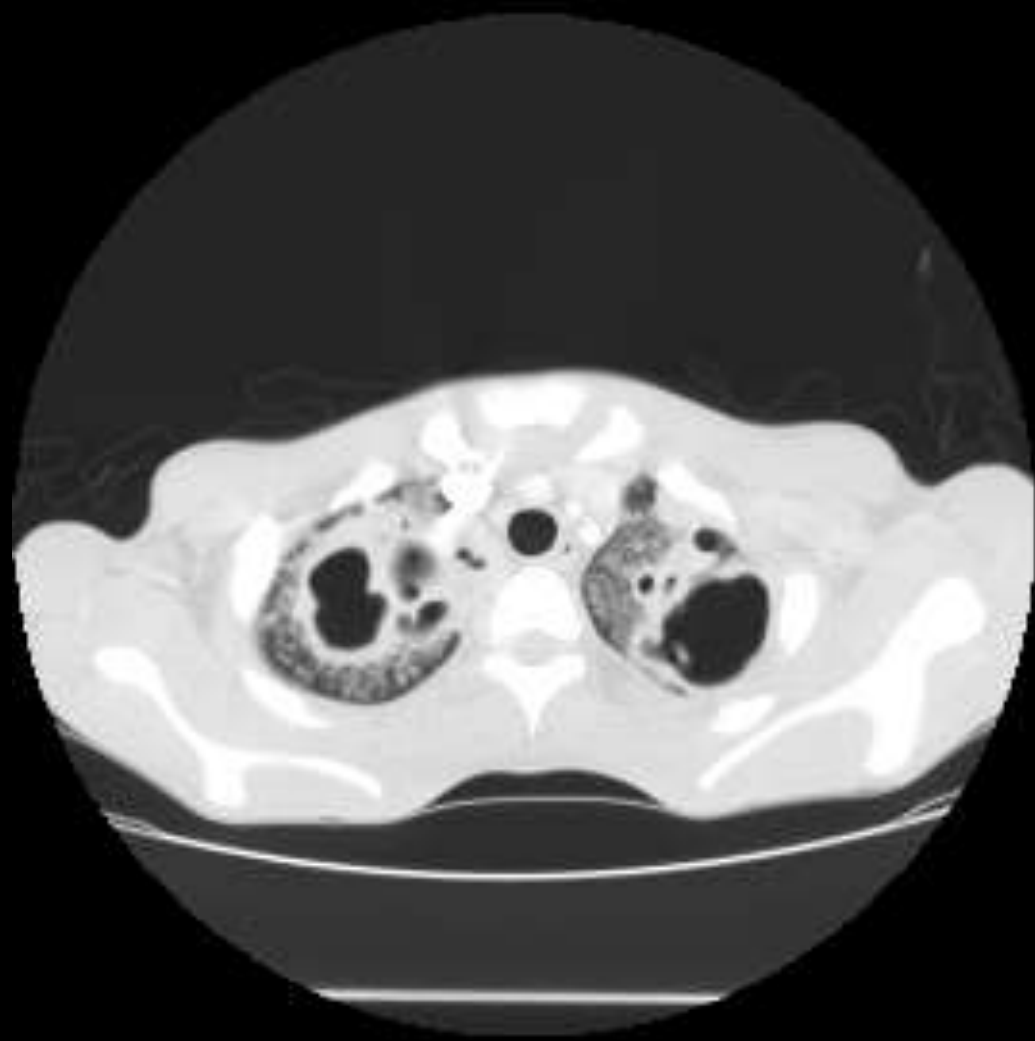
## AFB smear



AFB (shown in red) are tubercle bacilli









# Increased Risk of Progression of LTBI to Tuberculosis Disease

- **Age groups:**
  - Infants and young children
  - Post pubertal adolescents
- **Recent infection:**
  - Highest risk in first 6 months after infection
  - Remains high for 2 years
- **Recent immigration**
- **Immunodeficiency:**
  - HIV infection, Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, malnutrition
  - Immunosuppressive drugs:
    - Prolonged or high-dose corticosteroid therapy
    - Chemotherapy
    - Tumor necrosis factor (TNF-alpha) antagonists used to treat arthritis, Crohn's disease: Infliximab, etanercept, adalimumab, golimumab





# **Risk of Progression to TB Disease**

- **Immunocompetent adults: 5-10% lifetime risk of developing disease after infection**
- **Adults with TB infection and HIV infection: 5-10% annual risk of developing disease**
- **Children and the risk of TB disease:**



# Risk of Tuberculosis Disease by Age

	Risk of disease following primary infection			Comments
	Disseminated tuberculosis/ tuberculosis meningitis	Pulmonary tuberculosis	No disease	
<1 years	10-20%	30-40%	50%	High rates of morbidity and mortality
1-2 years	2-5%	10-20%	75-80%	High rates of morbidity and mortality
2-5 years	0.5%	5%	95%	..
5-10 years	<0.5%	2%	98%	"Safe school years"
>10 years	<0.5%	10-20%	80-90%	Effusions or adult-type pulmonary disease

Adapted from reference 30.

**Table 1:** Risk of pulmonary and extrapulmonary disease in children following infection with *Mycobacterium tuberculosis*



# **Significance of Tuberculosis in Children**

- **Public Health: Diagnosis of LTBI or tuberculosis disease in a child is considered a “SENTINEL PUBLIC HEALTH EVENT” usually representing recent transmission of TB within a community**
- **Personal Health: High rates of morbidity and mortality**



# **Control of Tuberculosis in the United States**

- **Case finding and treatment**
- **Contact investigations**
  - The most reliable TB control program is based upon aggressive and expedient contact investigations, rather than routine screening of large populations
  - Can be complex and may require lots of detective work
- **Targeted testing with tuberculin skin test or IGRA**

# Concentric Circle Principle in TB Control

## Identifying Contacts at Risk of Exposure

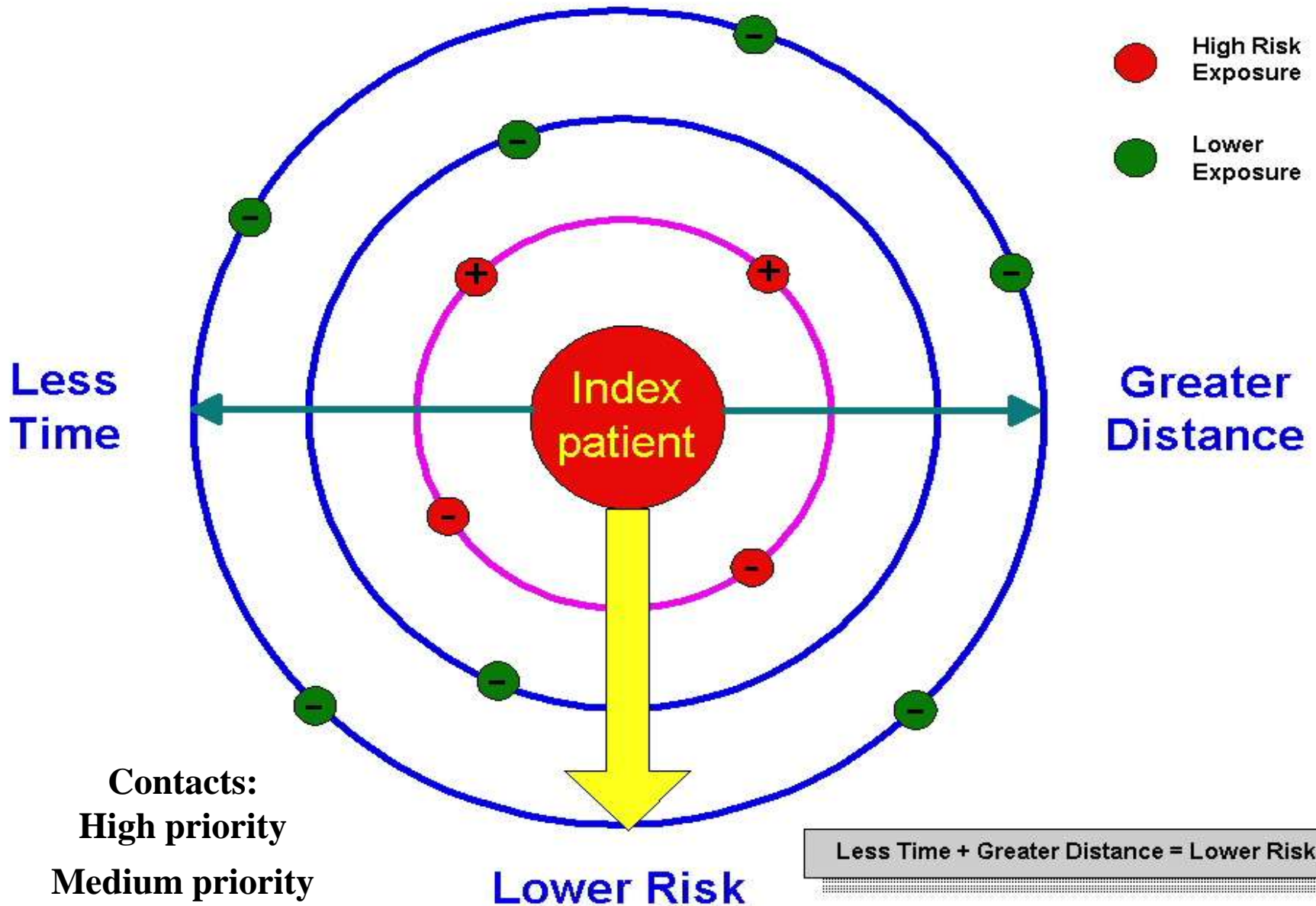
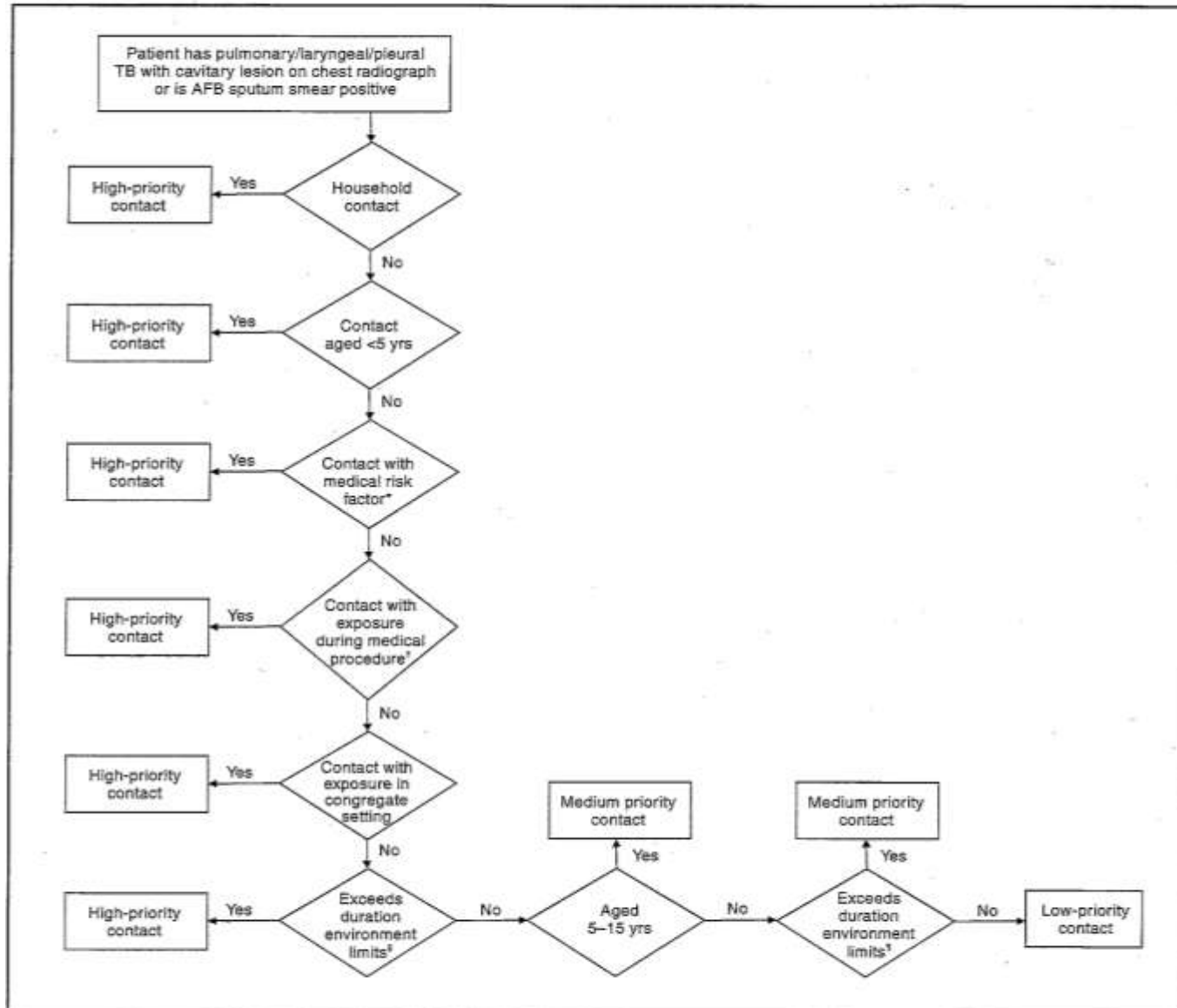


FIGURE 2. Prioritization of contacts exposed to persons with acid-fast bacilli (AFB) sputum smear-positive or cavitary tuberculosis (TB) cases



\* Human immunodeficiency virus or other medical risk factor.

† Bronchoscopy, sputum induction, or autopsy.

‡ Exposure exceeds duration/environment limits per unit time established by the health department for high-priority contacts.

§ Exposure exceeds duration/environment limits per unit time established by the health department for medium-priority contacts.



# **Prevention of TB in Children: Potential Missed Opportunities**

- Failure to find and appropriately manage adult source cases (Case finding)
- Delay in reporting the initial diagnosis of TB
- **Contact investigation interview failure**
- **Delay in evaluation of exposed children**
- **Failure to completely evaluate exposed children**
- **Failure to prescribe INH “window prophylaxis”**
- Failure to maintain a contact under surveillance
- LTBI diagnosed; treatment not prescribed
- **Failure to complete treatment for LTBI**



# Tuberculosis Exposure in Children

- **History, PE, TST, CXR are done**
  - CXR is done regardless of TST result
- **IF the child is:**
  - Asymptomatic and physical examination is normal
  - TST is negative (<5 mm)
  - Chest X-ray is normal
- **AND IF <4 years of age START: Isoniazid (INH) 10 mg/kg (max., 300 mg) PO once daily**



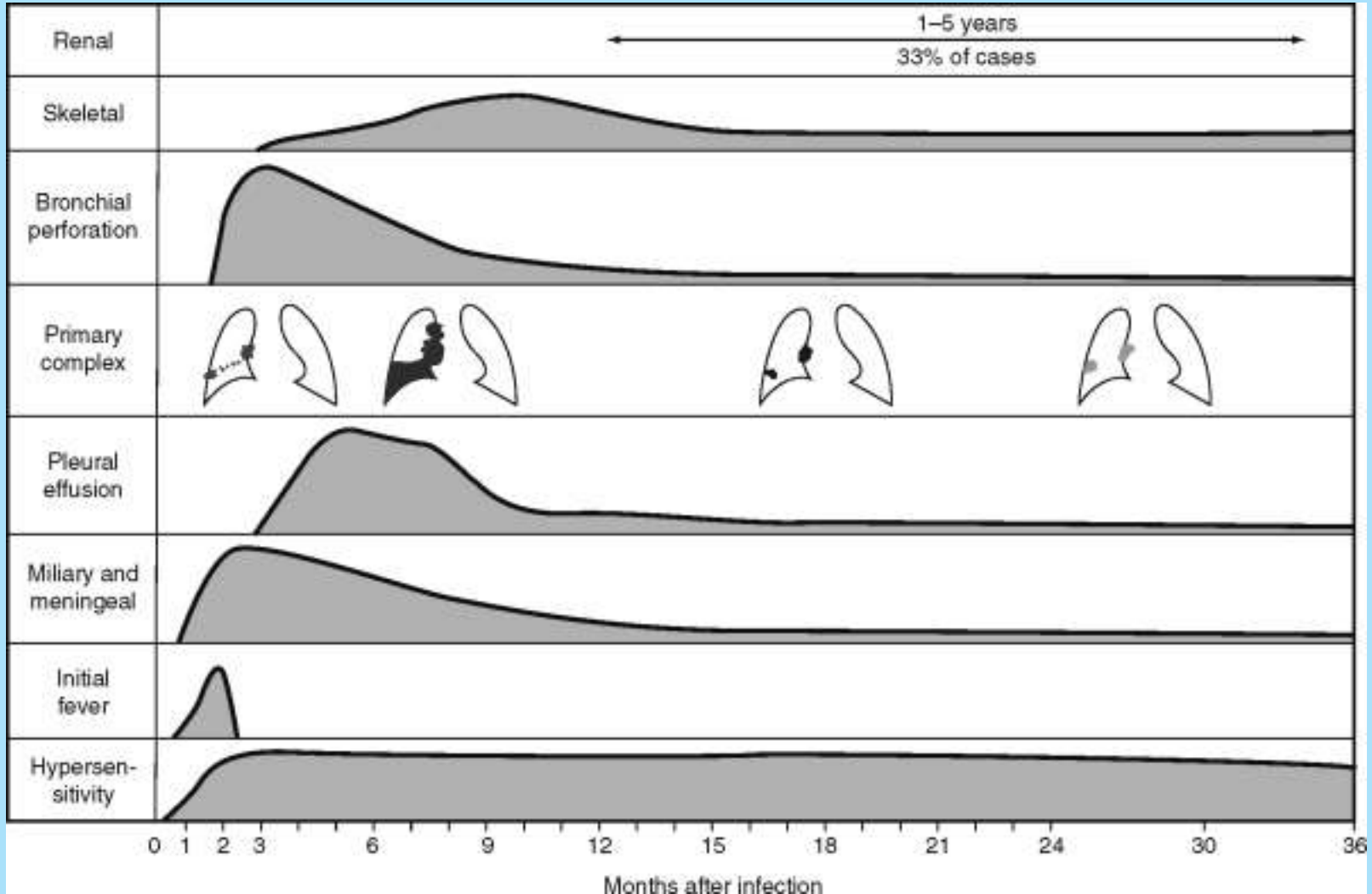


# **Tuberculosis Exposure in Children**

- **Why is INH given as “Window Prophylaxis” even if there is no evidence of TB infection or disease at the initial visit?**
  - May already be infected
  - Infection more likely to progress to disease
  - Infants and younger children are more likely to have disseminated disease or meningitis
- **TST repeated 8-10 weeks after contact broken with infectious adult:**
  - If TST (-), discontinue INH
  - If TST (+), re-evaluate child and treat accordingly



# Timetable of Tuberculosis in Children after Walgren





**4 yr old**  
**TST: 0.0 mm**





# **Case #1. Contact Investigations and TB-exposed Children: The Need for Speed or Nightmare in Daycare: Opportunities we almost missed but didn't....**



# **INDEX CASE (Patient)**

- **6/14 (Monday): 39 year-old female was admitted to a suburban New Jersey hospital with complaints of fever, decreased appetite, 23 lb weight loss, cough for 3 months, night sweats**
- **Chest radiographs were done**

GLG  
100





## **Background - 2**

- **6/19: Treatment initiated with RIPE**
- **6/21: Suspected case of pulmonary TB is verbally reported to local health department**





# Background – 3

- **6/21: LHD informed TB Control Program Manager of suspected case adding the following information**
  - Index case was a volunteer at a daycare center
  - Name, address and telephone of daycare center provided
  - Director of center is the sister of index case
  
- **Red flag day**
  - **Red flag # 1**



# Background – 4

- **6/21: Telephone call from TB Control Program Manager to director of daycare center who volunteered information that her aunt (“I know who this is...”) is diagnosed with suspected tuberculosis**
  - Purpose to schedule a meeting to discuss potential exposure to children and staff
    - Conduct on-site exposure assessment of center
    - Provide TB education to the director
    - Identify high-priority contacts during infectious period established at 3/17–6/14



## Background - 6

- **Near the conclusion of telephone call the following exchange occurred:**
  - Director: So, should my daughter be tested?
  - **TB Control:** Tell me about your daughter and how much exposure she had to your aunt.
  - Director: Not too much. She doesn't attend the daycare but we do spend some time socially (maybe 5 hours) together on the weekends going to the mall



# Background - 7

- **TB Control:** How old is your daughter?
- Director: 6 months
- **TB Control:** I'll make arrangements for your daughter to be tested tomorrow morning
- **TB Control:** By the way, how is your daughter feeling?
- Director: Well.... she was diagnosed with bronchitis a few weeks ago and is still coughing
  - **Red flag # 2**



## Background - 8

- **TB Control:** I'll make arrangements for your daughter to be tested *today* in your home and we will expect you to attend our pediatric clinic on Wednesday for skin test reading, chest x-ray and physician evaluation

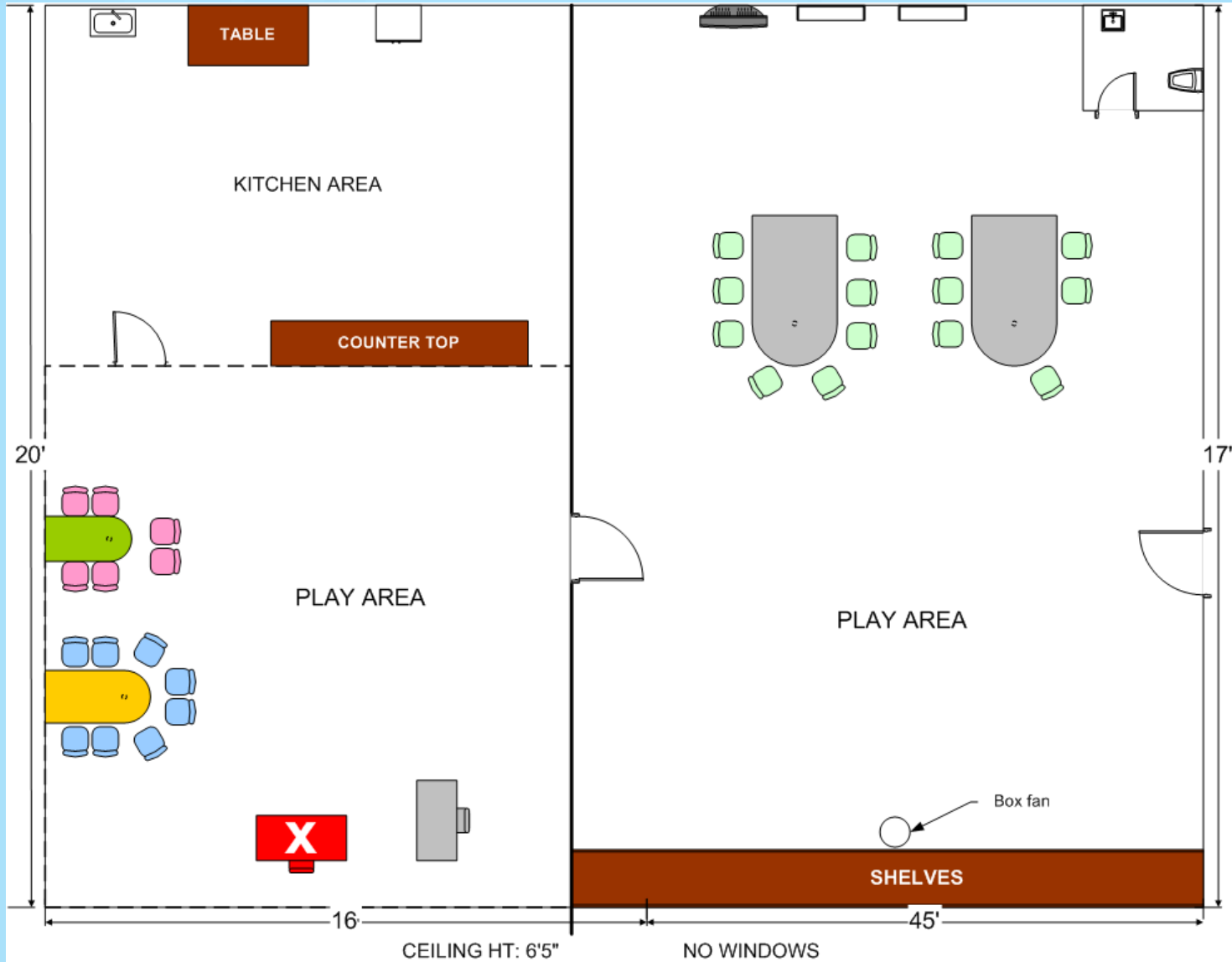


# Daycare Contact Investigation

- **6/23: On-site assessment of DCC conducted by TB controller:**
  - High priority contacts: 35
    - 30 children attend: All  $\leq 4$  years of age
    - 5 staff members: Adults and adolescents
  - The Daycare is in a church basement and the index case's desk is:



# Church Basement-Daycare





# Contact Investigation - 1

- **6/22: First of 4 TB interviews for contact investigation conducted by HCW in hospital**
  - Infectious period confirmed at 3/17-6/14
  - Index case may have spent more time in daycare than originally described
  - Index case indicates not much contact with children at daycare
  - 9 high-priority contacts identified
    - 2 household
    - 7 social
  - Despite director being aware of index patient's identity, written consent obtained by patient to release her identity





# **Contact Investigation - 2**

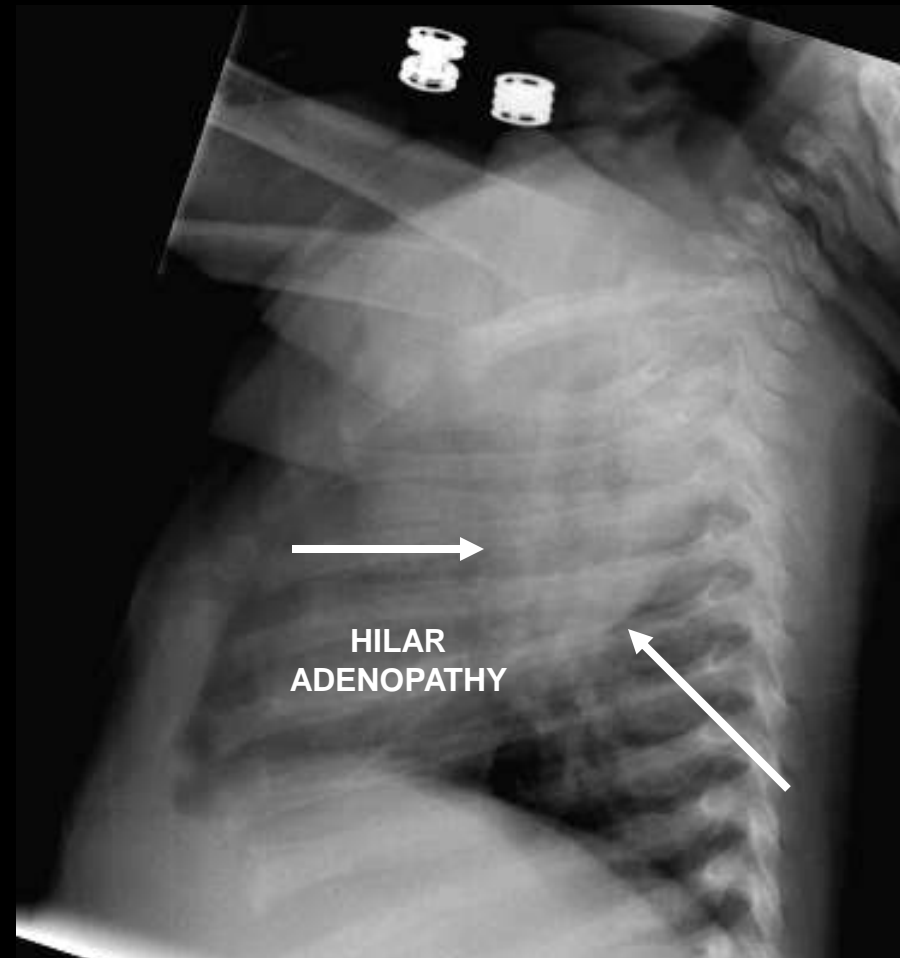
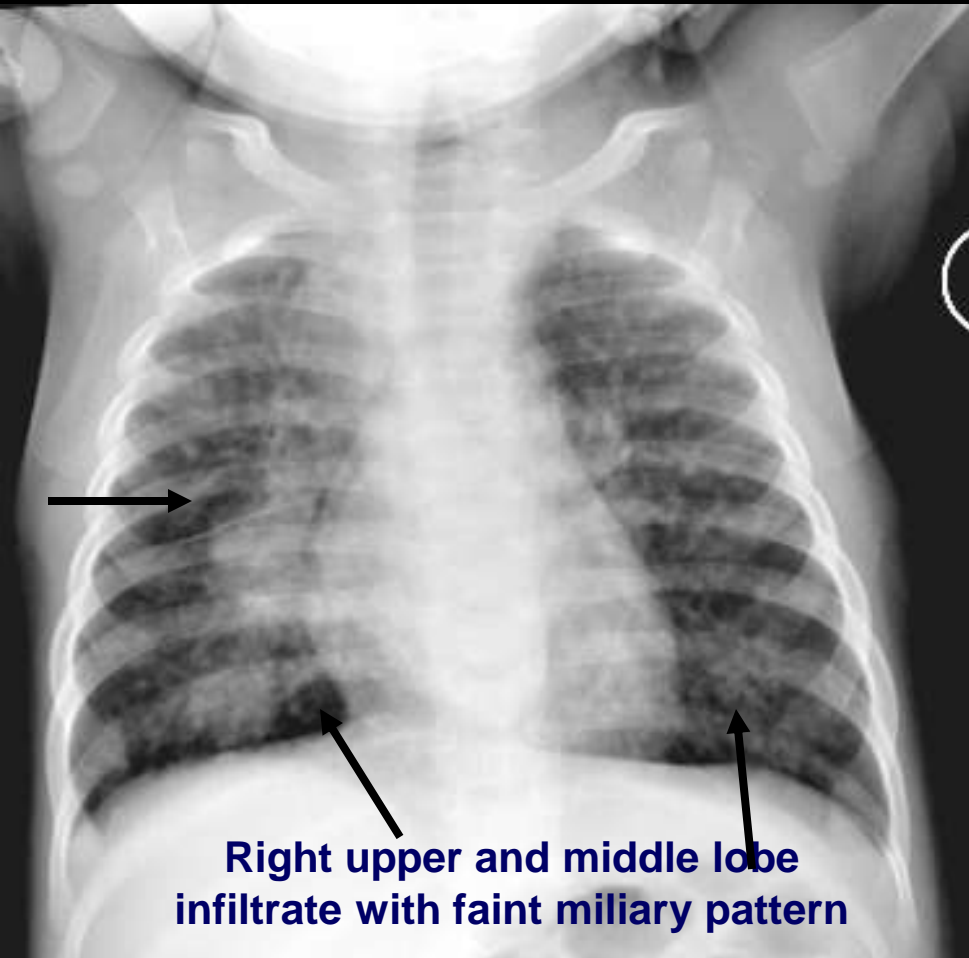
- **6/23: Initiation of on-site assessment of daycare center**
- **Written statement obtained by director indicating her obligation of respecting issues surrounding a patient's right to medical privacy**



# **Contact Investigation - 4**

- **6/23: 6 month old infant (director's daughter) evaluated at clinic**

# 6/23: 6 month old infant



TST: 20 mm

Admission PE: Somewhat lethargic

LP - 10 wbc's: nl protein, nl glucose;  
Gastric aspirates X3: (+) *M. tuberculosis*



# Contact Investigation - 5

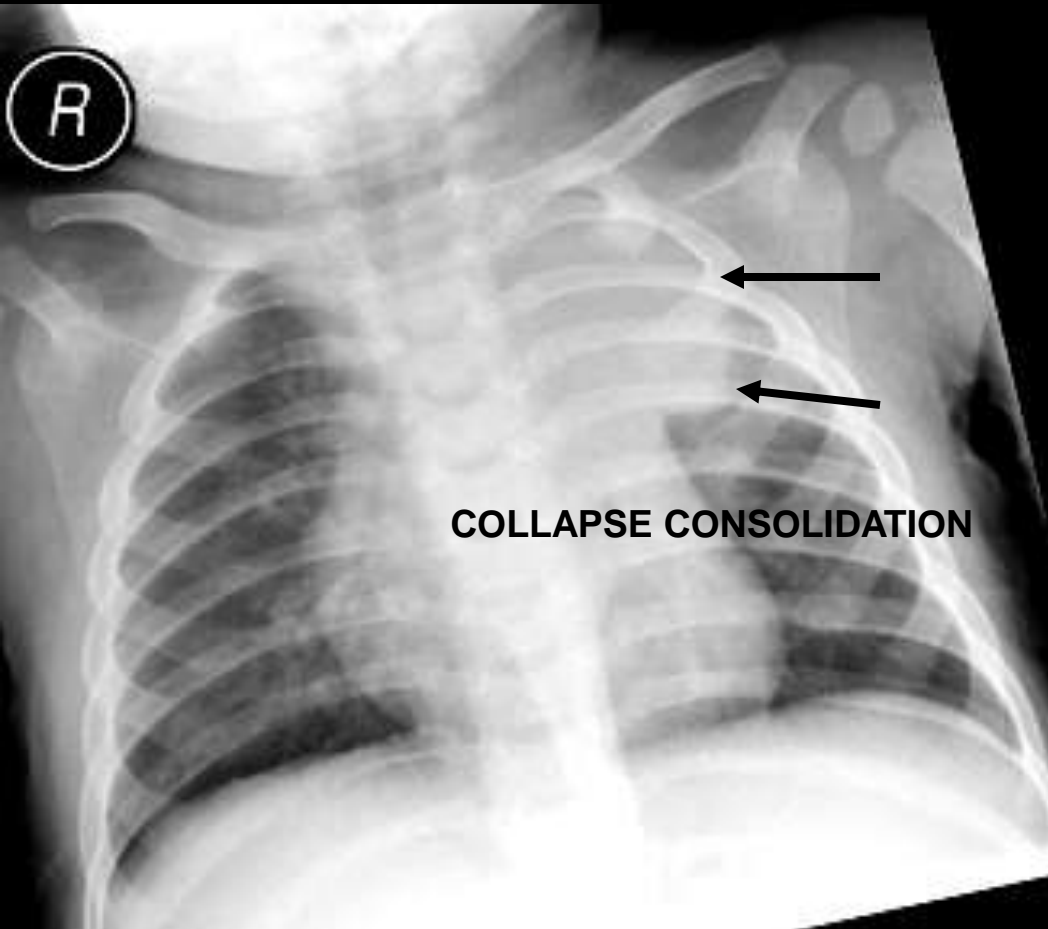
- **6/22-6/25: Process begins in collecting names and locating information of identified contacts in all exposure settings including household, social and workplace**
  - Notification process begins for testing
  - Education sessions provided to parents of daycare children
    - During these sessions it is learned that the 6 month old infant was at daycare center on regular basis



# Contact Investigation - 6

- **6/23: Field visit to social contact residence by HCW identifies a second 6 mo. old infant not named on initial interview**
  - 70 hours exposure per week during infectious period
  - Diagnosed with pneumonia 3 weeks ago
    - **Red flag # 3**
    - HCW & TB Control Program Manager consult with Pediatric Nurse Practitioner at clinic and infant is referred to ED, evaluated and admitted with diagnosis of suspected pulmonary TB

**2<sup>nd</sup> 6 month-old infant**



**TST: 17 mm**

**Gastric aspirates X3: (+) *M. tuberculosis***



# **Contact Investigation - 7**

- **6/29 - 6/30: TST administered on all 35 daycare contacts and chest x-ray taken on all 30 children from daycare**
- **6 extra clinic sessions scheduled at clinic in addition to 3 evening clinics at local health department to accommodate the medical evaluations of the 30 children**

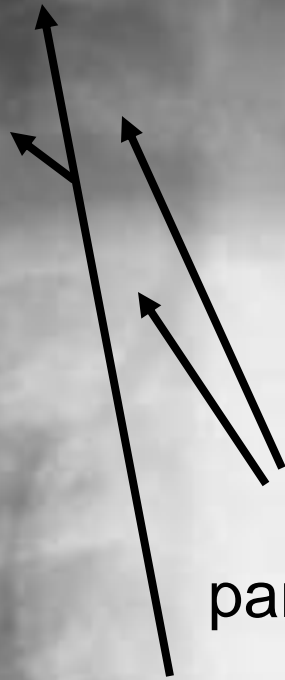
**3 year old**  
**TST: 20 mm**





3 year old

TST: 20 mm

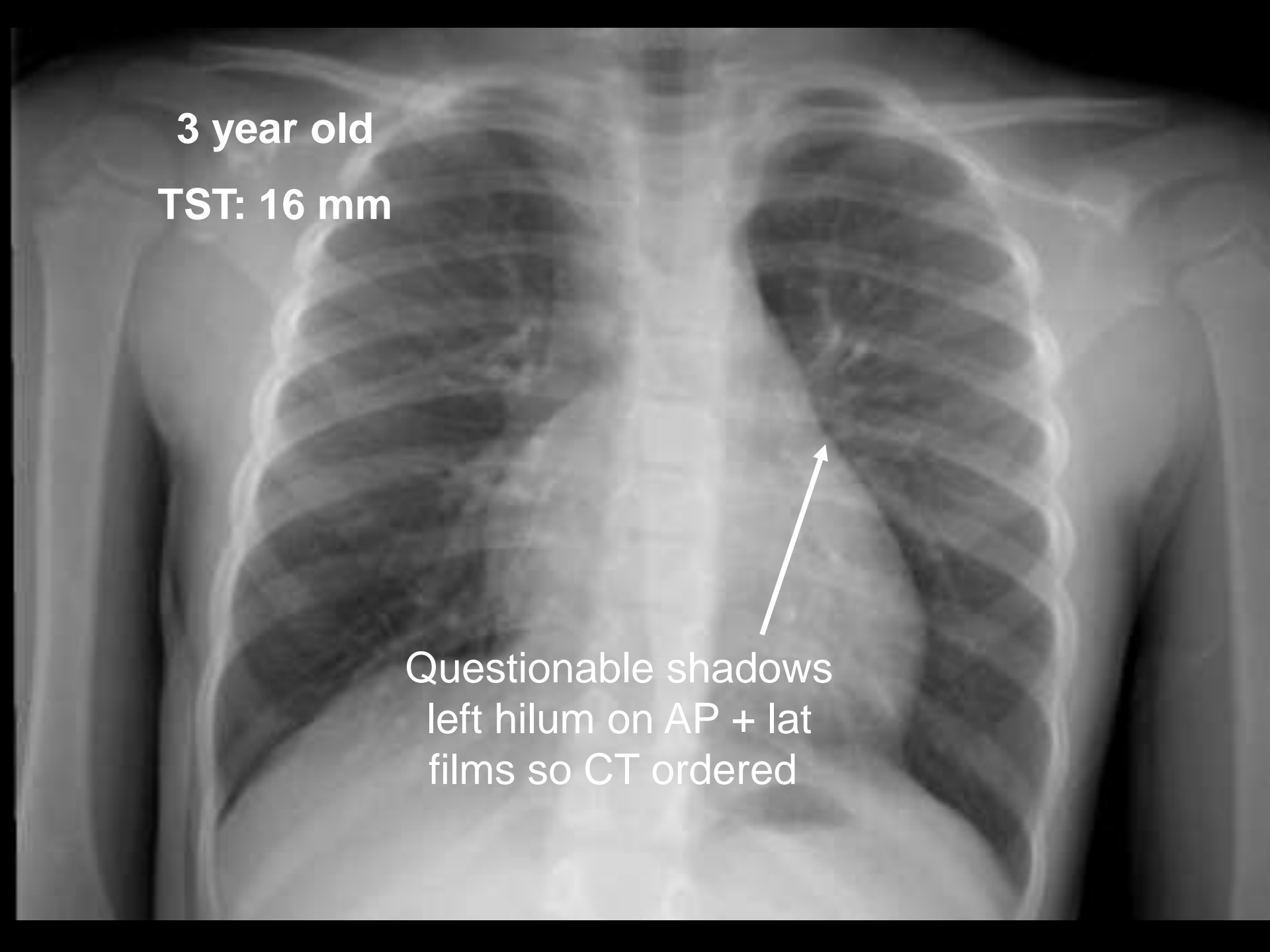


Hilar and probably  
paratracheal adenopathy  
with infiltrate

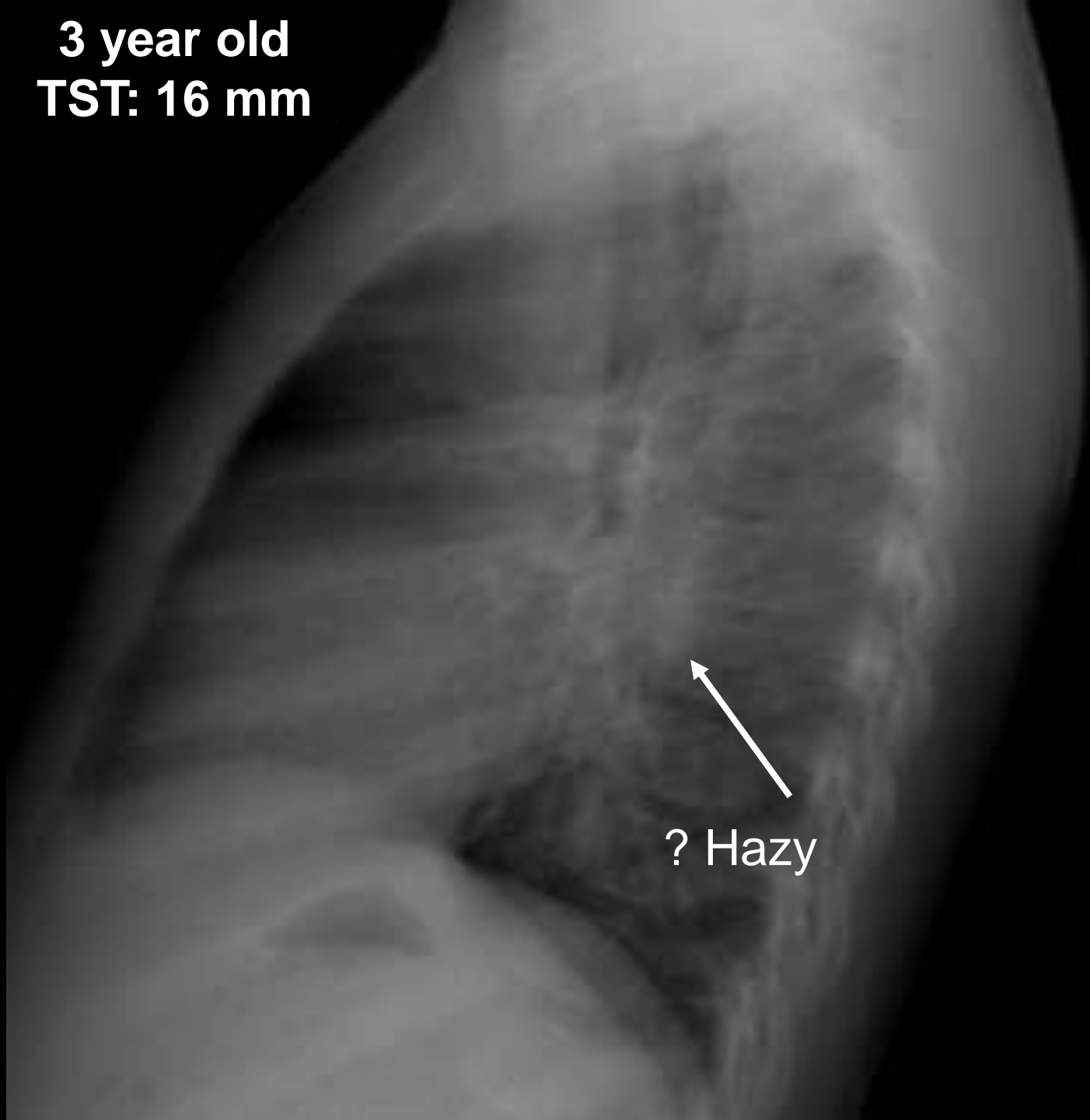
**3 year old**

**TST: 16 mm**

Questionable shadows  
left hilum on AP + lat  
films so CT ordered



**3 year old**  
**TST: 16 mm**



? Hazy

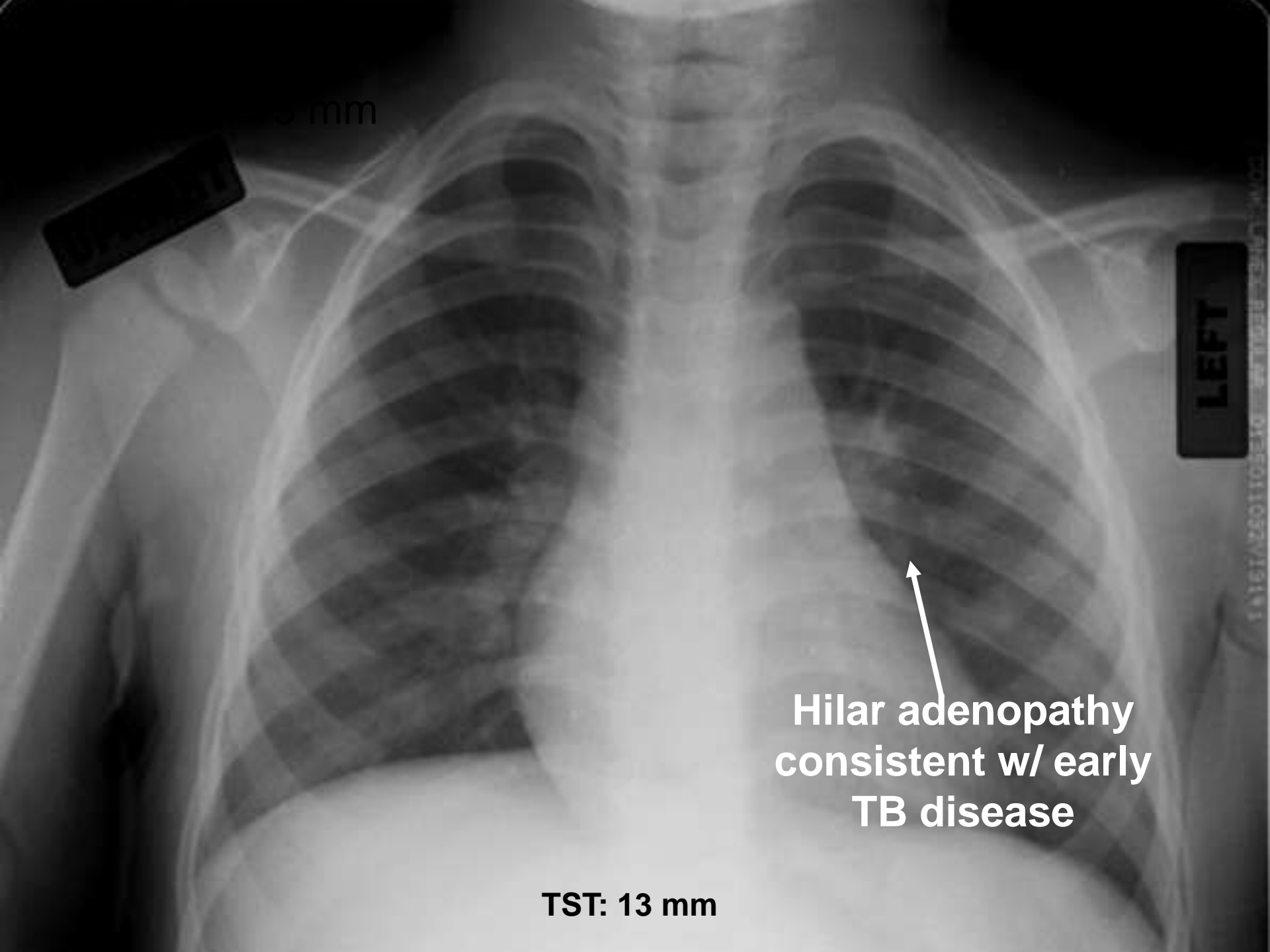
**4 year-old**

**TST: 17 mm**



**Hilar adenopathy  
consistent w/  
early TB disease**

The image is a frontal chest X-ray of a 4-year-old child. The lungs show bilateral hilar adenopathy, which is a finding consistent with early tuberculosis disease. The text 'Hilar adenopathy consistent w/ early TB disease' is written in white, bold font, with a white arrow pointing to the affected areas in the right lung. The text '4 year-old' and 'TST: 17 mm' is also written in white, bold font in the upper left corner of the image.



5 mm

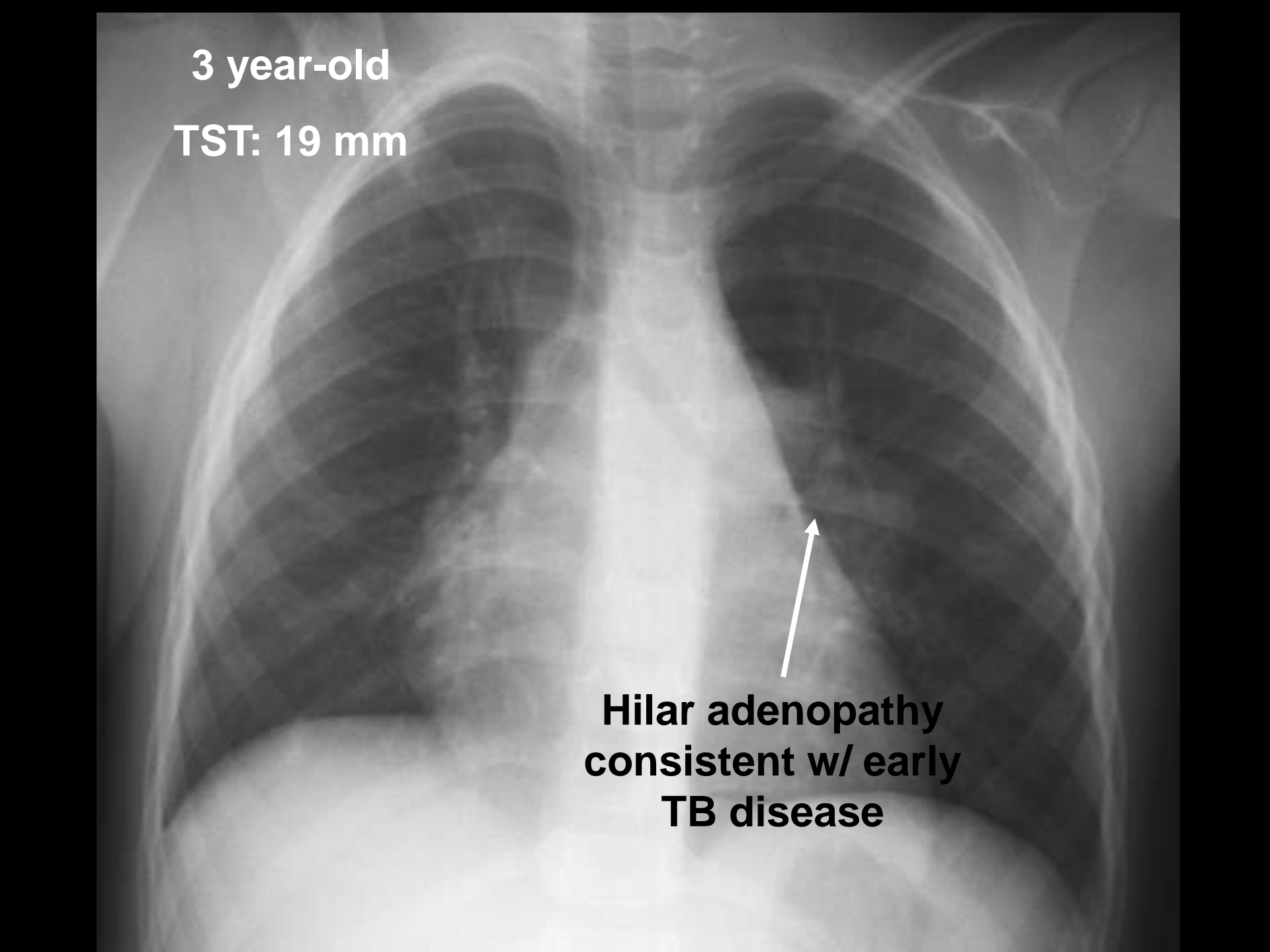
LEFT

Hilar adenopathy  
consistent w/ early  
TB disease

TST: 13 mm

**3 year-old**

**TST: 19 mm**



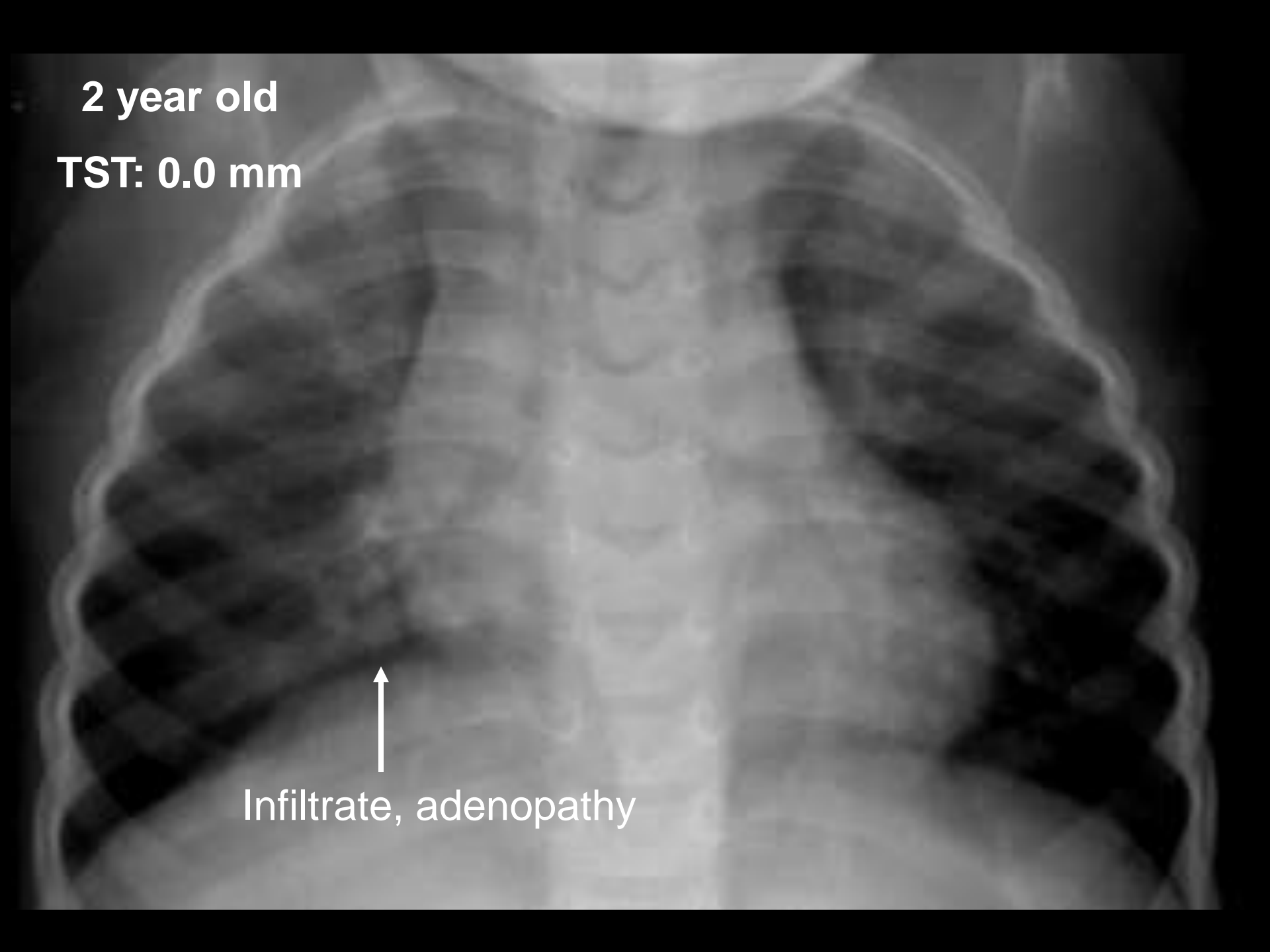
**Hilar adenopathy  
consistent w/ early  
TB disease**

A white arrow points to the right hilar region, where there is a noticeable enlargement of the lymph nodes, appearing as a soft, hazy opacity. The rest of the lung fields appear relatively clear, and the heart size is within normal limits for a child of this age.

2 year old

TST: 0.0 mm

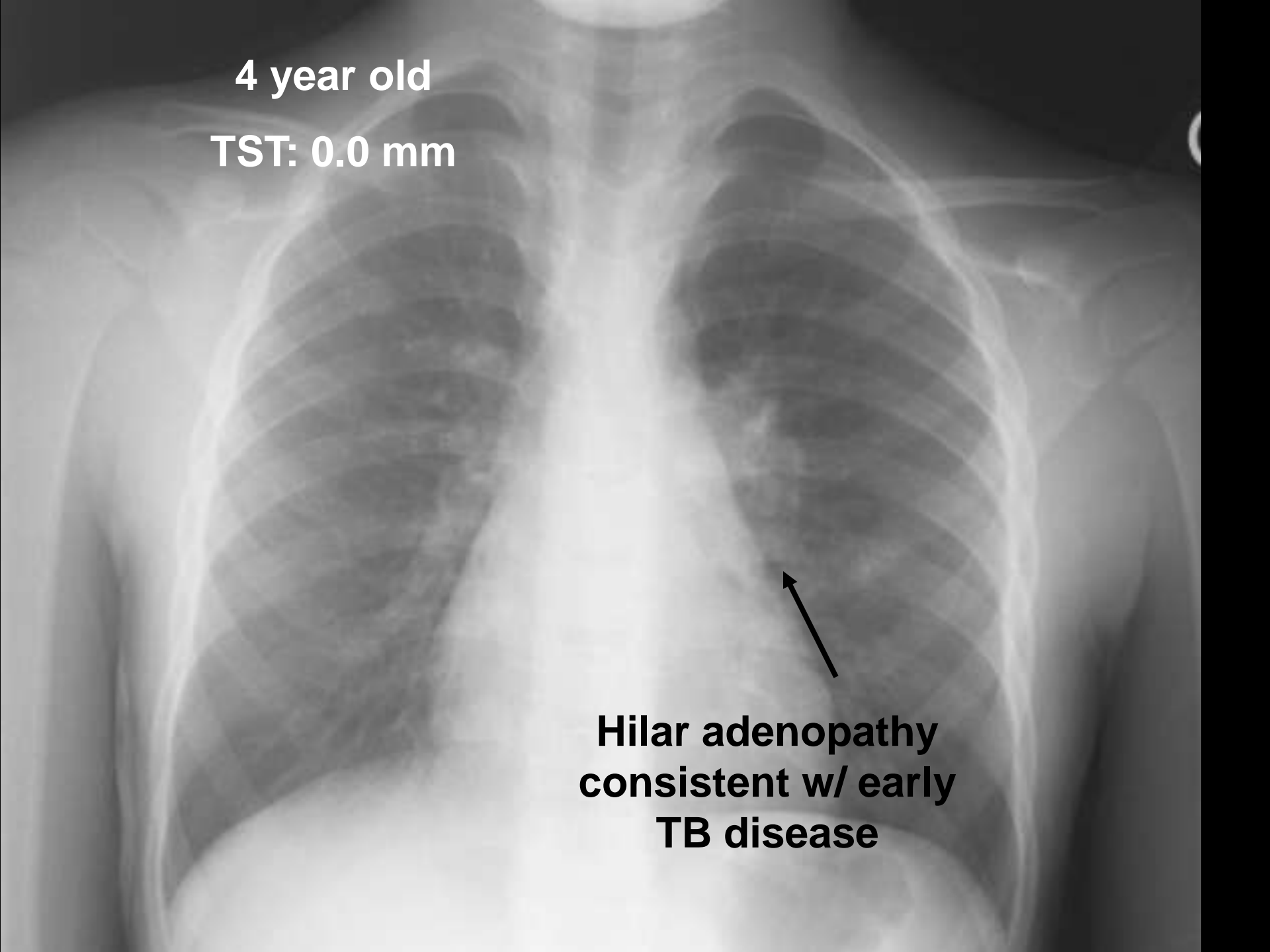
↑  
Infiltrate, adenopathy



**4 year old**

**TST: 0.0 mm**

**Hilar adenopathy  
consistent w/ early  
TB disease**



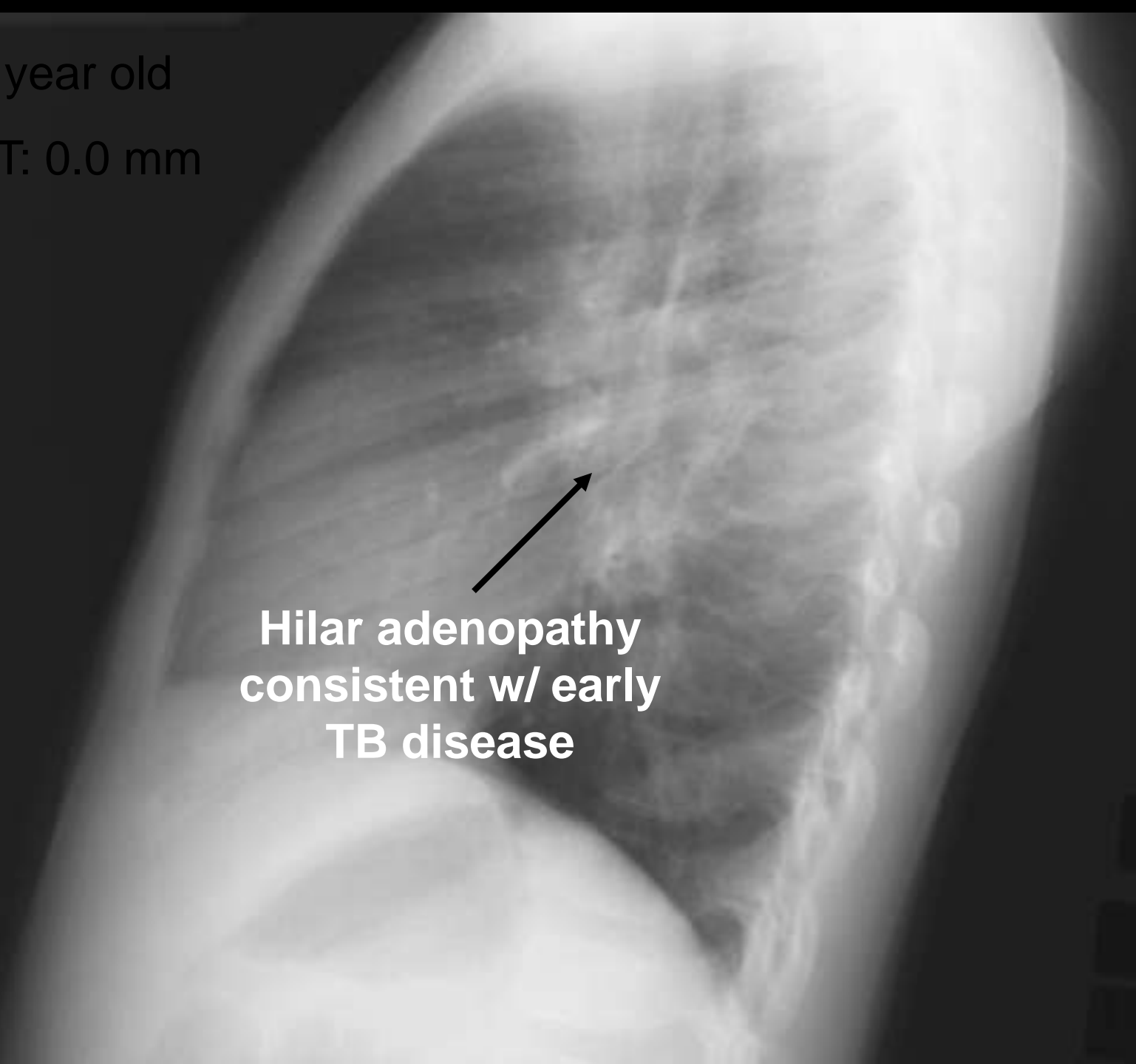


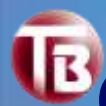
4 year old

TST: 0.0 mm



**Hilar adenopathy  
consistent w/ early  
TB disease**





# Contact Investigation, Initial Results: Infection and Disease at Daycare

## Children

30 ( $\leq 4$  years of age)

(+) TST

11/30 (37%)

(+) TST w/ disease

5/11 (45%)

(-) TST

19/30 (63%)

(-) TST w/ disease

2/19 (11%)

## Staff

5

(+) TST

3/5 (60%) - 2 adolescents

(-) TST

2/5 (40%)

No disease in adults



# Contact Investigation Results: Totals After Initial Testing

<u>Daycare Center</u>	35	30 $\leq$ 4 yrs old
(+) TST	14/35 (40%)	
(-) TST	21/35 (60%)	
TB disease	7/35 (20%)	All $\leq$ 4 yrs old
<u>House Hold + Social</u>	9	2 $\leq$ 4 yrs old
(+) TST	5/9 (56%)	
(-) TST	4/9 (44%)	
TB disease	2/9 (22%)	Both <1 yr old



# Contact Investigation: Totals After Initial Testing

## Investigation Totals

	44		32 $\leq$ 4 yrs old
(+) TST	19/44	(43%)	All $\leq$ 18 yrs old
(-) TST	25/44	(57%)	
TB disease	9/44	(20%)	All $\leq$ 4 yrs old

## Children $<$ 4 yrs old

(+) TST	13/32	(40%)	7 with disease
(-) TST	19/32	(60%)	2 with disease
TB disease	9/32	(28%)	



# Observations on Private Pediatrician Involvement in Contact Investigations

- **6 of 30 (20%) of the exposed children were initially evaluated in conjunction with their pediatricians:**
  - TSTs read by pediatricians were reported in at least one case as negative, i.e.: Not in millimeters
  - TSTs 0.0 (zero) mm: (3)
    - H & PE, CXR done: None
  - TSTs 0.0 (zero) mm + CXR (-): (2)
    - H & PE done: None
  - INH prescribed for prophylaxis for 6 contacts  $\leq 4$  yrs of age: None
  - In each case TCs made to assure proper evaluation were followed by a referral to TB Center for the evaluation



# Importance of Pediatric Radiologic Expertise

- **7 of 30 (23%) chest X-rays taken during the initial investigation either needed to be repeated or were misinterpreted**
  - In 5 cases the technique used did not yield evaluable films
    - Repeats done at the same institution as the initial films, even when requests were made for a specific technique, did not address the question the initial films raised
  - In 2 cases, CXRs with evidence of disease were read normal



# **Just Two Examples Why Quality Contact Investigations Are Important....**

- **43% of infants aged 0-1 develop TB disease within 1 year of infection**
  - 25% of these pediatric cases are extra-pulmonary
    - 66% are diagnosed with lymph node TB
    - 6% are diagnosed with miliary TB
- **Of those infants who are identified as a contact to a known infectious or potentially infectious TB case 10% who are TST negative develop TB disease**



# Day Care Graduation





**TB  
in  
Daycare**



**6 mo old infant**



**6 mo old infant**



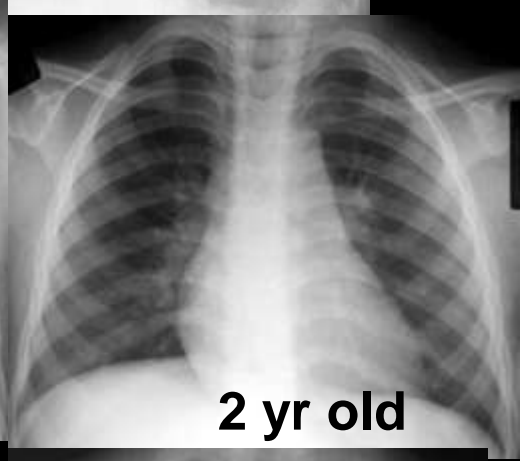
**3 yr old**



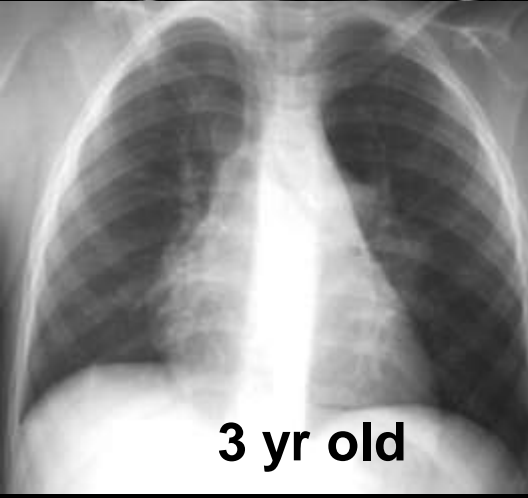
**3 yr old**



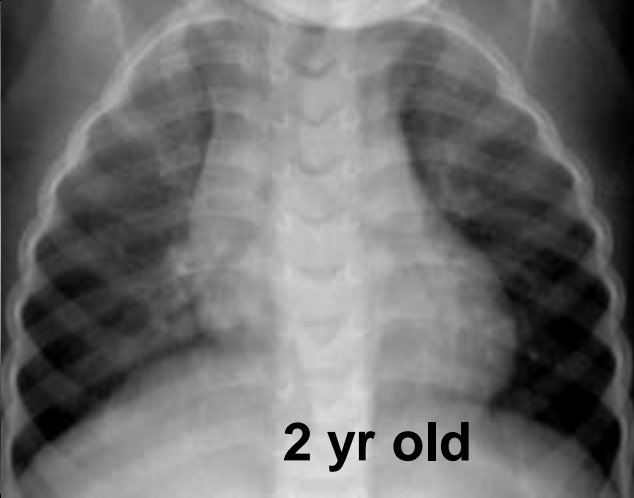
**4 yr old**



**2 yr old**



**3 yr old**



**2 yr old**



**4 yr old**



# **Prevention of Tuberculosis in Children: Missed Opportunities**

- Failure to find and appropriately manage adult source cases (Case finding)
- Delay in reporting the initial diagnosis of TB
- **Contact investigation interview failure**
- **Delay in evaluation of exposed children**
- **Failure to completely evaluate exposed children**
- **Failure to prescribe prophylactic INH**
- Failure to maintain a contact under surveillance
- LTBI diagnosed; treatment not prescribed
- Failure to complete treatment for LTBI (Adherence)



# Contact Investigation: Lessons

- **Large scale contact investigations require thoughtful planning**
  - Don't want to over test
  - Don't want to under test
- **Importance of on-site assessment**
  - Testing recommended?
  - Magnitude of the problem
  - Answer questions of why some convert and not others
- **Critical to provide follow-up TB interviews of index patient to allow for:**
  - Clarification of previously collected contact information
  - Collection of additional information
  - Provision of additional TB education
  - Different interviewers if no contacts identified, rapport is an issue



# Contact Investigation: Lessons

- **Despite the rapidity of the contact investigation 9 cases of TB disease occurred in young children**
  - Children develop disease soon after infection so it is imperative to move quickly
- **Pediatricians are generally not familiar with standard evaluations of children exposed to tuberculosis and use of INH in such situations**
- **Radiological expertise with young children is important:**
  - In this CI, 7/30 CXRs either needed to be repeated or were interpreted incorrectly
- **Education: Parents, students, teachers, media**



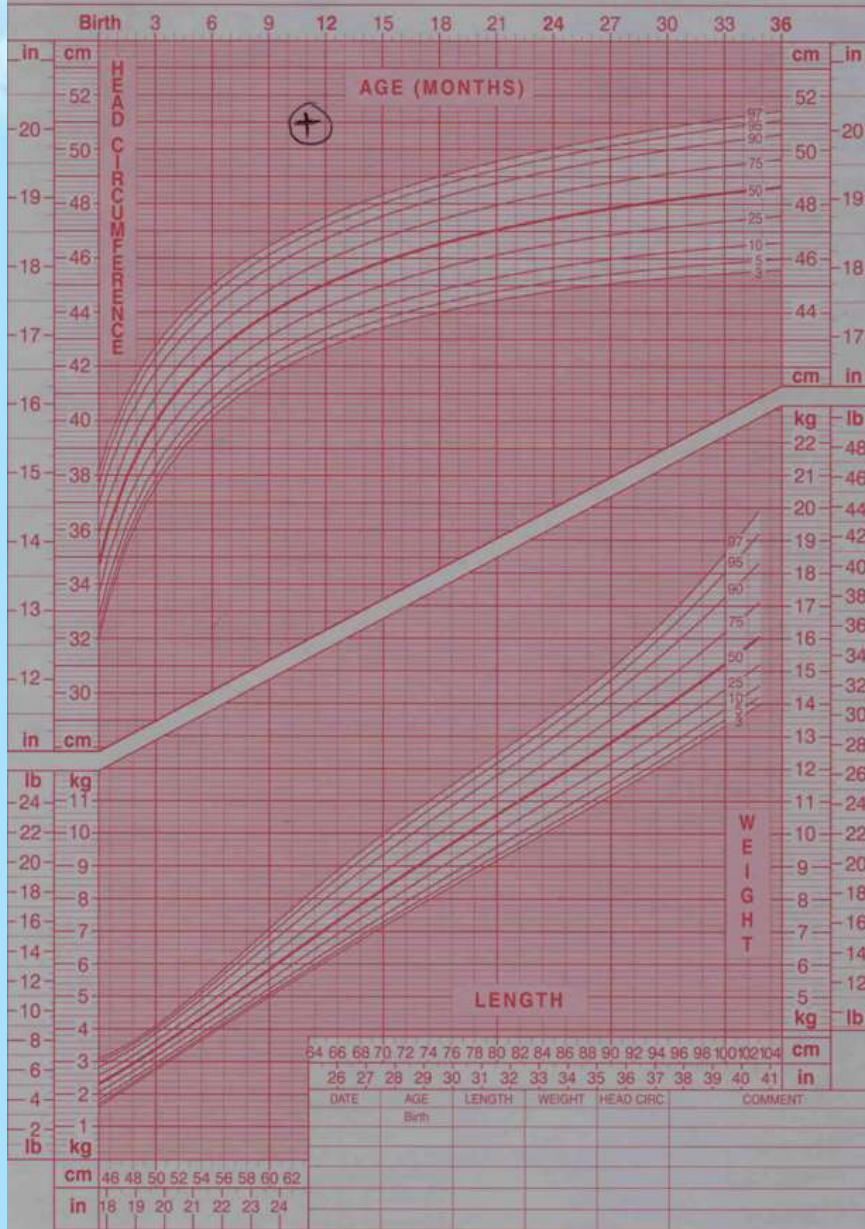
## **Case #2. Three generations, two families and a pediatrician....**

**Or, Source cases, index cases, and contact investigations.... you never know what you'll get if you keep your eyes open....and keep asking the right questions...THE IMPORTANCE OF EPIDEMIOLOGY, i.e., is this TB? If we could only find an adult source case?**



**GIRLS: BIRTH TO 36 MONTHS**  
**CDC US GROWTH CHARTS\***

Name \_\_\_\_\_ Record # \_\_\_\_\_



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 Oral Electrolyte Maintenance Solution/Packet Pops

**Similac® 2**  
 Infant & Toddler Formula With Iron

**Isomil® 2**  
 Infant & Toddler Soy Formula With Iron

**PediaSure®**  
 Complete, Balanced Nutrition®

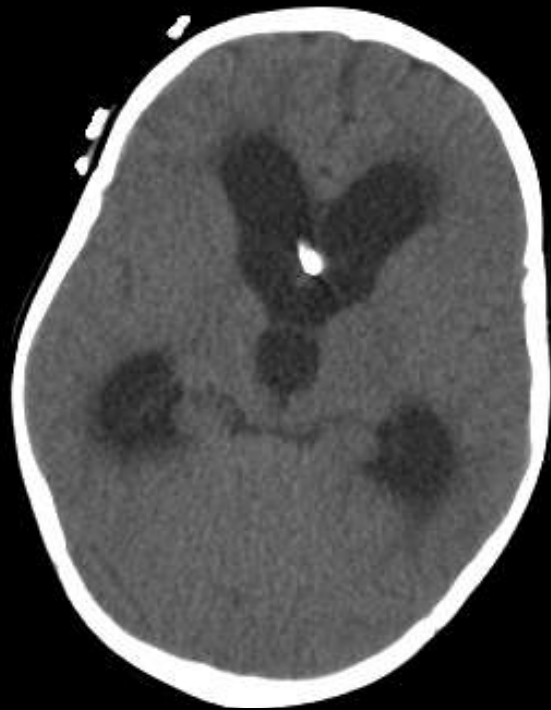
**EleCare®**  
 Nutritionally Complete Amino Acid-Based Medical Food

\* Adapted from the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000). Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC Growth Charts, United States. Advance data from vital and health statistics No. 314. Hyattsville, Maryland: National Center for Health Statistics, December 4, 2000.

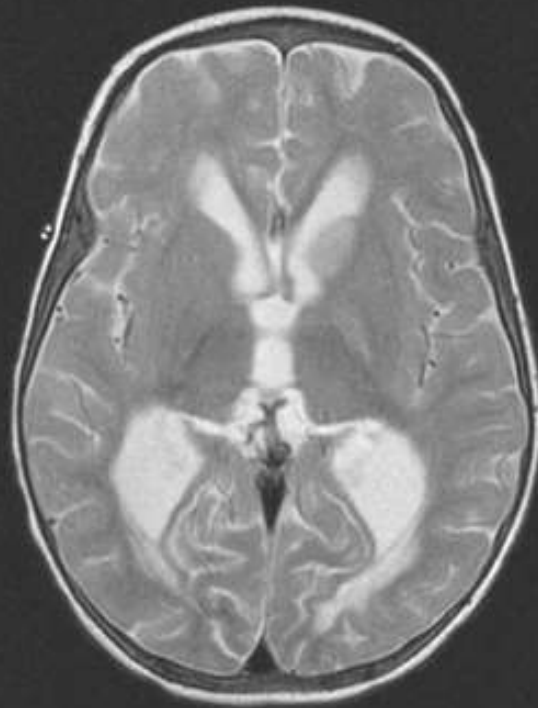
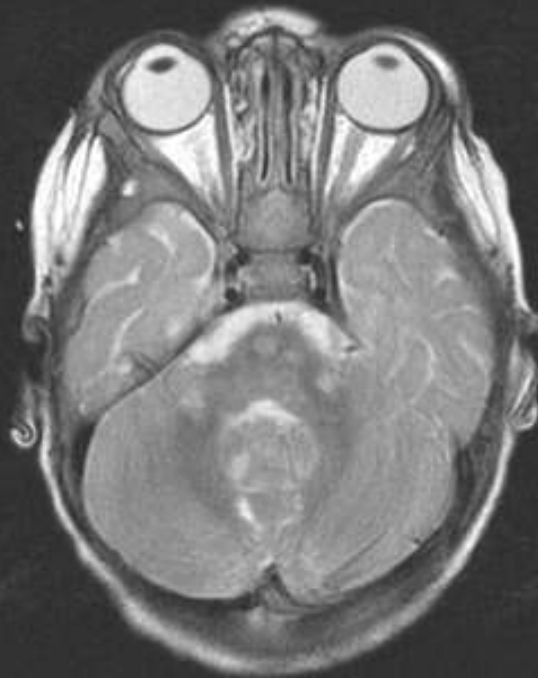
This chart is consistent with CDC growth data as of July 2001.

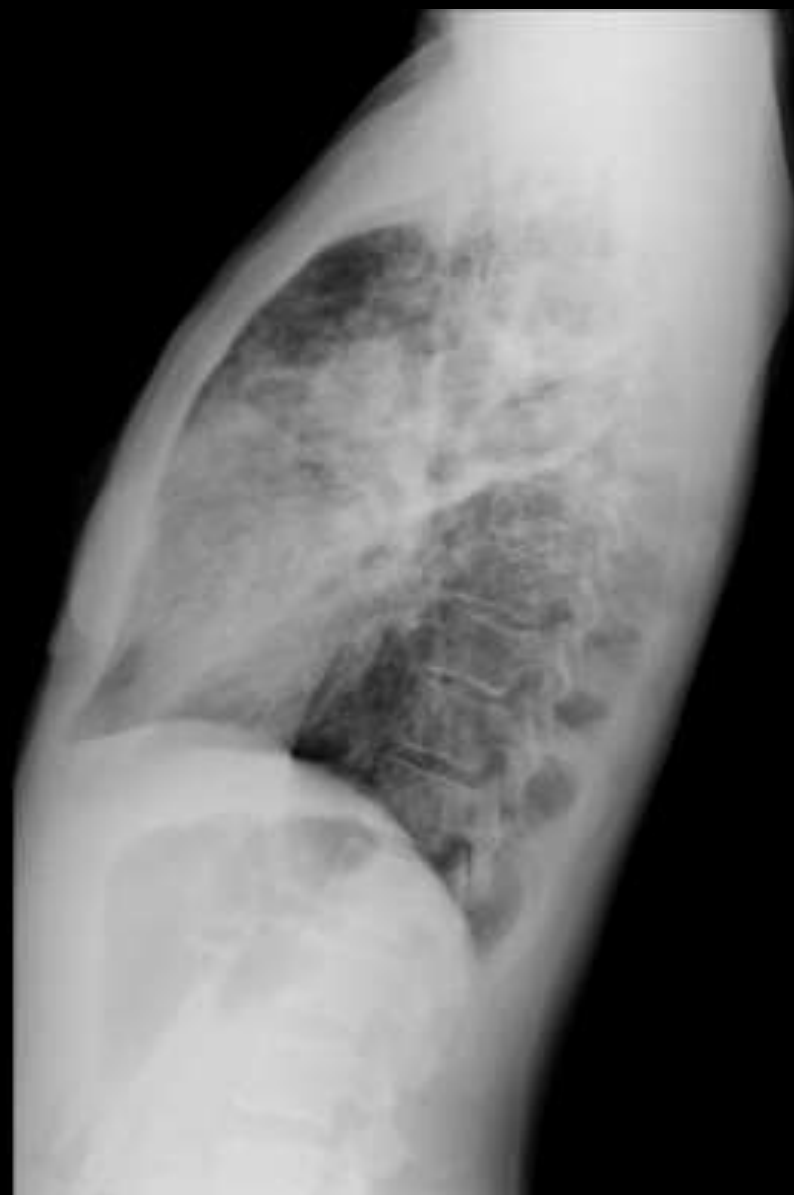
Internet: <http://www.cdc.gov/growthcharts>

**CT**



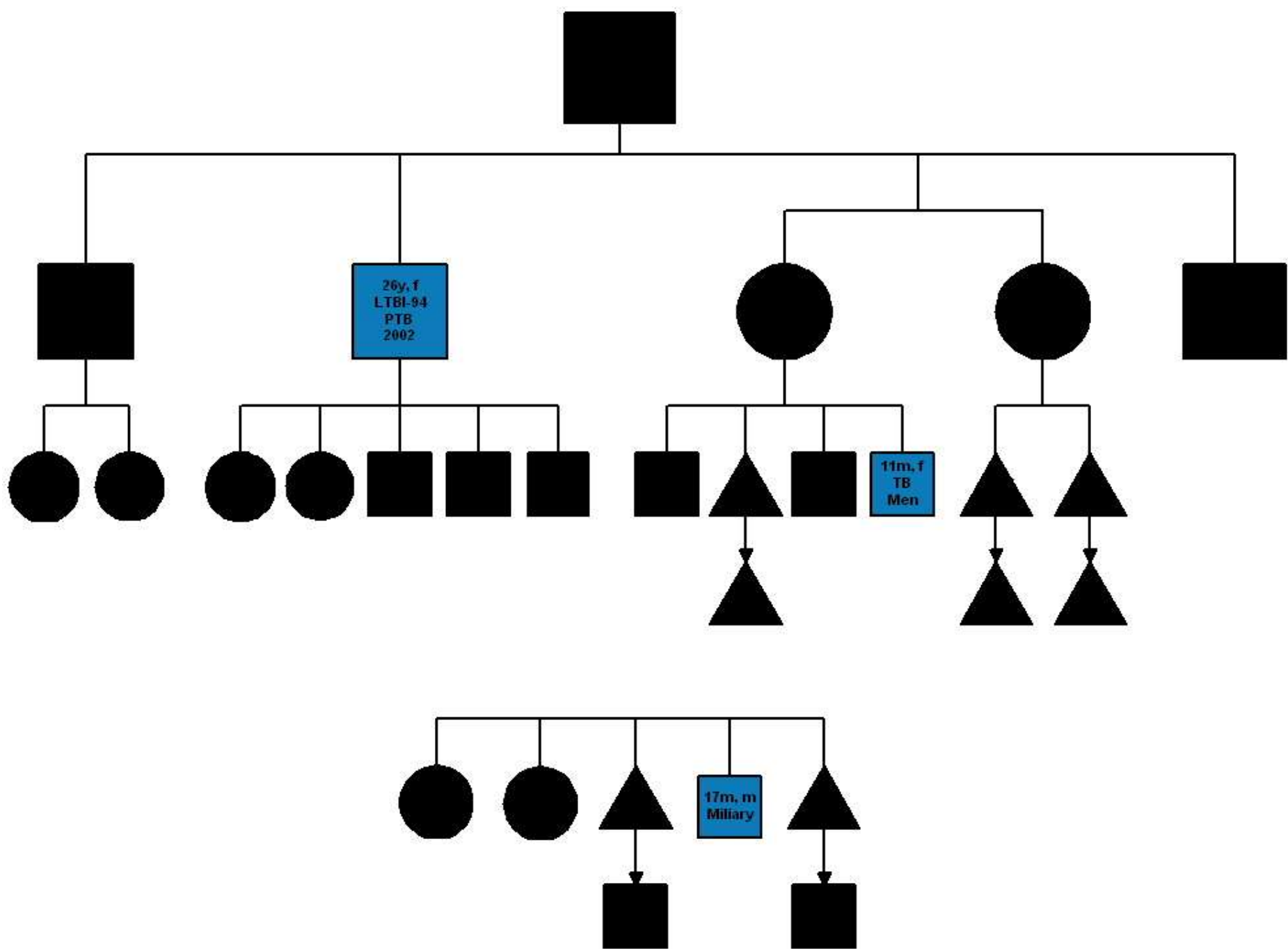
**MRI**

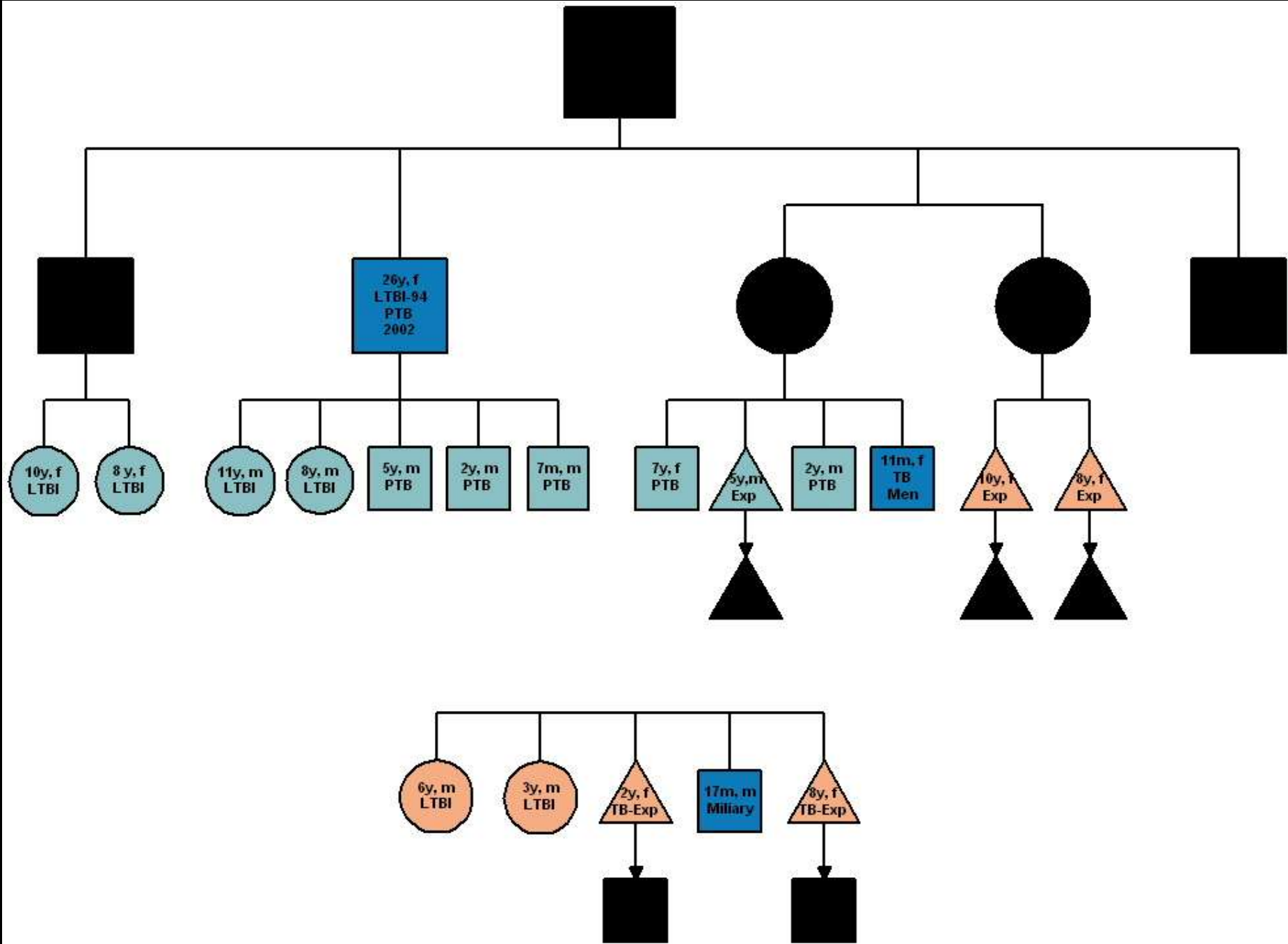














# Potential Missed Opportunities in TB Control

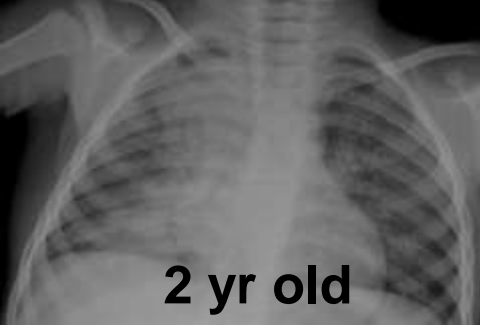
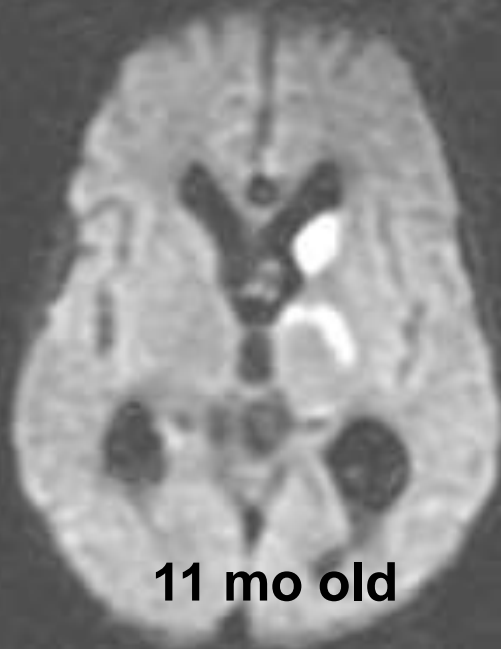
- **Two children with LTBI from one family see their private pediatrician for evaluation and management after mother insists to health department that she would like them seen by the pediatrician:**
  - Receive prescriptions for INH plus 8 refills
    - No follow-up appointments are given
    - Social history: Homeless, 5 children, mother with her own serious health problems, holding down a full-time job
  - Set-up for another missed opportunity? Strong probability
    - Will therapy for LTBI be completed?
    - Was it? Yes, why? DOT of infection (DOTI).

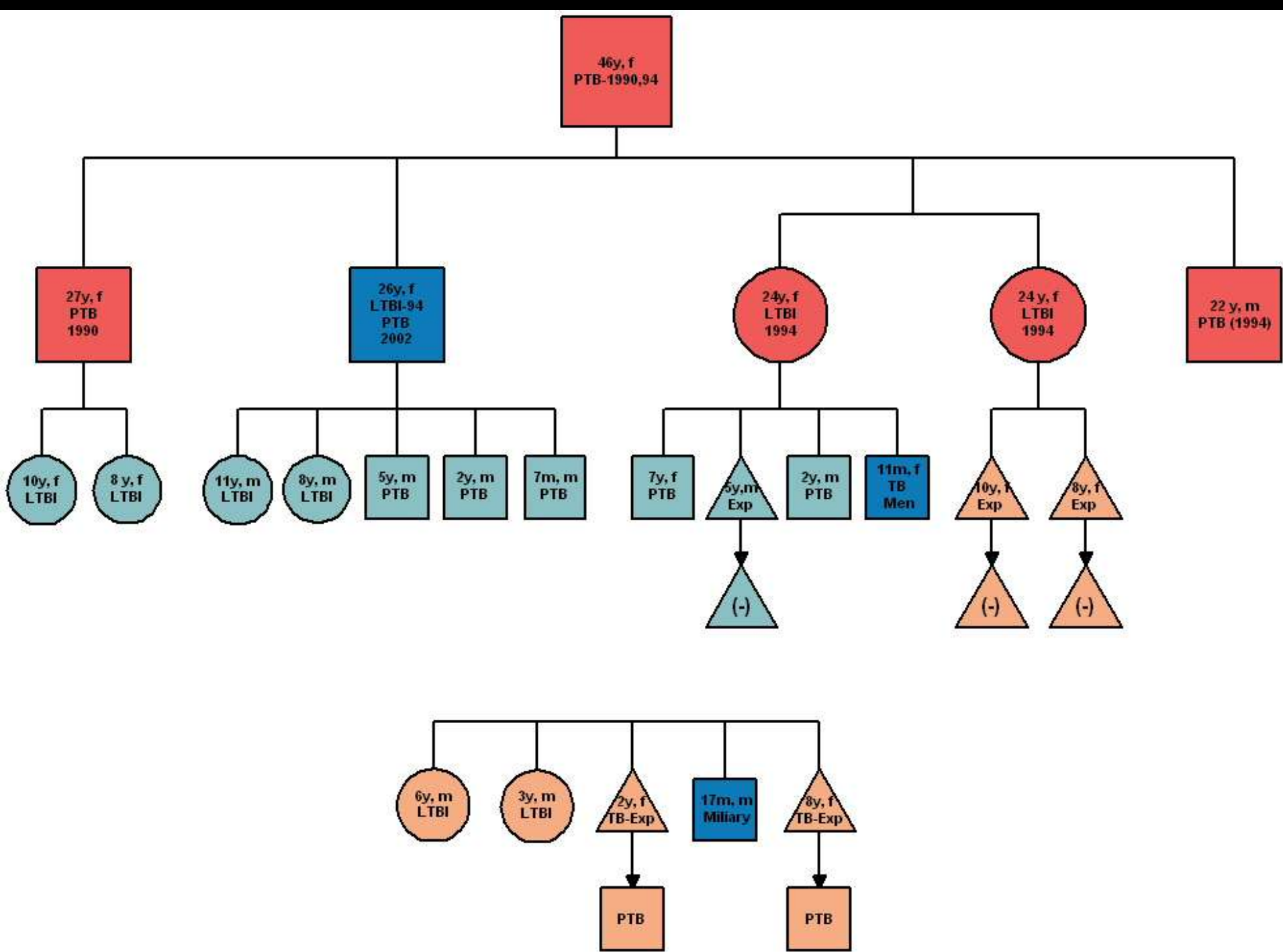


# Potential Missed Opportunities in TB Control

- **Initially, 5/18 children are diagnosed as TB-exposed**
  - Two (Ages 6 & 28 months) identified in the contact investigation have 0.0 mm TSTs and normal CXRS at the health department
  - Mother (same family as above) insists to health department that she would like to them to be seen by their private pediatrician
    - No PE done
    - No INH “window prophylaxis” given











**GRANDMOTHER 1990, 34 YRS OF AGE**



# Case History: Final Numbers

- **Eighteen children were exposed to a 26-year old woman with bilateral cavitory pulmonary tuberculosis:**
  - 15/18 (83%) children are infected
    - 9/15 (60%) develop TB disease
      - Two after initial negative TST (Missed opportunity)
      - 1 TB meningitis, 2 miliary
    - 6/15 (40%) have LTBI
  - 3/18 (17%) are TB-exposed but not infected
- **Through 3 generations: All 2<sup>nd</sup> and 3<sup>rd</sup> generation cases preventable**
  - TB-infected child of today may become the index pt. of tomorrow without treatment for LTBI

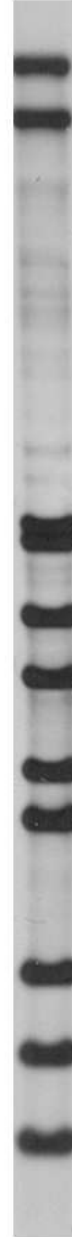


TN21812  
GD254

TN 22398 and 22399  
W976



GD308





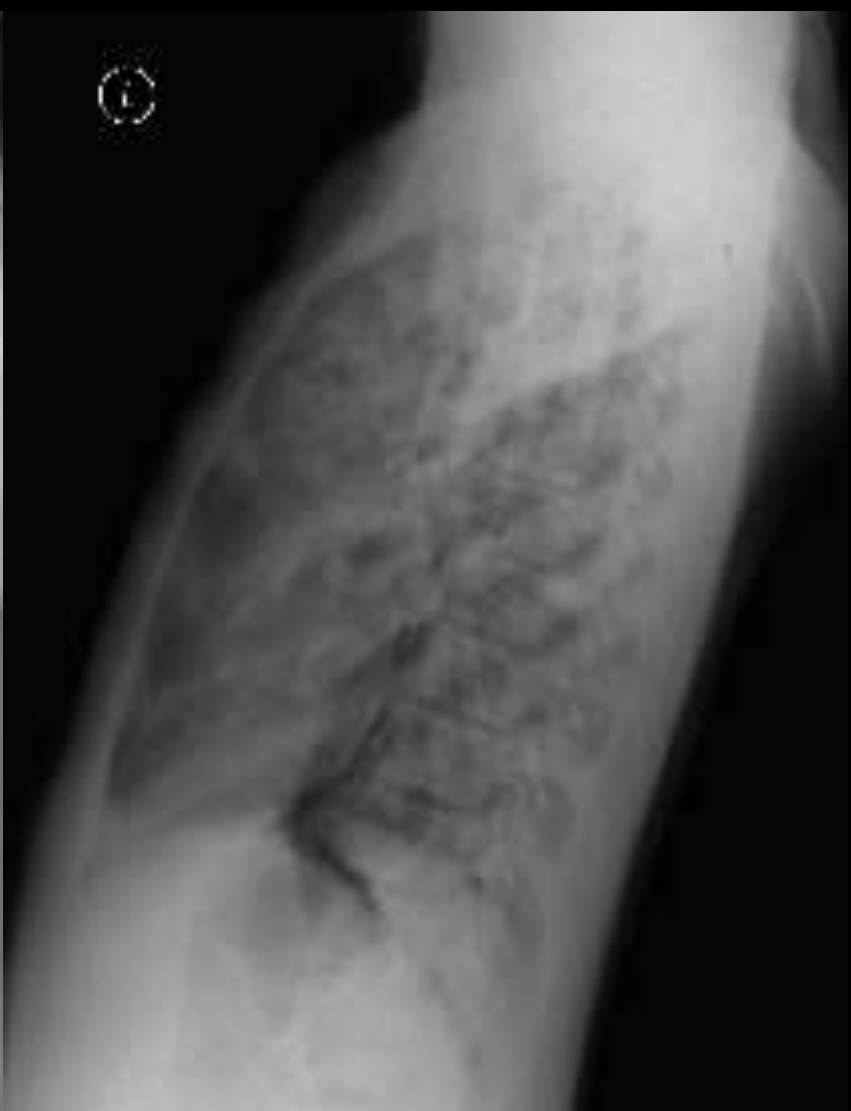
**Case #3. The six year-old boy who was not a household contact but was....so says Dr. Kreiswirth....and a memory of LTBI treatment long ago....**





## **The six year old boy....**

- **A 16 year old male was referred to oncology for evaluation of a lump in the neck**
  - There was history of decreased appetite, 20 lb weight loss, and intermittent, nonproductive cough
  - A CXR was done:





## **The six year old boy....**

- **A 22-year-old aunt remembered being treated for LTBI about 10 yrs ago**
  - An uncle who had a cough and may have had TB but was not sure of the diagnosis
- **Using the name provided, the TB controller was able to find the uncle's medical record**
  - Was a highly infectious case 9 years earlier
  - Review of the contact investigation showed 5 household contacts including the niece and 4 work contacts
    - The 6-yr-old boy who spent several hours in the uncle's apartment each day after school was not mentioned







## **The six year old boy....**

- **RFLP analysis was a match between the uncle and the 16 year-old (Dr. Kreiswirth)**
- **The contact investigation of the now 16 year-old (now a computer whiz) involved evaluation of his H.S. (1600 students) and targeted testing of 50 high priority classmates and teachers**

# **Tuberculosis in Children and Adolescents 2011- Part II**

**George D. McSherry, MD  
Division of Infectious Diseases  
Penn State Hershey Children's Hospital  
and  
Pediatric Section  
Northeastern Regional Training and Medical Consultation  
Center  
NJMS Global Tuberculosis Institute**

**TB Intensive Workshop  
April 12-14, 2011**



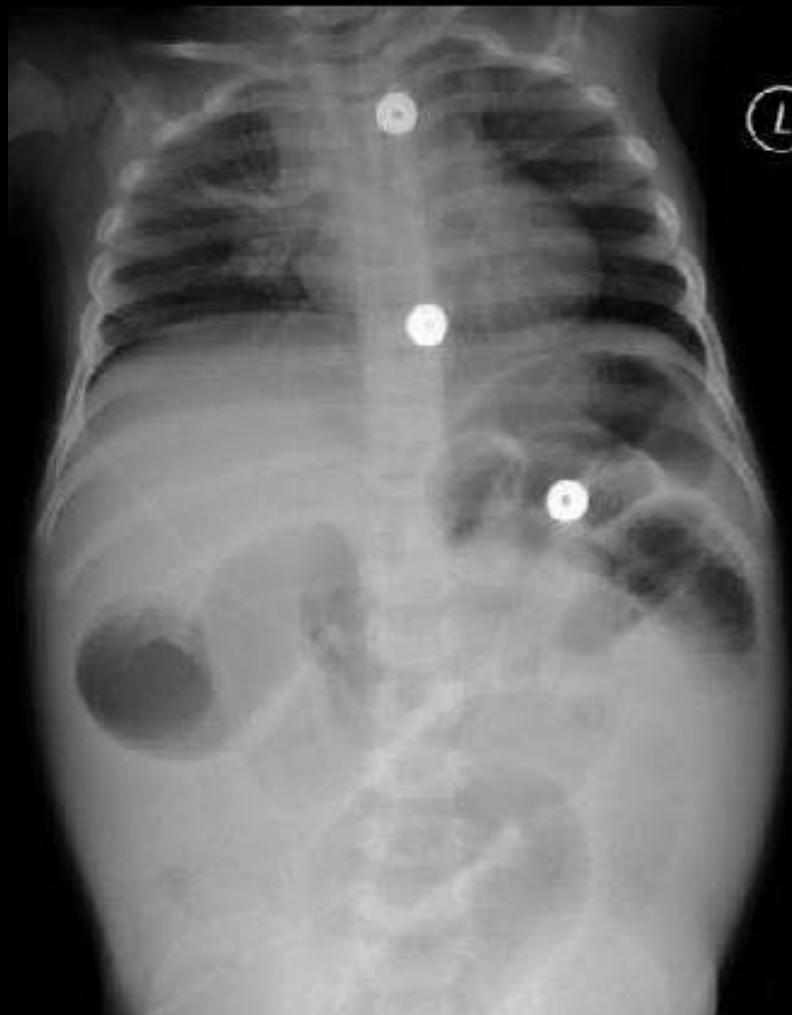


**#4. “Have never seen him, didn’t know he existed”....Dr. Barry Kreiswirth says you have and you did....or, the DNA doesn’t lie....**



# **“Have never seen him, didn’t know he existed”....**

- **21 month old boy is admitted to the hospital due to severe dehydration brought on by 2 days of vomiting.**
- **He had fever, was lethargic and had had no urine output for 12 hours**
- **Bilious vomiting is noted suggesting intestinal obstruction**
  - X-rays and CT scan of the abdomen are done:





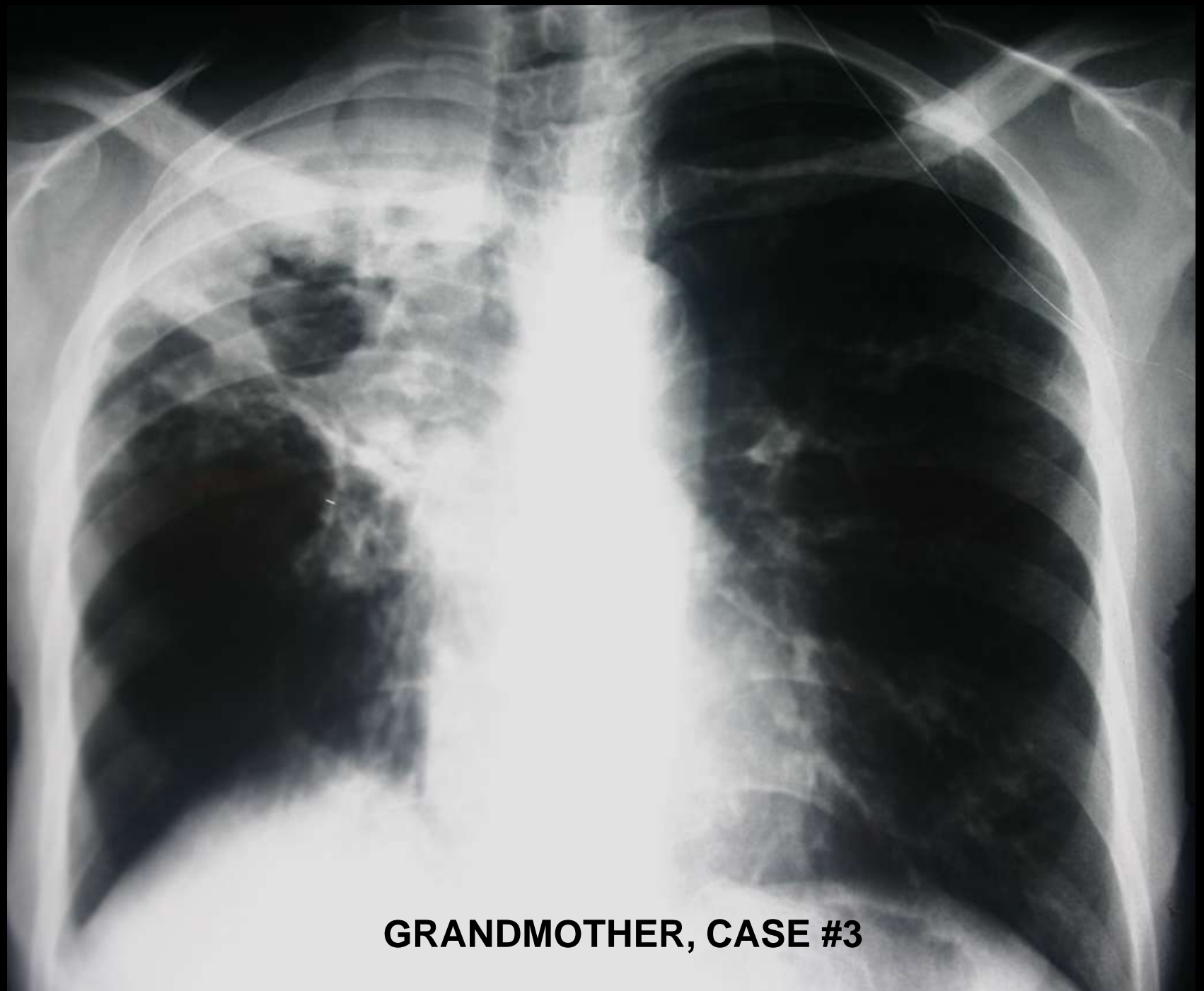
# **Have never seen him, didn't know he existed"....**

- **Child undergoes emergency laparotomy and ileostomy**
  - 2 ft. of necrotic small intestine is removed
    - Hemorrhage, necrosis, multiple granulomas noted in bowel wall and the mesentery
      - Cultures of gastric drainage grow *M. Tuberculosis*
    - Thrombosis of small vessels
- **Months of hospitalization (Acute and rehab)**
  - Two additional surgeries
  - NGT placed for feeding
  - Has to re-learn to eat and walk
- **Months of outpatient rehab and TB treatment**



# **Have never seen him, didn't know he existed"....**

- **Children are usually infected by an adult or adolescent in the immediate household**
  - Source case investigation:
    - Paternal grandmother with “chronic lung disease”
    - Diagnosed with smear/culture positive pulmonary TB 8 months previously
    - Did not name grandson or his family in contact investigation maintaining: “Have never seen him, didn't know he existed....”
  - Dr. Kreiswirth's opinion:
    - RLFP: Match between grandson and grandmother



**GRANDMOTHER, CASE #3**





# The High Cost of Missed Opportunities

- Missed opportunities documented:
  - Failure to find and appropriately manage adult source cases (Case finding)
  - Contact investigation interview failure
  - Delay in evaluation of exposed children
  - Failure to completely evaluate exposed children
  - Failure to prescribe prophylactic INH
  - Failure to complete treatment for LTBI (Adherence)
- Resulted in: 20 cases of TB in children (23 total cases):
  - 3 military
  - 1 TBM, 1 GI TB
  - Extended hospitalizations (acute and rehab), CIs, DOT





# **AAP Recommendations: Targeted TB Testing**

- **What is Targeted TB Testing?**
  - Identifies persons at high risk for TB who would benefit by treatment of LTBI
- **Risk of exposure to TB should be assessed at routine healthcare evaluations:**
  - Risk Assessment Questionnaire
  - Only children with an increased risk of TB infection or disease (a positive response to a question on the questionnaire) should be considered for tuberculin skin testing



# Why Use Risk-Assessment-Based Targeted TB Testing?

- Why not use routine, universal, administratively mandated TB testing? Why not use the TST or IGRA as the screening tool?
  - Daycare
  - Schools
  - Colleges
  - Summer camps
- **Answer: Limitations of the TST (Mantoux Skin Test)**
  - Universal testing means that large numbers of low risk children will be tested
  - Even if the specificity of the TST approaches 99%, testing of persons in low-prevalence groups would result in mostly false-positives
  - **IGRA** specificity reduces but does not eliminate all false positives in low risk population



# Targeted TB Testing

- **Risk assessment:**
  - Signs and symptoms consistent with TB disease
  - Contact and source-case investigations
  - $\geq 1$  risk factor identified on screening risk-assessment questionnaire
    - General pediatric practice
    - School-based healthcare
  - High risk of progression due to underlying conditions



# Targeted TB Testing Risk-Assessment Questionnaire

- Has a family member or contact had TB disease?
- Has a family member had a positive TB skin test?
- Was your child born in a high-risk country (i.e. outside US, Canada, Australia, New Zealand, or Western European countries)
- Has your child traveled to a high-risk country and spent >1 week with the resident population?



# Using the Risk Assessment Questionnaire

- At first contact with child and every 6 months until age 2 years
- After age 2 years, ask risk assessment questions every year if possible
- Anytime a risk factor is identified, a TST or IGRA should be performed



# **BCG Vaccine and Tuberculin Skin Testing**

- **History of a BCG is never a contraindication to tuberculin skin testing**
- **Interpretation of TST results in BCG recipients is the same as for people who have not received the vaccine**
- **Difficult to distinguish between (+) TSTs caused by infection with *M. tuberculosis* and those caused by BCG**
  - Reactivity does not occur in some children after receipt of BCG
  - If BCG does cause a positive TST, the reaction is generally negative by 5 years of age
  - If child is from a high-burden country, (+) PPD is almost always due to LTBI
- **Therefore, management of children with a history of BCG and a (+) TST includes:**
  - Diagnostic evaluation including a chest radiograph
  - Appropriate treatment





# **Interferon gamma release assays: Use in children**

- **Published experience less in children**
- **Can be used in children  $\geq 5$  yrs of age**
- **May be useful in children who received BCG vaccine**
- **Do not distinguish between LTBI and TB disease**
  - Negative IGRA does not rule out either in child with suspicious findings
- **Interpretation of negative IGRA in child with (+) TST is not clear**
  - No longitudinal studies to establish negative predictive value



# **Evaluation of the Child with a positive TB test (TST, IGRA)**

- **Evaluation of all children with a positive TB test should include:**
  - A careful history for symptoms of disease
  - Physical examination
  - Chest radiographs (PA & lateral)
  - Household investigation



# Treatment of Latent Tuberculosis Infection

- **INH 10-15 mg/kg (max., 300 mg) PO daily for 270 doses**
  - Efficacy approaches 100%
- **Alternative: Twice weekly directly observed (DOT) INH 20-40 mg/kg (max., 900 mg) PO for 72 doses**
- **Monitor index case isolate sensitivities**
- **Hepatotoxicity from INH is rare in children:**
  - A monthly assessment for clinical evidence of hepatotoxicity should be made: malaise, loss of appetite or weight, nausea, vomiting, abdominal pain, jaundice
  - Routine monitoring of LFTs is not indicated



# Treatment of Latent Tuberculosis Infection

- Rifampin 10-15 mg/kg/day (max. 600 mg) po daily for 6 months is an alternative
  - INH not tolerated
  - Index patient isolate INH-resistant
- **MDR-LTBI: TREAT????NOT TREAT?????**
  - Treatment can reduce risk of disease by up to 2/3
  - Regimen based on susceptibilities of index patient isolate
- **Child from a country with “a lot of resistance” shouldn’t treat with more than just INH? No.**

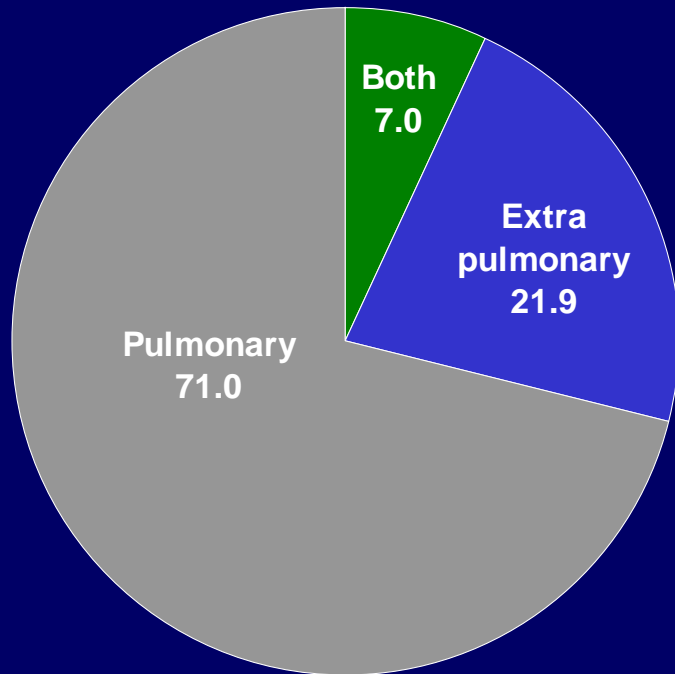




# **How Children with Tuberculosis are Identified**

- **Presentation with a symptomatic illness**
- **Discovery of a child with pulmonary tuberculosis during contact investigation of an adult with tuberculosis**
  - Few or no symptoms
  - Evaluation: (+) TST and abnormal CXR
  - In some areas of U.S. up to 50% of children with PTB are discovered in this manner
    - Before significant symptoms have developed

# Pediatric TB Cases by Site of Disease, 1993–2006



## Any extrapulmonary involvement\* (totaling 28.9%)

Lymphatic	18.9%
Meningeal	3.1%
Miliary	1.5%
Bone & Joint	1.5%
Other	3.9%

\*Any extrapulmonary involvement which includes cases that are extrapulmonary only and both. Patients may have more than one disease site but are counted in mutually exclusive categories for surveillance purposes.



# Mycobacteriologic Diagnosis of Tuberculosis

- **Adults:** 70-90% have a sputum that is (+) for *M. tuberculosis*
- **Children:**
  - Tubercle bacilli are relatively few in number
  - Sputum generally cannot be obtained from children <10 yrs old
  - Gastric aspirates in children with PTB
    - 30-40 % sensitive in children
    - 60-70% sensitive in infants
  - Bronchoalveolar lavage (BAL): Sensitivity may be less than gastric aspirates
  - CDC: 15,946 pediatric cases, 1993-2006: 24% lab (+), 51% clinical criteria, 24% provider diagnosis



# **Difficulties in the Diagnosis of Tuberculosis in Children**

- Children are often asymptomatic or symptoms are nonspecific: Fever, poor appetite, poor weight gain or weight loss
  - Approximately 25-30% of disease is extrapulmonary
  - Meningitis and miliary disease tend to develop soon after infection
    - 70-80% occur in children 0-4 years of age
- Epidemiologic link (The adult source case)
  - Crucial to identify the adult source case for the child
    - Provides strong evidence that the child suspected of having TB disease actually has TB
    - May be the only isolate available for susceptibility testing

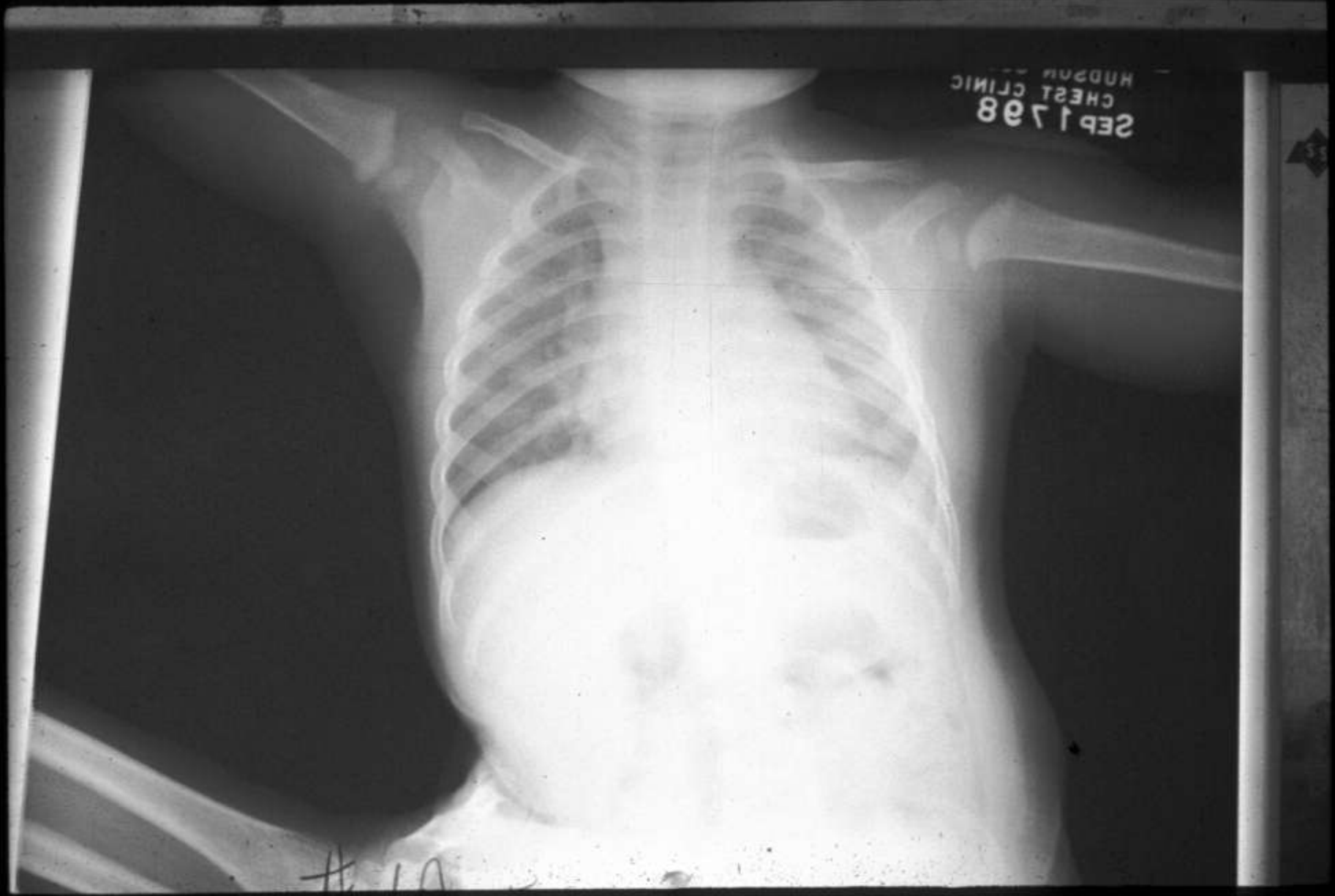


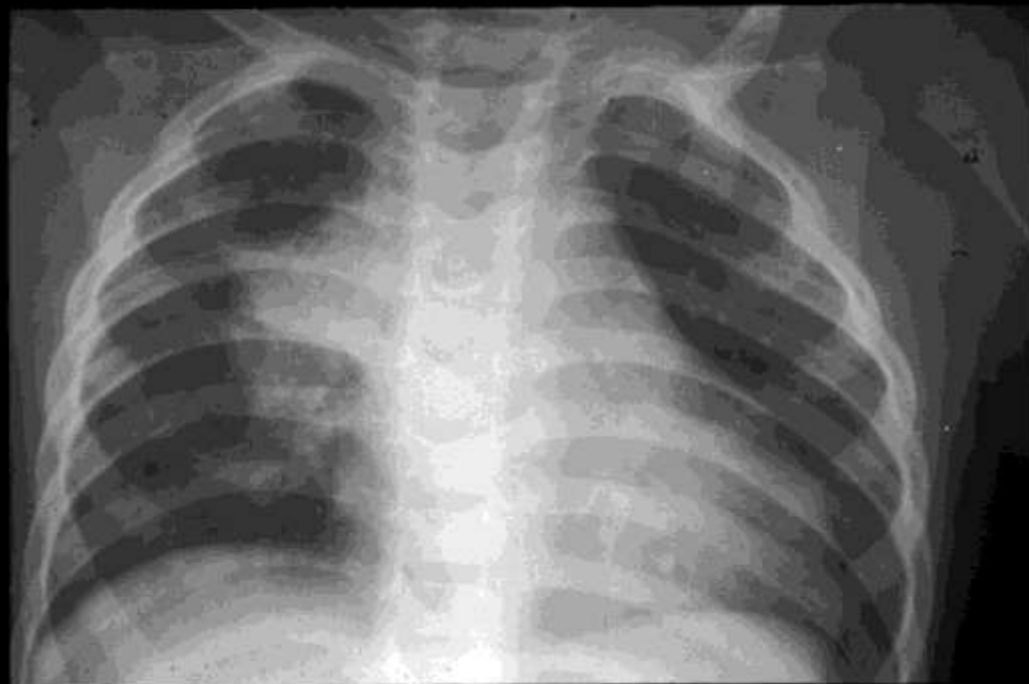
# Difficulties in the Diagnosis of Tuberculosis in Children

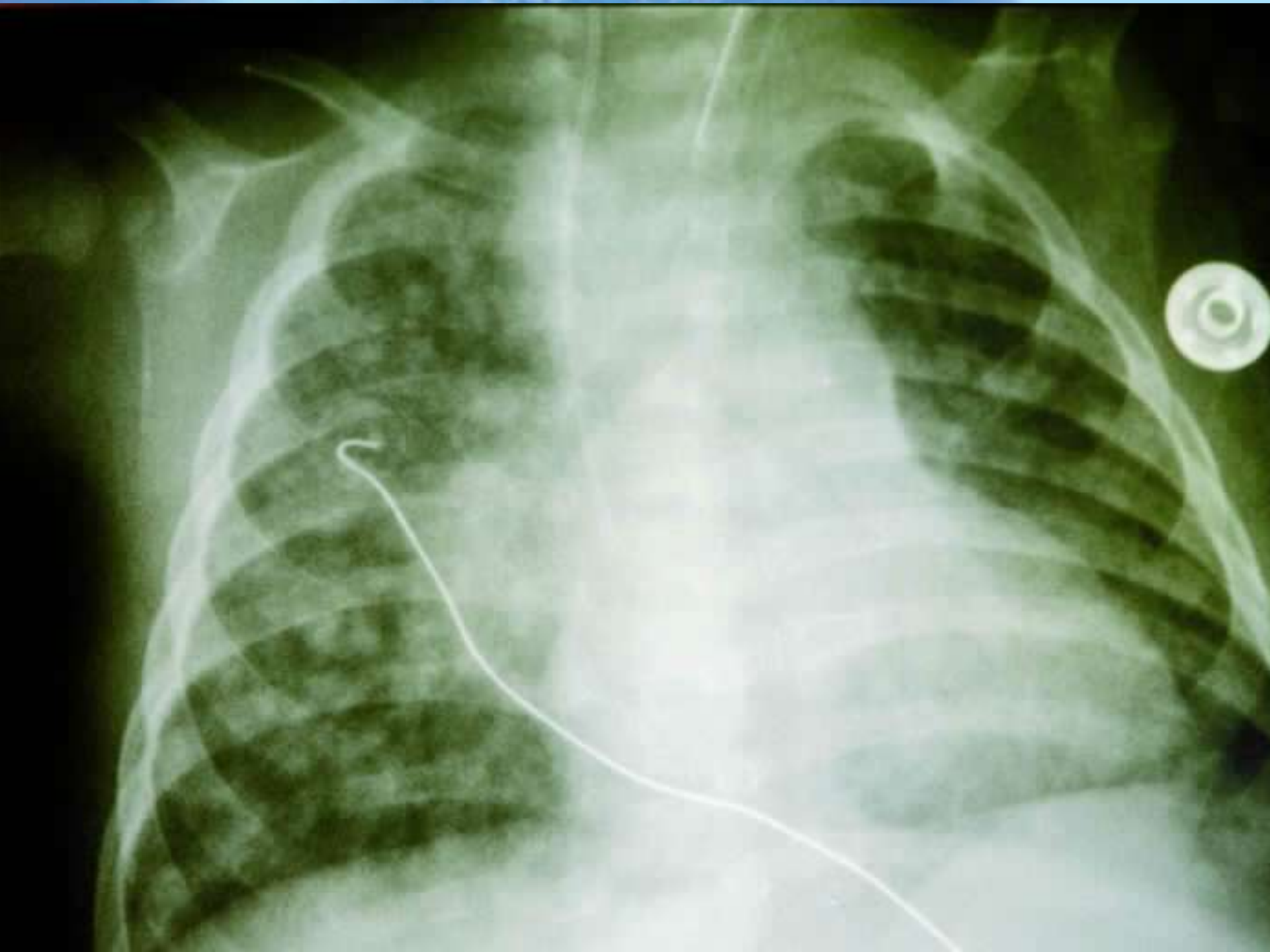
- Physical examination may be normal
- TST may be negative (10%)
- Chest radiograph: Any lobe of the lung may be involved
  - Good technique/Experience with children
  - Two views
  - Careful interpretation

HUDSON  
CHEST CLINIC  
SEP 17 98

# 10







Sc 8  
SE/M  
SL 11

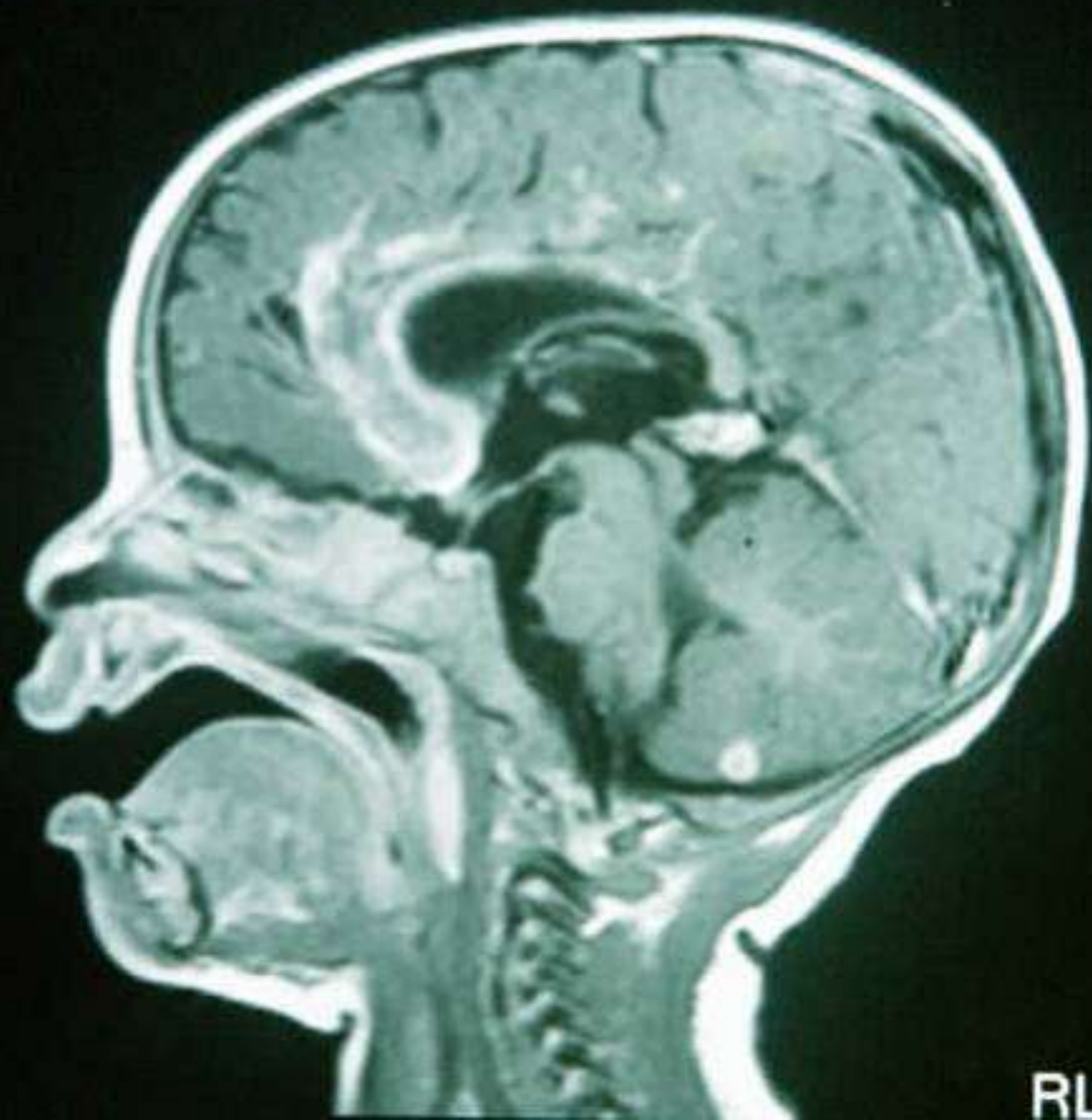
H

P  
5 cm

P  
5 cm

2 left

RL -3 right

















NOT BLOCK  
HAUST VENT

EMERGENCY



# **Tuberculous Spondylitis**

- **Spinal TB accounts for 50% of cases of skeletal TB**
- **Usually involves the thoracic spine**
- **May occur by direct extension from a paravertebral node or by local lymphohematogenous spread from a neighboring bone**
- **May have non-specific symptoms of restless sleep and low-grade fevers**











# Tuberculosis in Adolescents

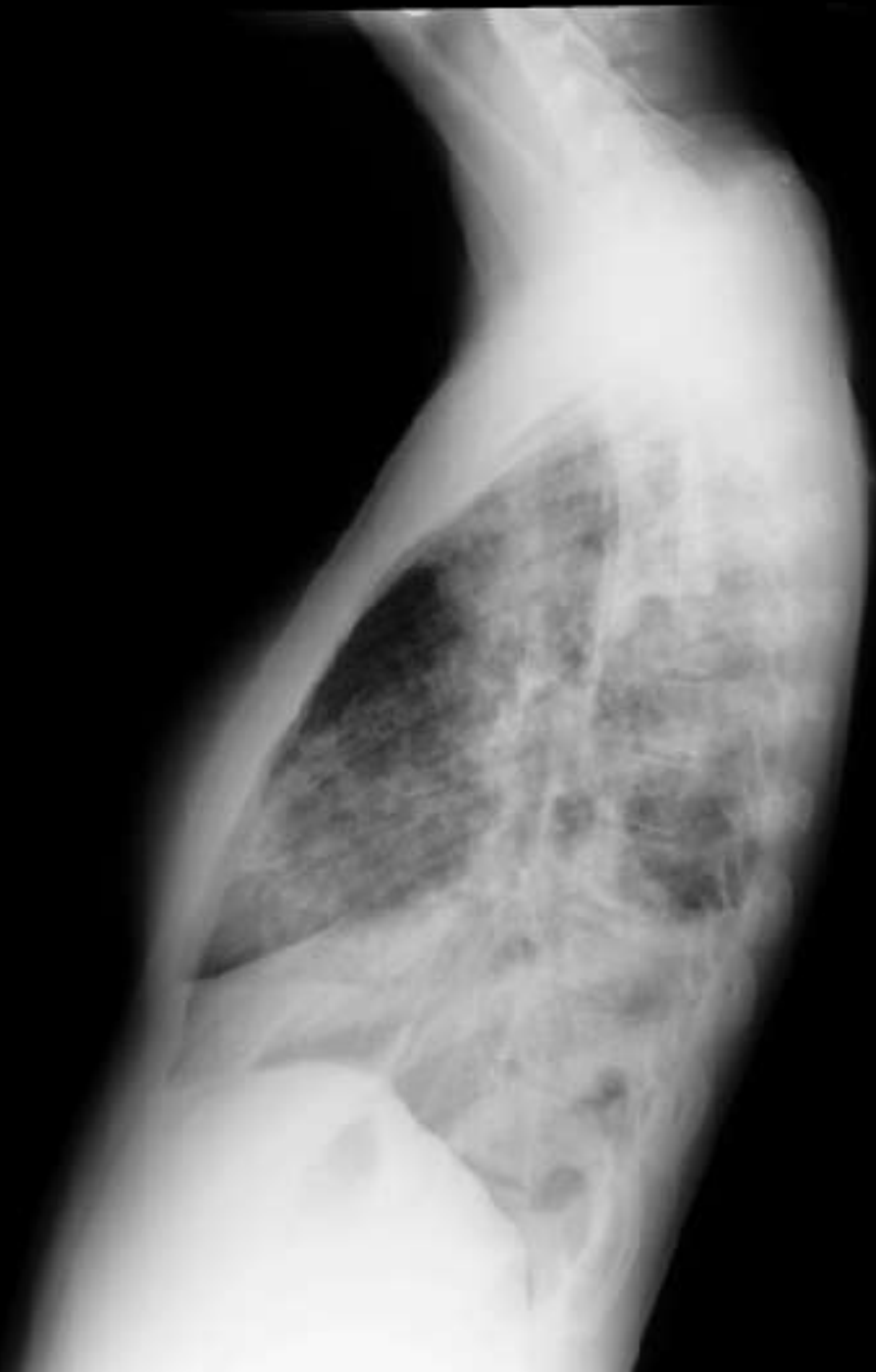
- **Adolescents develop tuberculosis in one of two ways:**
  - Reactivation of infection acquired during childhood
    - Chronic pulmonary tuberculosis
    - The closer to puberty at the time of infection the greater the risk of reactivation
  - Progression of infection acquired during adolescence to disease:
    - Classic primary disease
    - Progressive primary pulmonary tuberculosis
    - Chronic pulmonary tuberculosis





IK

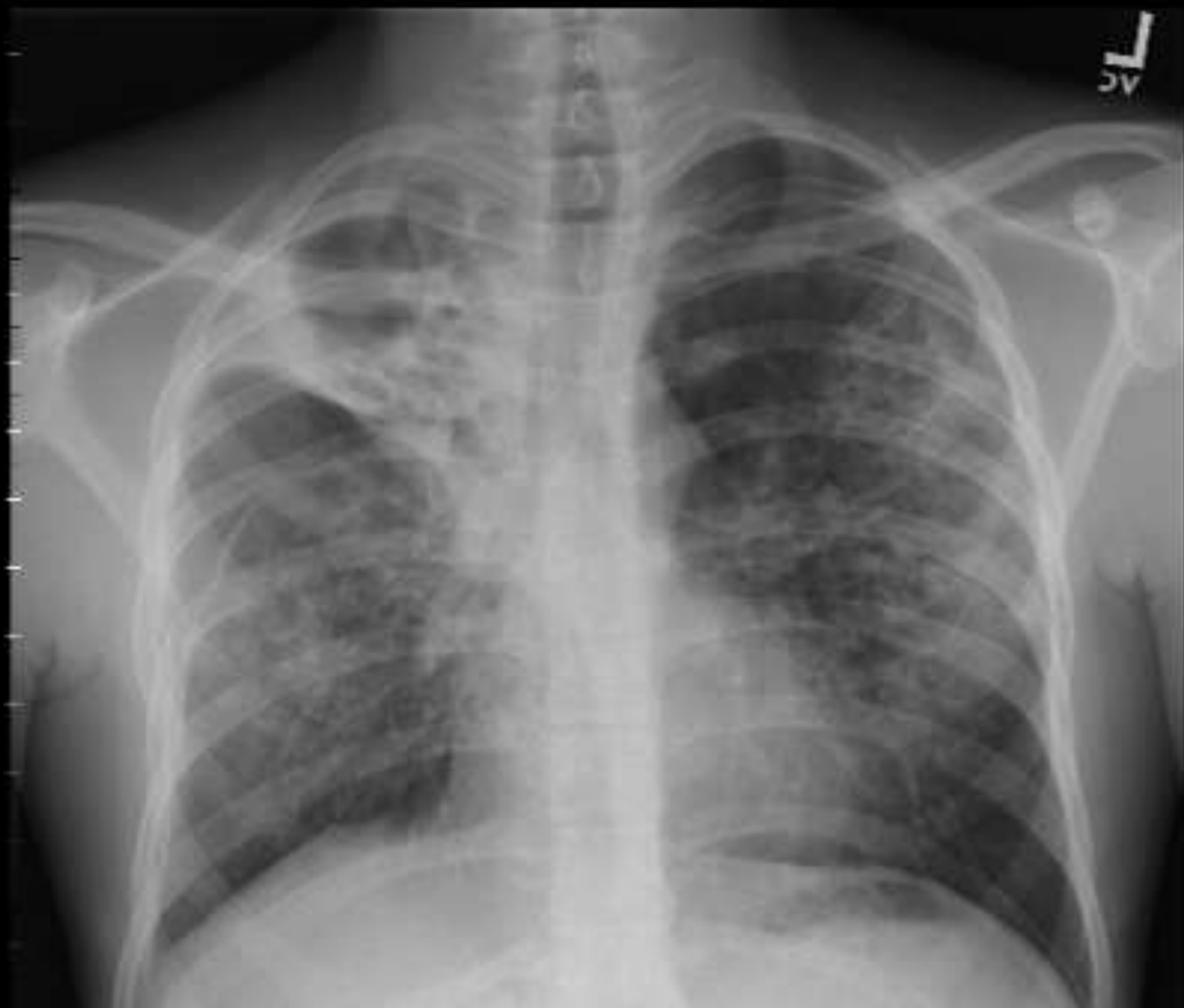
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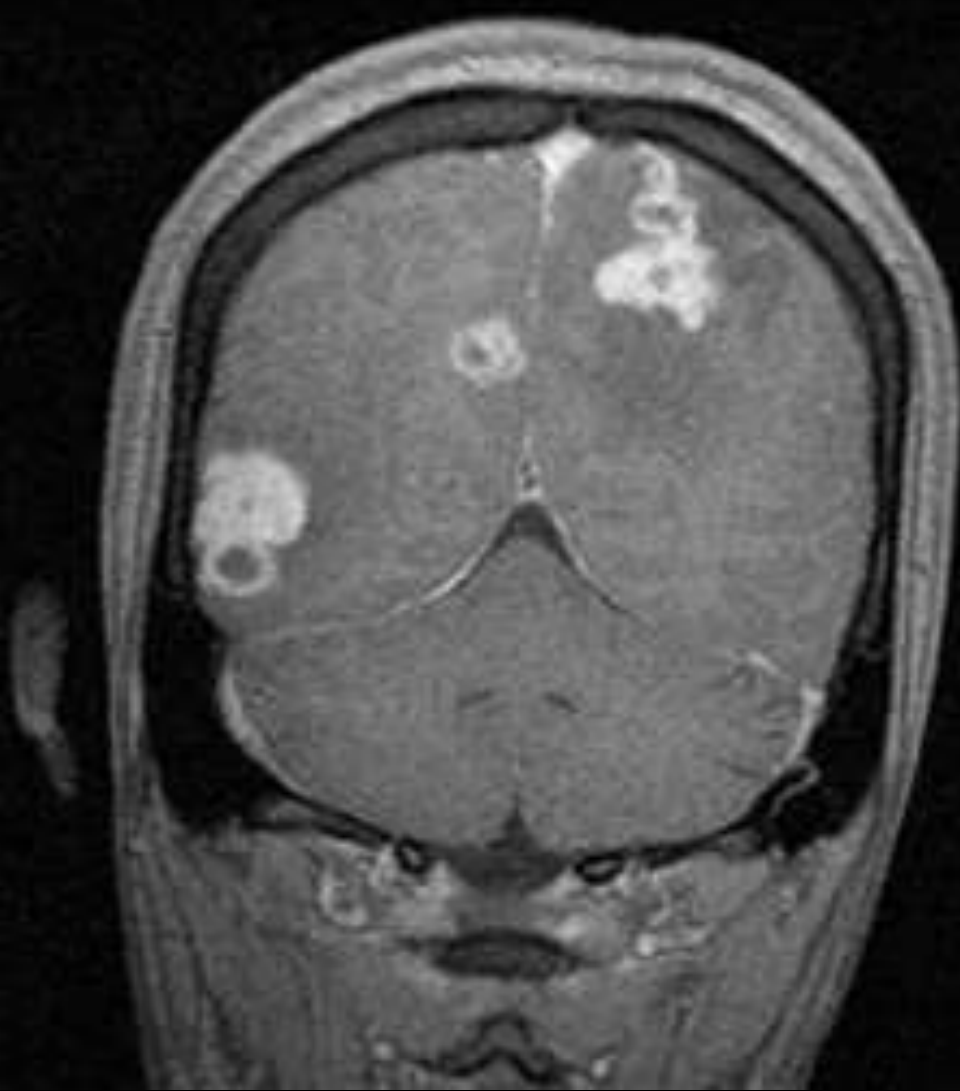


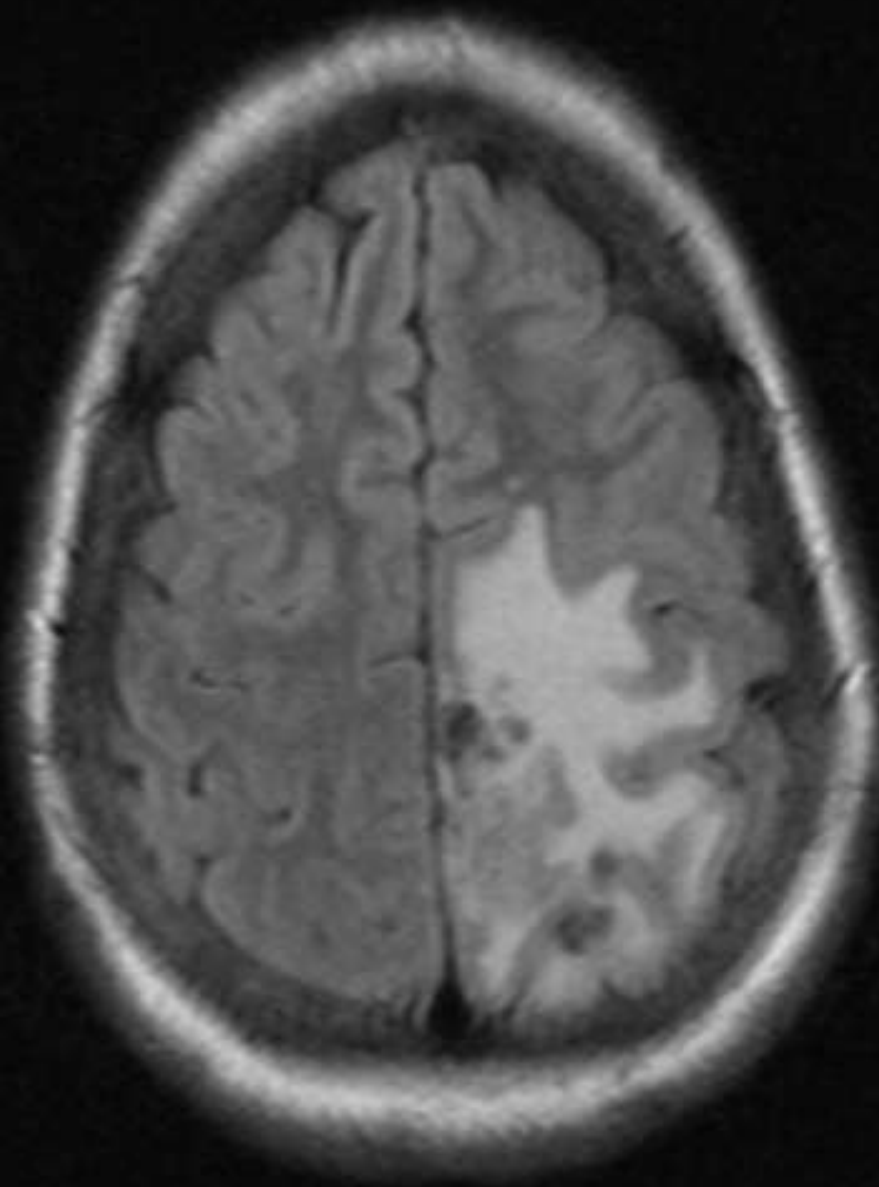
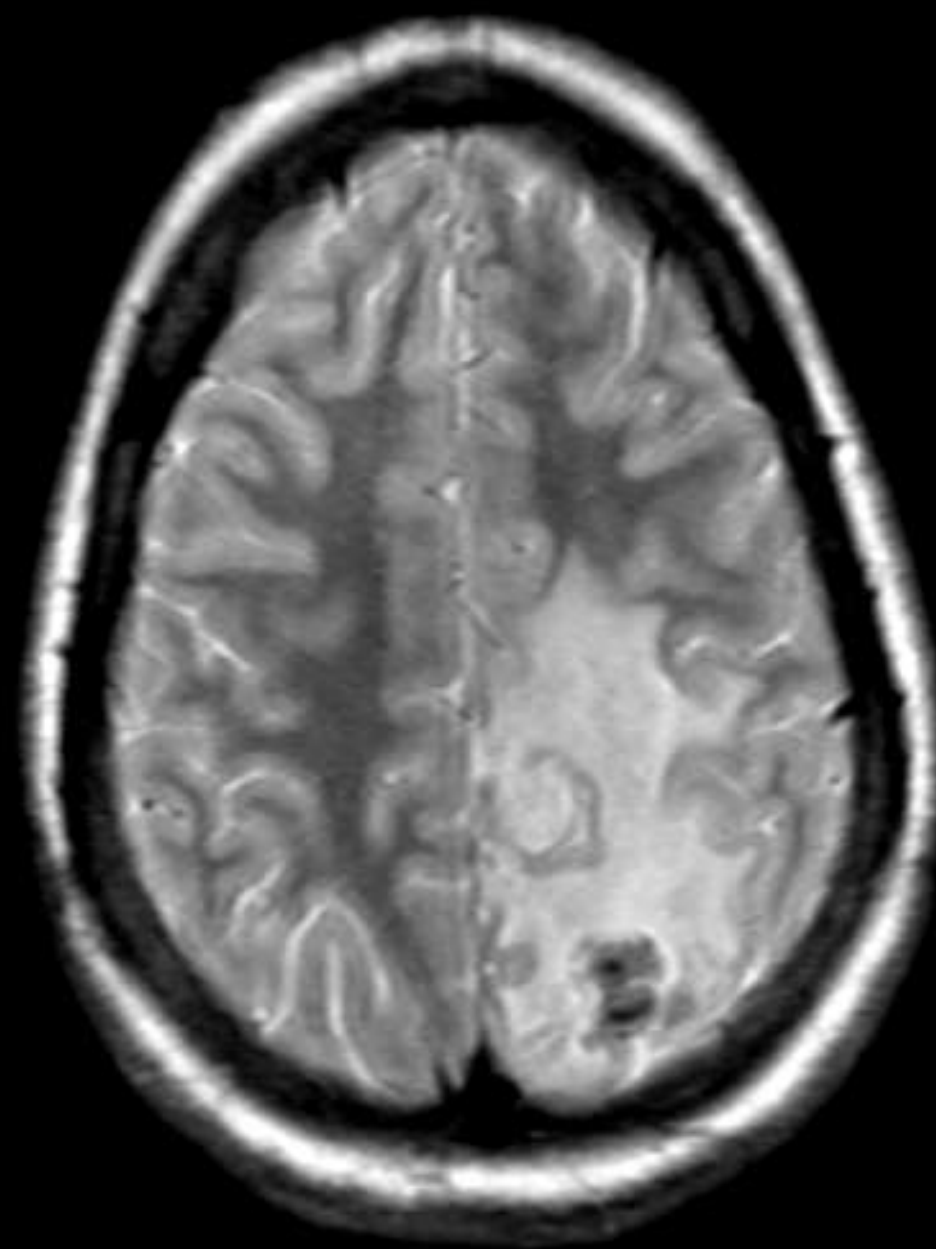


# Reactivation Tuberculosis

- **Constitutional symptoms often more prominent than respiratory symptoms**
  - Weight loss and fever are very common
  - Cough, chest pain, hemoptysis
  - Drenching night sweats occur several times per week
- **Cavitary lesions frequently seen**















**Another missed opportunity:**

**Can you die from TB if you are a teenager?**

**OR**

**Another example of why  
LTBI is important**

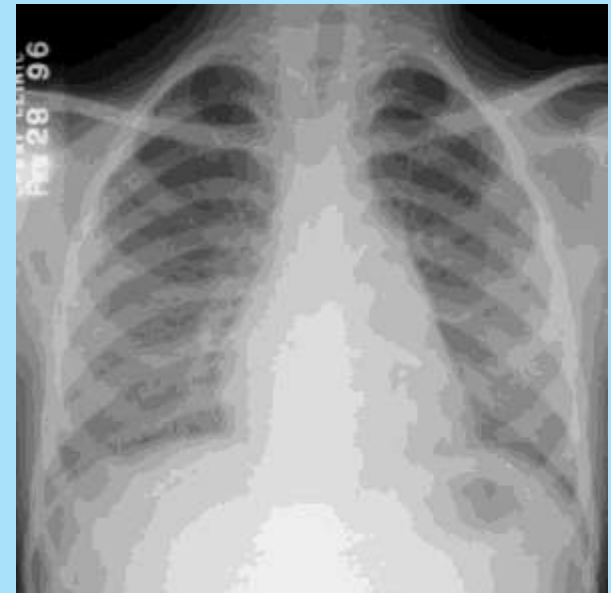
**AND**

**Sometimes you just have to  
buy 'em an air conditioner**



## Case

- 8-year old girl, recently arrived from Haiti was evaluated at the DOH for a 12 mm TST reaction
- There were no symptoms of TB disease and PE was normal
- A chest radiograph was done:





## Case

- **INH 200 mg po once daily; #30 tabs were dispensed**
- **There are no notes in the chart until 6 months later when the following is written: “Overdue for medication refill.”**
- **There were no further notes....until 5 years later.**



# Hospital Admission

- **The pt., now 13-years of age was admitted to an outside hospital with a 3 week history of fever, cough, increasing dyspnea, weakness**
  - She had been sent home by the school nurse on 4 occasions over 2 months for the fever and cough and then for weight loss and weakness
  - She was seen on 2 occasions by her PCP and was given antibiotics (azithromycin) And twice in EDs of local hospitals:
    - The last ED visit was 9 days PTA when chest radiographs were done and amoxicillin-clavulanate (Augmentin) was given
    - There was no improvement with antibiotic





## Case

- **PE: Cachetic, weak appearing female with flat affect and in mild respiratory distress**
- **T – 103.2°F HR – 160' RR – 22' O<sub>2</sub> sat = 92%**
- **Wt: 78.7 lbs UBWt.: 96.7 lbs**
- **Admitted**
- **Treatment IV ceftriaxone and oral azithromycin**





# Case

- **Sputa sent:**
  - Smear: Few AFB; culture (+) MTB; pansensitive
  - Smear: Few AFB; culture (+) MTB
  - Smear: Rare AFB; culture (+) MTB
- **Anti-TB medications started:**
  - INH 300 mg po daily
  - RIF 600 mg po daily
  - PZA 500 mg po, three times a day
  - Emb 400 mg po, twice daily
- **Received letter from local pediatric TB doctor and doses were adjusted**
- **Ensure given tid**







# Case

- **No notes on chart from 7/2-7/7**
- **Concern with continued fever, a short note appears in the chart:**
  - Please arrange social service consult for pt. “noncompliance” with medications, family safety.
  - ? Should we obtain court intervention? Or possible referral to DYFS?
- **Health insurance medical director recommend conference call between PCP and a Dr. Lee Richman of TB Center at UMDNJ in Newark**



# Case

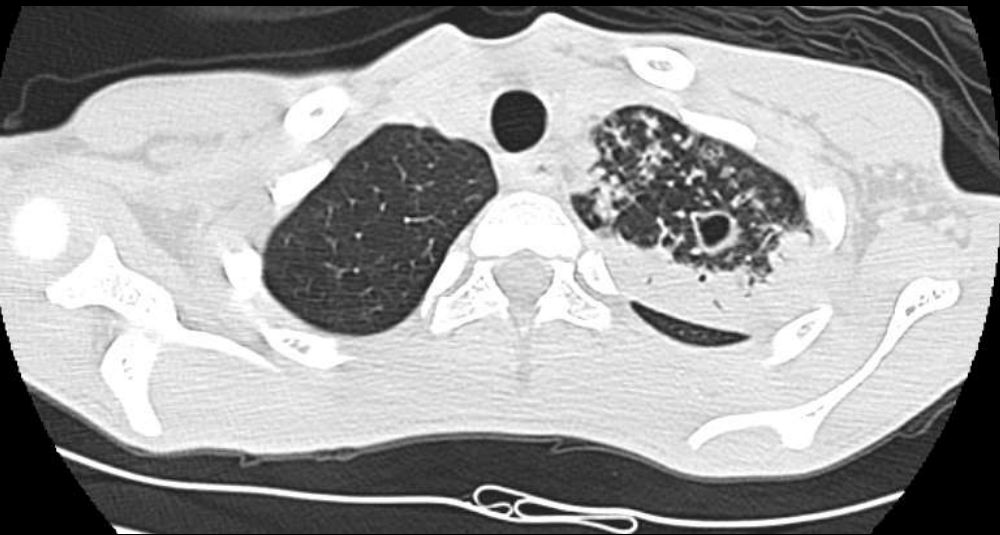
- **7/12: Discharge**

- Remains febrile
- Came directly to Hudson County Chest Clinic with “TB escort” and brother and sister
  - Cachectic, weak with unsteady gait
  - Continued treatment added supplement, ibuprofen
  - DOT by RN
  - Home visit by CRNP (ped NP)
    - Weak, tires easily, bed ridden, bed-bathroom, bedroom had no windows, home was very warm (no AC)
    - Poor oral intake
    - Tachypneic, tachycardic



# Case

- **7/19: Wt 72 lbs**
- **7/24: CT scan chest (high resolution)**
  - Call from CRNP, pt. very weak, tachypneic, may need admission





## Case

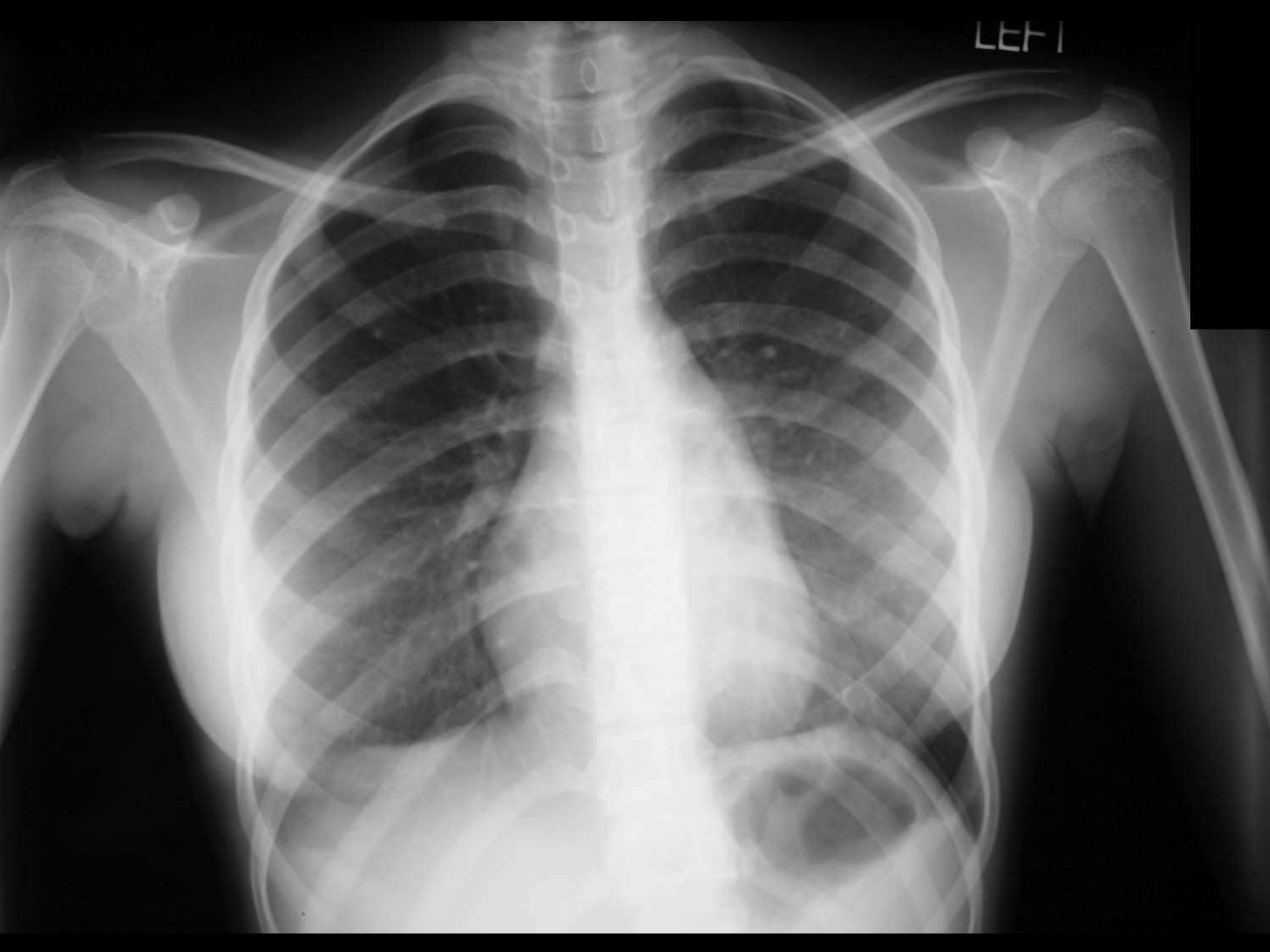
- Hospitalized 7/24-8/17: TB, weaker, hypoxia, cachexia; wt down to 66 lbs
- RR - 40' O<sub>2</sub> sat 90%
- Continued TB meds; oxygen
- NGT placed for continuous nutritional supplementation
- Gradually regained strength and began to walk
- Discharge: 8/17 RR – 20' on 1L oxygen; Wt 76 lbs
  - TB meds and supplement
  - AC purchased and placed in home





## Case

- 8/23: Wt. 88 lbs; RR = 18' O<sub>2</sub> sat 97% on RA
- 9/20: Wt. 97 lbs; RR = 18''
- 11/1: Wt. 99 lbs
- 12/13: Wt 102 lbs





# What happens to adolescents who survive the healthcare system and TB?

## Some become all-state volleyball players (actually many!), All-American college softball players, summa cum laude college graduates in IT, physicians



TOP 20		FINAL GROUP, PREP TEAM LEADERS	
1-Delmarcrest (26-1)	2-Cherry Hill East (22-2)	3-Union Catholic (25-4)	4-Pascack Valley (21-2)
5-Bridgewater-Raritan (29-2)	6-Cresskill (23-4)	7-Old Tappan (17-5)	8-Cherry Hill East (18-4)
9-Newark East Side (29-2)	10-Southern (26-1)	11-Huneydon Central (27-4)	12-North Arlington (23-2)
13-West Morris (25-4)	14-Williamstown (18-4)	15-Elizabeth (18-4)	16-Ridgewood (25-3)
17-Lakeland (21-4)	18-DelPax (20-8)	19-Hawthorne (29-2)	20-Laconedele (16-3)

ALL-BERGEN	
<b>FIRST TEAM</b>	<b>SECOND TEAM</b>
Britney Bellamy, Pasack Valley Janiya M. Alani, Crestall Alycia DeRosa, Pasack Valley Kathryn Nowinski, North Arlington Harriet Meyers, Demarest Tiffany Proctor, Crestall Sasha Kozak, Demarest Madison Spafford, Old Tappan	Christina Curletti, Crestall Rachy Figueroa, Ridge Maddy Roca, Pasack Valley Christy Walker, Demarest Janiya Madachni, Old Tappan Neyler Mousaka, Highland Park Anastasia O'Connell, Ina Alycia Woods, R. Ridgewood
<b>FIRST TEAM</b>	<b>SECOND TEAM</b>
Justis Carlin, Rte. 208 Lynn Giamonte, Old Bridge Katie Giamonte, Pasack Valley Hannah Holsinger, Lincroft Justine Pajunen, W. Milford Alycia Proctor, Ridge Yara Stone, Bridgewater Rte. 208 Laurie Tull, Huneydon Central	Nicole Bekasova, Bridgewater Janiya Madachni, North Arlington Christy Walker, Demarest Justine Pajunen, W. Milford Alycia Proctor, Ridge Yara Stone, Bridgewater Rte. 208 Laurie Tull, Huneydon Central
<b>FIRST TEAM</b>	<b>SECOND TEAM</b>
Adria Jackson, Livingston Maddie DeAngelis, Chatham Larissa Karamanidis, Chatham Maddy Kelly, Chatham Ursula Perini, East Hill Alana Rae Williams, Lincroft Hannah Zornice, East Hill Sara Zornice, East Hill	Erilyn Senkovic, Livingston Tara Bordignon, East Hill Jiyoung Lim, Livingston Maddie DeAngelis, Chatham Christy Walker, Demarest Justine Pajunen, W. Milford Alycia Proctor, Ridge Yara Stone, Bridgewater Rte. 208 Laurie Tull, Huneydon Central
<b>FIRST TEAM</b>	<b>SECOND TEAM</b>
Isabella Bernini, Scotch Plains Sofia Chiriac, Emerson (NJ) Aria Hanks, Chatham Corynne Haskilly, Emerson Caitlin Meehan, Hawthorne (NJ) Sara Murphy, Hawthorne (NJ) Megan Nunez, Hawthorne (NJ) Megan Nunez, Hawthorne (NJ)	Isabella Bernini, Scotch Plains Sofia Chiriac, Emerson (NJ) Aria Hanks, Chatham Corynne Haskilly, Emerson Caitlin Meehan, Hawthorne (NJ) Sara Murphy, Hawthorne (NJ) Megan Nunez, Hawthorne (NJ) Megan Nunez, Hawthorne (NJ)







# Treatment of Tuberculosis in Children and Adolescents

- **If INH resistance rate >4% or if other risk for resistance include four drugs in initial regimen:**
  - Isoniazid (10 mg/kg/day, range 10-20, max. 300)
  - Rifampin (15 mg/kg/day, range 10-20, max. 600)
  - Pyrazinamide (20-30 mg/kg/day)
  - Ethambutol (15-25 mg/kg/day)
- **Treatment complicated by child unfriendly preparations of the medications**
- **Directly observed therapy (DOT)**
- **Monitor LFTs – Depends on severity of disease**
- **Follow susceptibility studies of Mtb isolate (Index and/or child isolate)**
  - Important to be familiar with resistance patterns in the community



# **Difficulties in Treatment**

- **Lack of symptoms initially**
- **Lack of observable improvement**
- **Lack of culture “proof”**
- **Education of the caregiver**
- **Multiple caregivers**
- **Chronic dosing**
- **Language/cultural differences**
- **Child unfriendly dosing forms**
- **Communication with the child**



# **Negotiating a Plan for DOT**

- **Establish plan for DOT while patient is in the hospital or at first out-patient visit**
  - Assess child/family
  - Coordinate necessary resources/services
  - Individual treatment regimens:
    - Time/food/place/who
    - Daily vs. intermittent
  - Involve outreach worker/school nurse
- **Plan should be discussed with child and family**
- **Renegotiate if non-adherence occurs**



# Assessing Adherence Barriers

- **Parents: Adherence can be influenced by:**
  - Parenting skills
  - Motivation
  - Personal health beliefs, stigma
  - Other competing life circumstances
- **In children and adolescents adherence can be influenced by:**
  - Developmental level
  - Behavioral characteristics





# Barriers to (TB) Care of the Foreign Born

- **Cultural Beliefs**

  - “There’s no TB in my country”

  - Social consequences of diagnosis

- **Language**

  - Trained volunteer or professional medical translator

- **Healthcare system**

  - Seek care late

  - Little follow-up

- **Lack of insurance**

  - Fragmented care

  - Use of ED

- **Effect of employment on adherence**

  - Need to work to get paid

- **Misconceptions of BCG vaccine: Parents and**





# Cultural Variables

- **Ethnicity**
- **Race**
- **Gender**
- **Spirituality/religion**
- **Class**
- **Age**
- **History of the culture**
- **Caste/status**
- **Urban/rural origin**
- **Sexual orientation**
- **Language or dialect**
- **SES**
- **Sub-cultures**
- **Other?**



# **School-Based DOT**

- **School nurse can administer DOT in school**
- **Clinician will provide regimen for nurse to follow**
- **School nurse can give feedback to clinician on frequency of dosing that works well for child (medication must be given only once a day, but can vary the amount of times per week as per physician order)**
- **School nurse can also provide feedback on child's medical condition**



# Evaluation of Immigrant and Adopted Children

- Hepatitis B profile: HBsAg, anti-HBs, anti-HBc
- Hepatitis C antibodies: Children from China, former Soviet Union countries, Eastern Europe, Southeast Asia
- HIV testing
- TST
- Stool for ova and parasites
- RPR for syphilis
- CBC with diff
- Lead level
- Urinalysis by dipstick
- Vision, hearing and dental screening
- Developmental examination



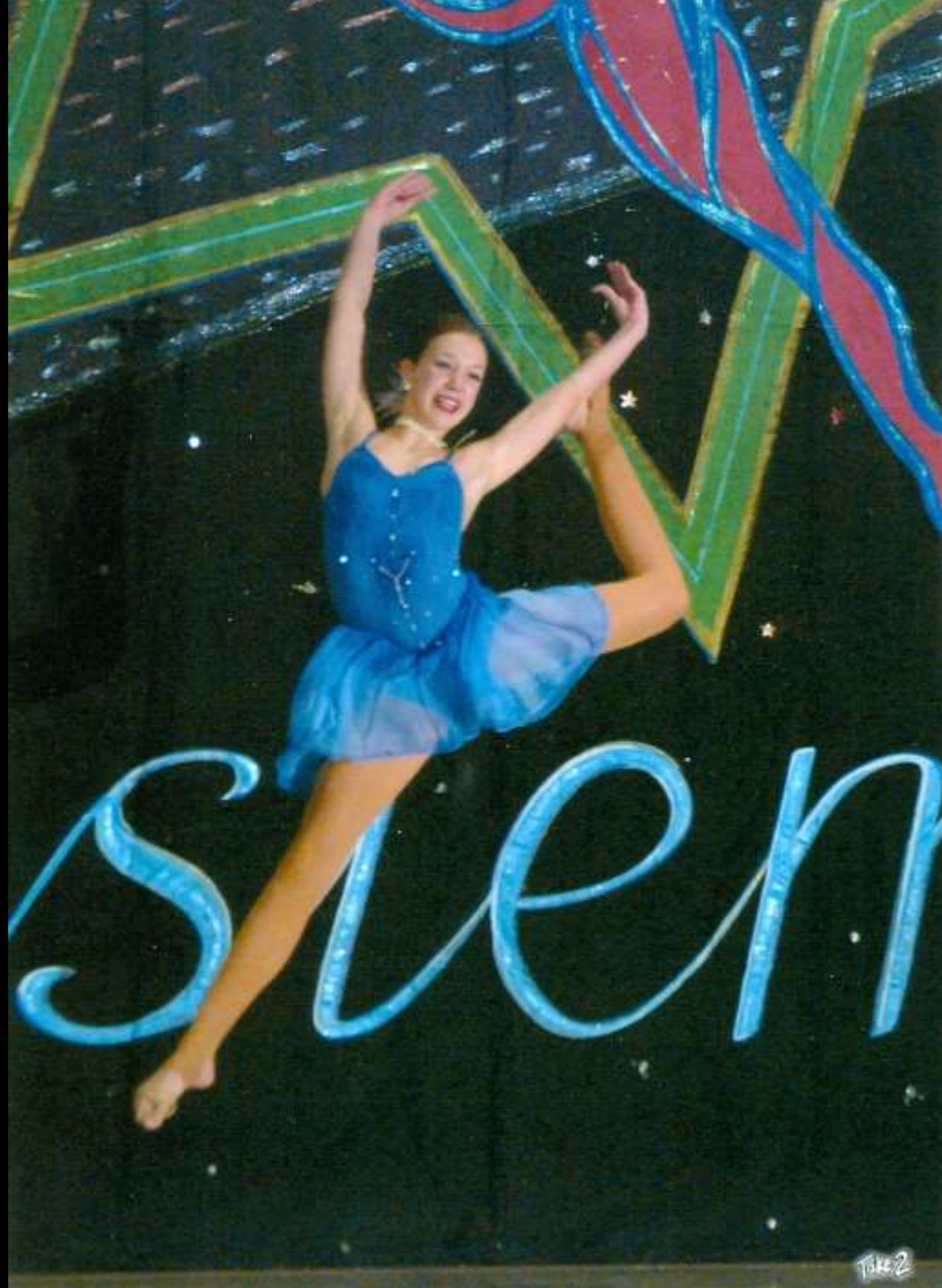
# **TB Clinic: Non-TB Diagnoses among Immigrant Children**

- **Bacterial pneumonia: S. aureus, S. pneumoniae**
- **Sinusitis**
- **Brain tumor, lymphoma**
- **Psychoses-schizophrenia**
- **Cystic fibrosis**
- **Diabetes mellitus**
- **Glomerulonephritis**
- **Lead poisoning: By chest radiograph**
- **Scoliosis**
- **Scabies: Entire families**
- **Tinea corporis**



# Indications for Isolation of the Hospitalized Child with Pulmonary Tuberculosis

- **Most children with tuberculosis are not contagious and require only standard precautions**
- **Exceptions are:**
  - Potential adult source case not yet identified
  - Cavitory disease
  - Laryngeal involvement
  - Extensive pulmonary disease
  - (+) sputum AFB smears
  - Suspected congenital tuberculosis
  - Productive cough





# Summary

- Reported cases of tuberculosis in the U.S.:
  - More than 2/3 occurs in nonwhite racial and ethnic groups
  - More than 50% occur in foreign born persons
  - Among children case rates are highest in infants and postpubertal adolescents
- Children are usually:
  - Infected by adult or adolescent household contacts
  - Not infectious (contagious)
- Contact investigations and targeted TB testing are mainstays of TB control in the U.S.
  - Evaluation of TB-exposed child: PA, CXR, window prophylaxis
  - Risk assessment questionnaires are the most effective screening tool to detect children at risk for LTBI
- TB diagnosis in young children requires a high index of suspicion
- DOT is key to successful treatment