Contact Investigation and Prevention in the USA

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Control of Tuberculosis in the United States

- Case finding and treatment
  - 2016: 9,272 cases: incidence 2.9 cases/100,000
  - 4.2% in children
- Contact investigations
  - Source case investigations
- Targeted testing of persons with risk
  - Diagnosis and treatment of LTBI is critical to control and elimination of TB in the U.S.

Red Book 2012

Objectives of the Contact Investigation

- Identify all high and low risk contacts
- Medically evaluate all appropriate contacts
- Identify contacts diagnosed with LTBI and provide appropriate treatment to completion of therapy thus *preventing future disease*
- Identify contacts diagnosed with TB disease and provide appropriate treatment to completion of therapy thus *preventing further transmission*
- Identify contacts at high risk of developing TB disease (e.g., children, immunocompromised) and provide appropriate treatment until infection and disease is ruled out

Control of TB in the United States

- Case finding + treatment -> Contact investigations
  - The most reliable TB control program is based upon aggressive and expedient contact investigations, rather than routine screening of large populations

High priority contact:

Household

Age <5 yrs

Med risk condition

Procedure

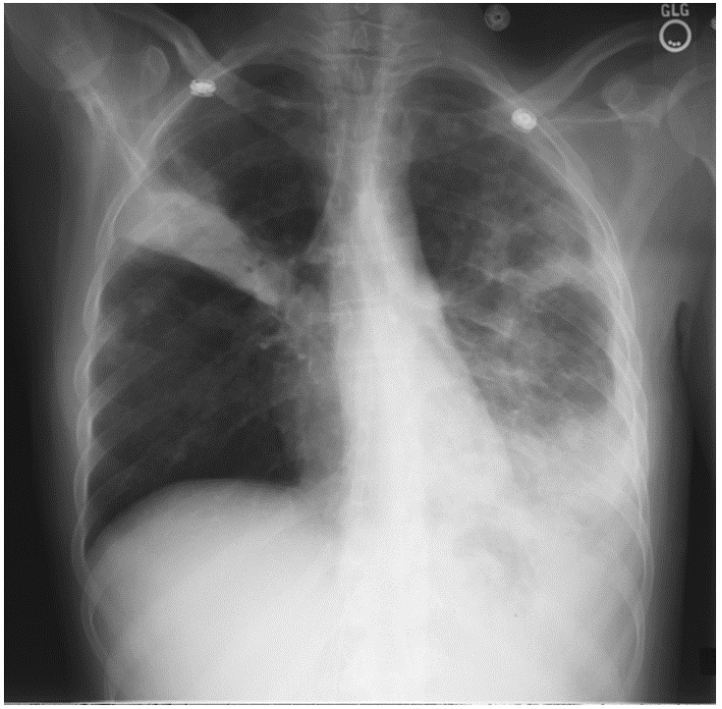
Congregate, Time

  - Can be complex and may require lots of detective work

Red Book 2009

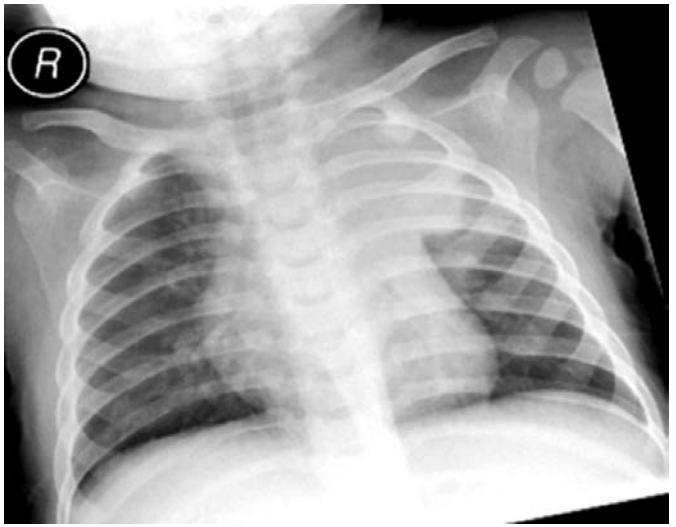
Contact Investigation

- A 39 year-old female was admitted to a New Jersey hospital with fever, decreased appetite, 11 kg weight loss, cough X 1-3 months, night sweats
- Chest radiographs were done
- Sputa were 4+ AFB, later identified as pansensitive M. tbc
- Presumptive case of TB reported to local health department
  - Place of employment-Daycare Center
  - Health department nurse contacted TB controller for the county

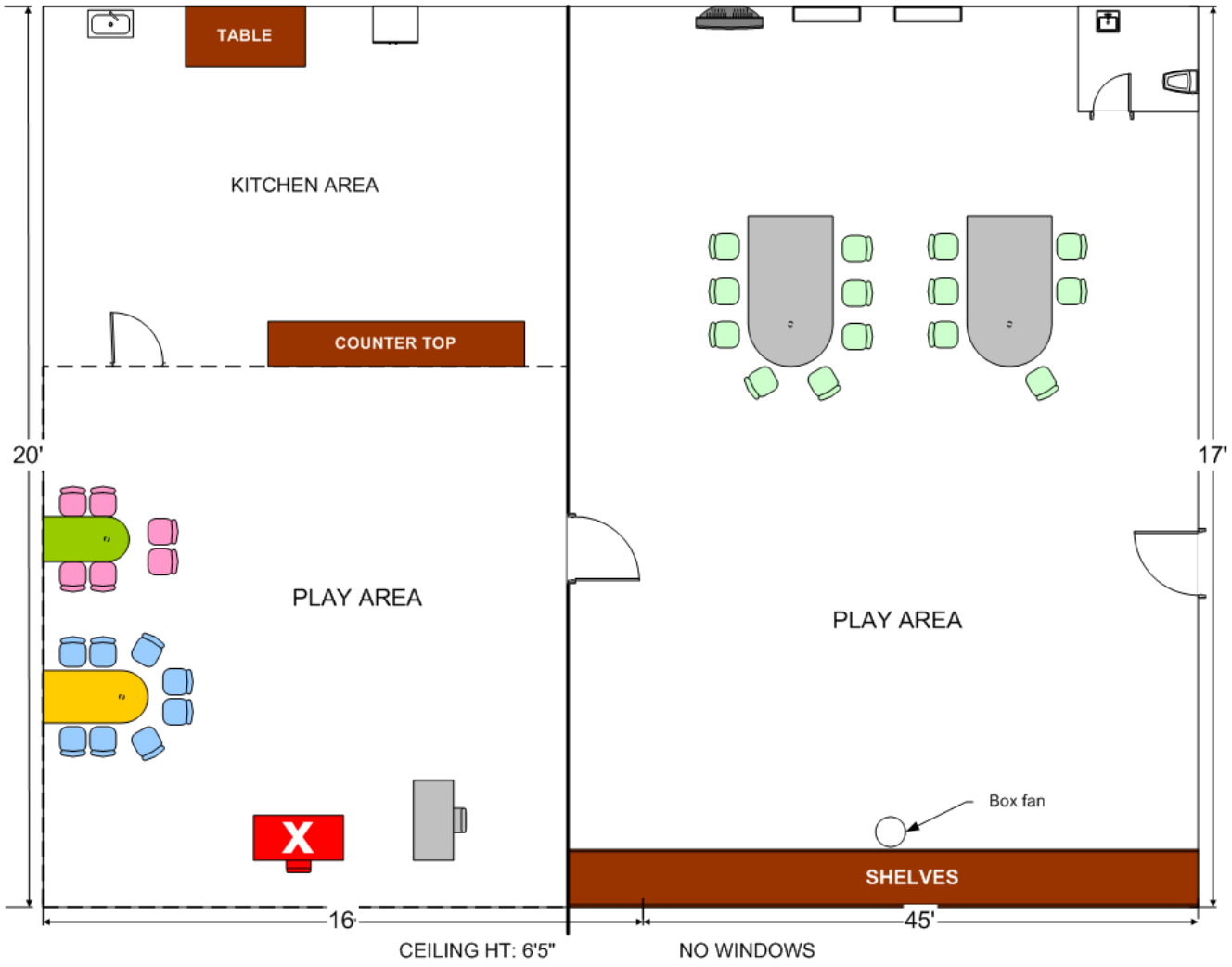


Daycare Contact (DCC) Investigation

- On-site assessment of DCC conducted by TB controller:
  - High priority contacts: 35
    - 30 children attend: All ≤4 years of age
    - 5 staff members: Adults and adolescents
  - Daycare is in a church basement
  - Index patient was secretary with “little” contact with the children
- Household and social contacts
  - High priority contacts: 9; field staff felt index pt. did not reveal all contacts
  - 4 are children: 2 are ≤1 year of age with recent history of pneumonia

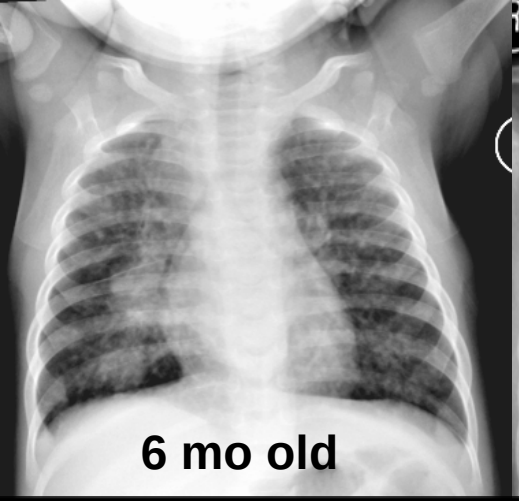


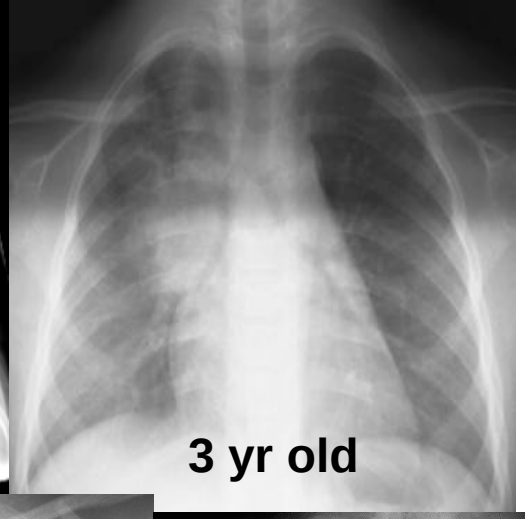
Church Basement-Daycare



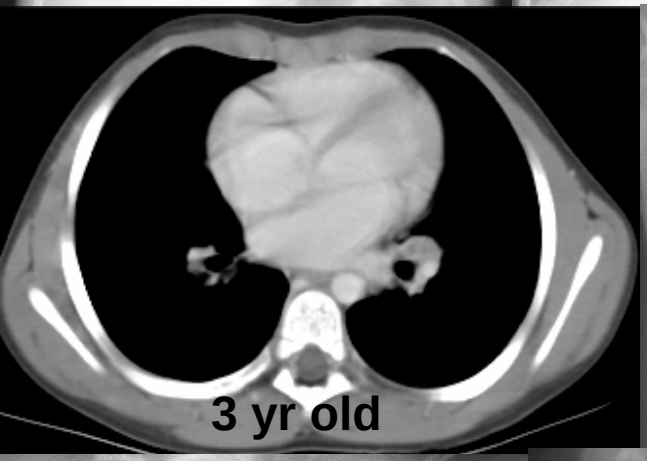
Contact Investigation Results: Totals After Initial Testing

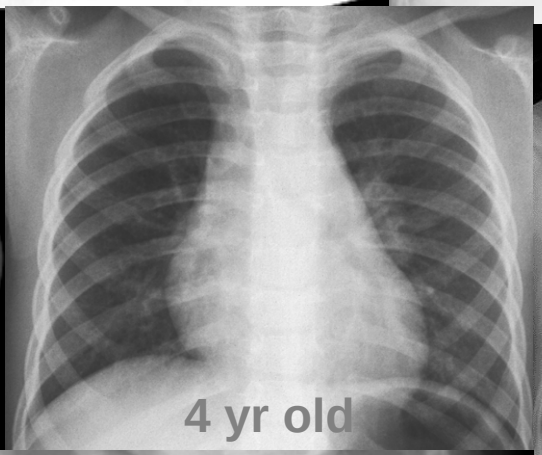
Daycare Center	35		30 ≤4 yrs old
(+) TST	14/35	(40%)	
(-) TST	21/35	(60%)	
TB disease	7/35	(20%)	All ≤4 yrs old
Household + Social	9		2 ≤4 yrs old
(+) TST	5/9	(56%)	
(-) TST	4/9	(44%)	
TB disease	2/9	(22%)	Both <1 yr old

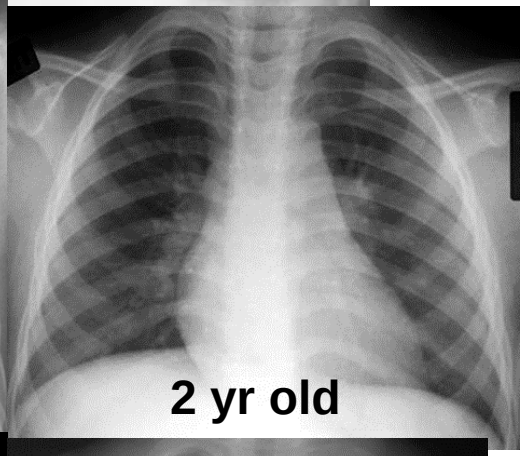


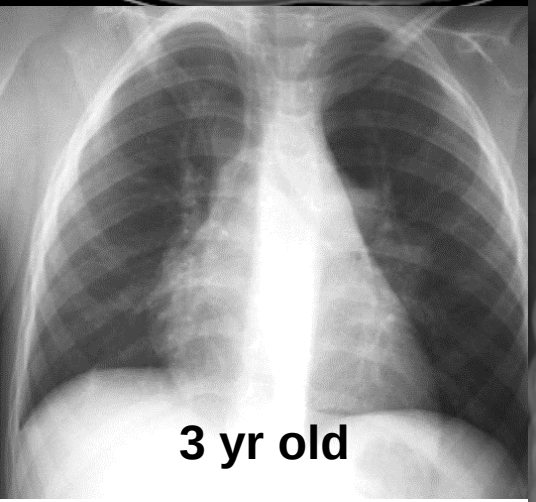


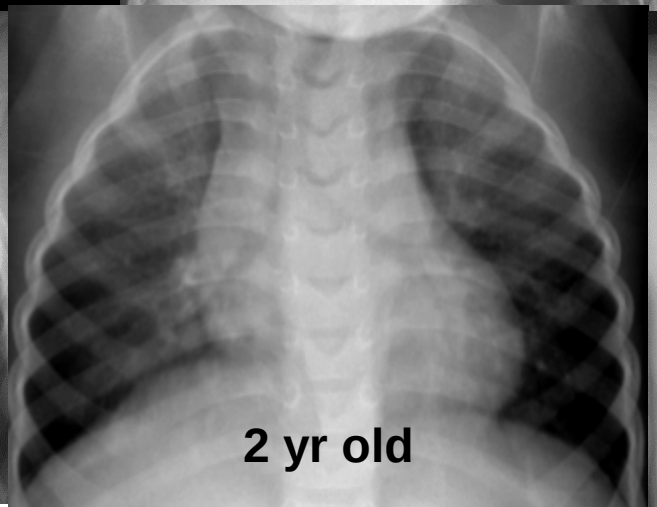
TB in Daycare

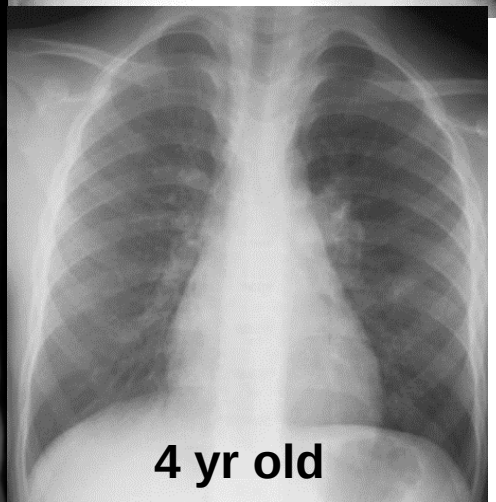




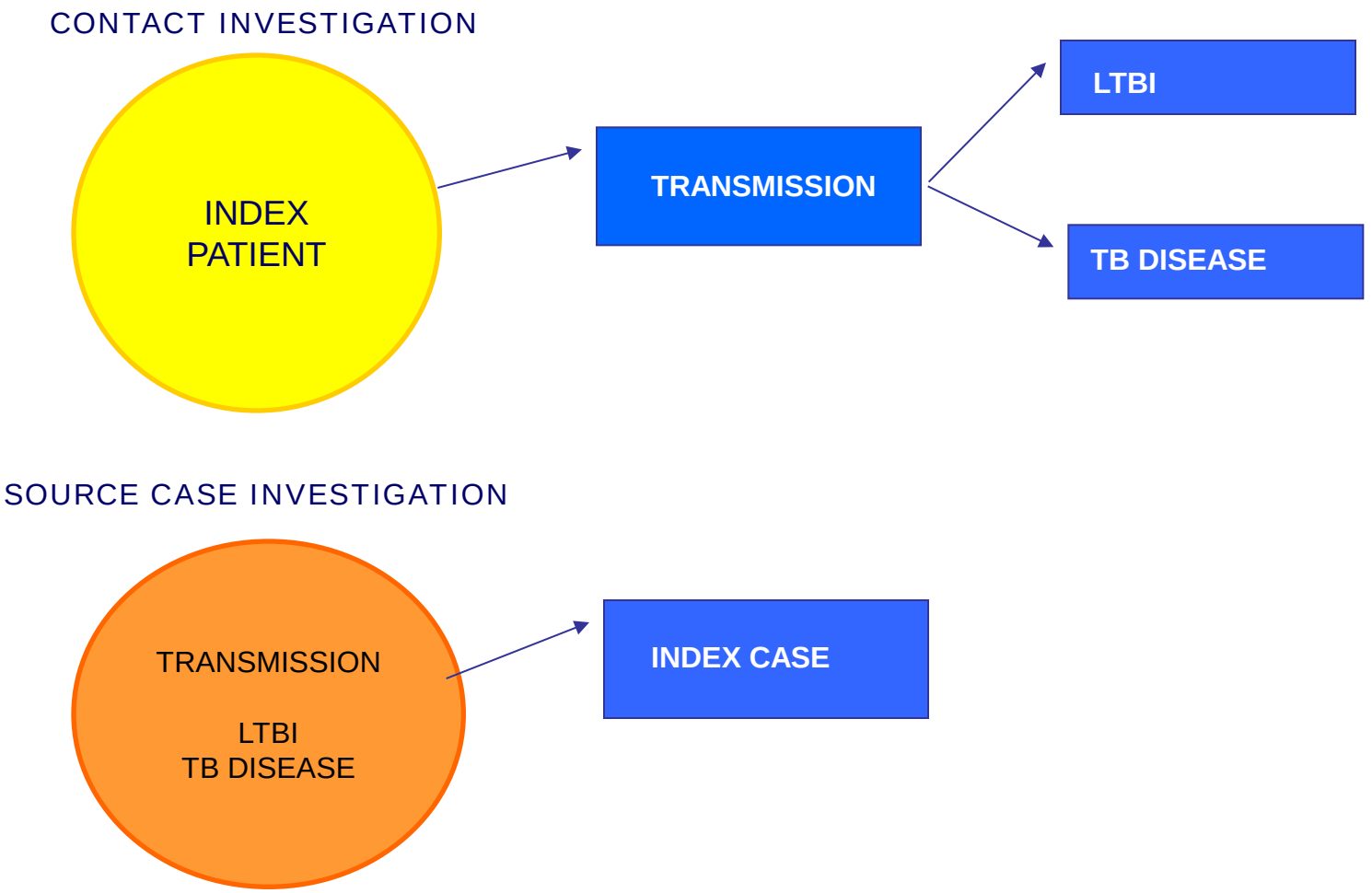


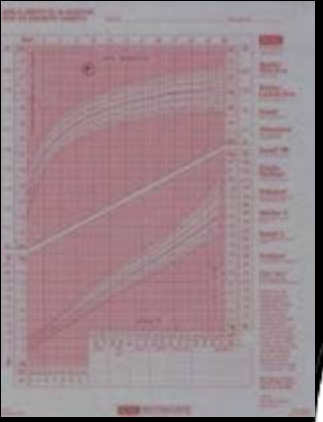






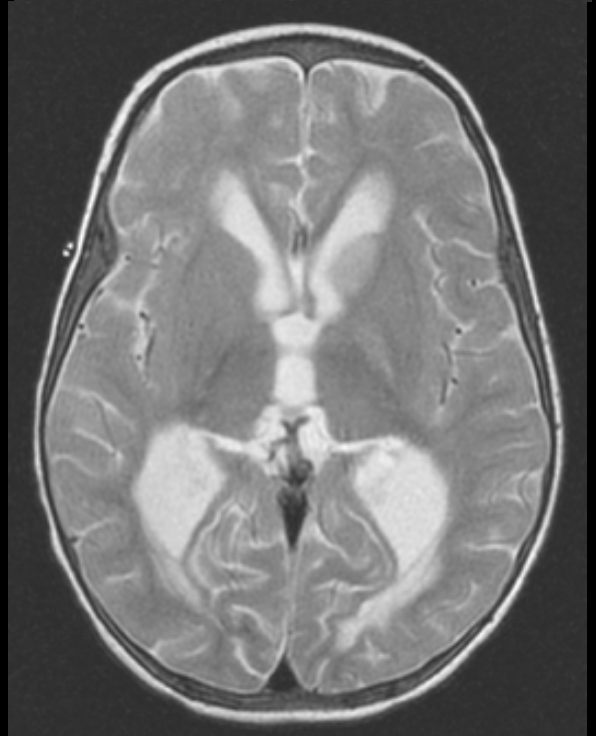
Contact vs. Source Case Investigation

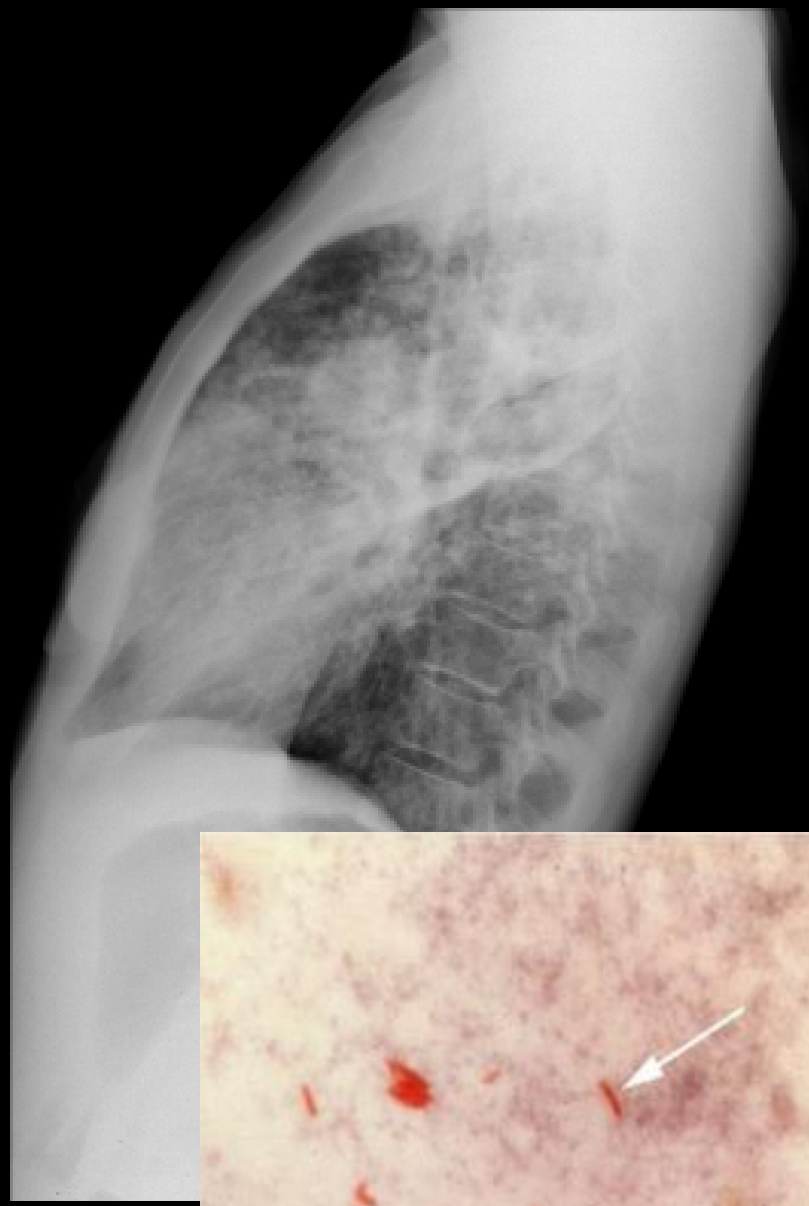


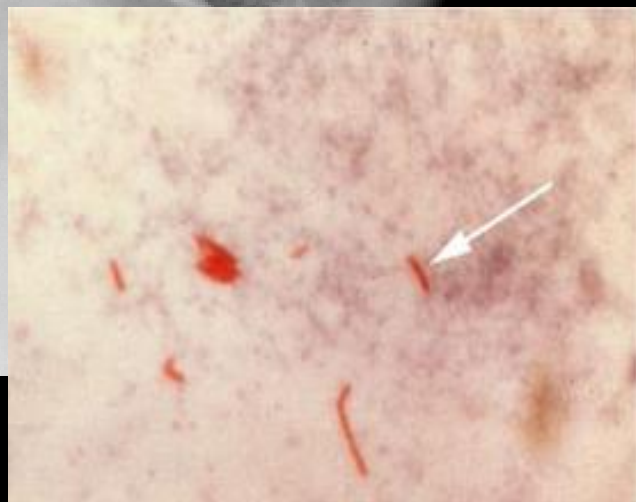


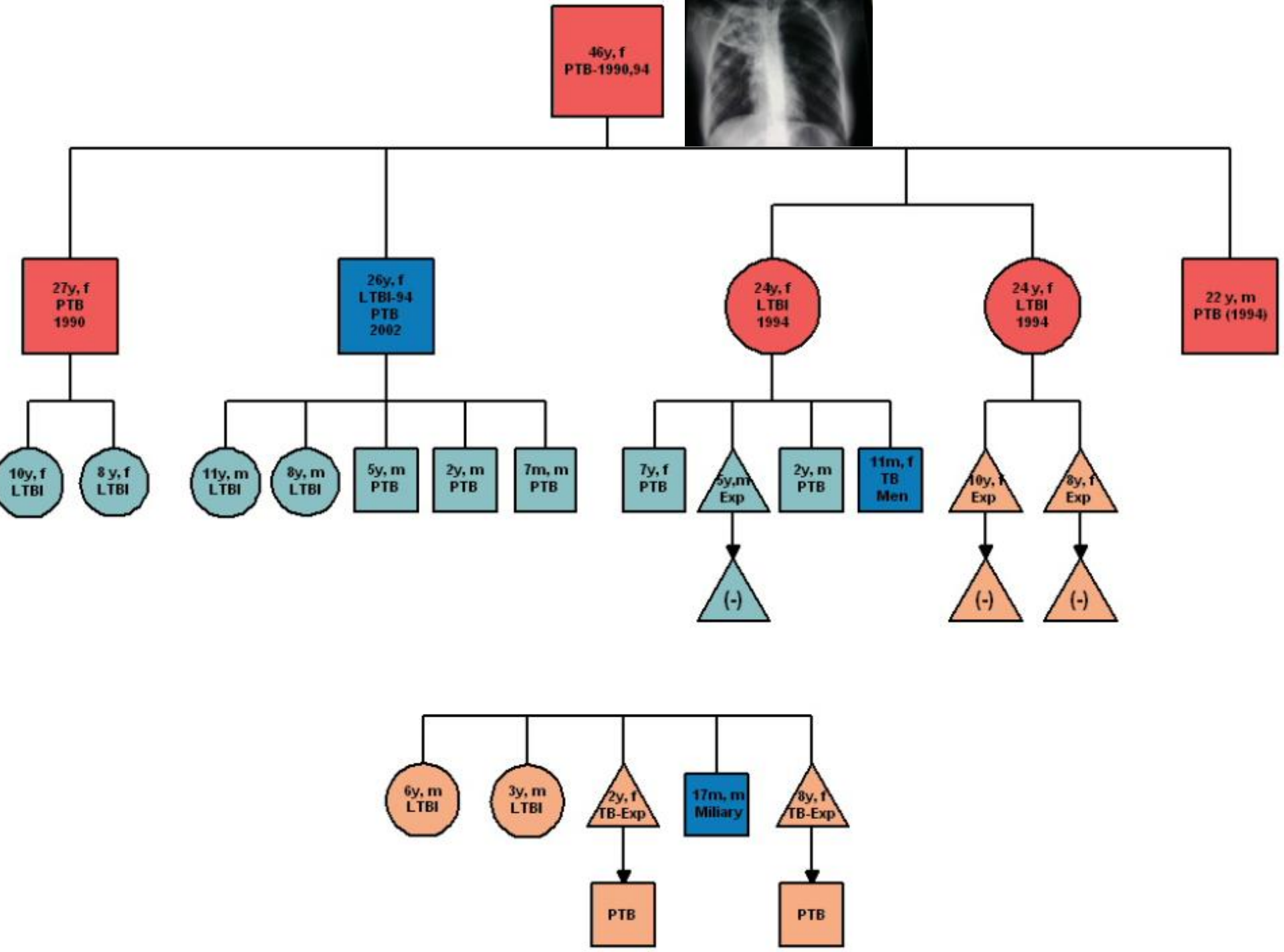
CT

MRI








46y, f
PTB-1990,94
27y, f
PTB
1990
26y, f
LTBI-94
PTB
2002
24y, f
LTBI
1994
24 y, f
LTBI
1994
22 y, m
PTB (1994)
10y, f
LTBI
8 y, f
LTBI
11y, m
LTBI
8y, m
LTBI
5y, m
PTB
2y, m
PTB
7m, m
PTB
7y, f
PTB
5y,m
Exp
2y, m
PTB
11m, f
TB
Men
10y, f
Exp
8y, f
Exp
(-)
(-)
(-)
6y, m
LTBI
3y, m
LTBI
2y, f
TB-Exp
17m, m
Miliary
8y, f
TB-Exp
PTB
PTB

US Contact Investigations Outcomes - Sputum AFB Smear (+)

Year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	
# Cases	14061	13727	13282	12895	11520	11163	10517	9951	9550	9406	
Sputum sm (+)	4828	4649	4776	4084	3668	3368	3417	3687	3648	3609	
# Contacts ID	73281	75410	76298	69542	66628	63068	72050	73677	69063	64148	
Evaluation Indices											***National Objective***
Contact index	**15.2**	**16.2**	**15.5**	**16.7**	**18.2**	**18.7**	**21.1**	**20.0**	**18.9**	**17.8**	
No contacts ID	8%	8%	7%	7%	6%	5%	5%	5%	6%	6%	
Evaluated	58624	60010	62630	57306	52259	53019	58785	60189	56464	52029	**93%**
Not evaluated	14656	15400	13668	12236	14369	10049	13265	13488	12599	12119	
TB disease	1%	1%	1%	1%	1%	<1%	<1%	<1%	<1%	<1%	
Infected	24%	23%	*23%*	22%	20%	19%	19%	19%	19%	17%	
LTBI treatment initiated	69%	72%	71%	74%	67%	74%	70%	68%	71%	72%	**91%**
LTBI treatment completed	63%	66%	68%	64%	67%	67%	66%	66%	71%	74%	**81%**

Targeted Testing for Tuberculosis in Children and Adolescents

- Children for whom immediate TST or IGRA is indicated:
  - Contacts of people with confirmed or suspected contagious TB (contact investigation)
  - Children with radiographic or clinical findings suggesting tuberculosis disease
  - Children immigrating from high rates of infections (Asia, Middle East, Africa, Latin America, counties of the former Soviet Union)
  - Children with history of significant travel to countries with endemic infection who have substantial contact with the resident population
- Children who should have annual TST or IGRA:
  - Children with HIV infection
- Children at increased risk of progression of TBI to TB disease
  - HIV infection, Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, malnutrition, prolonged or high-dose corticosteroid therapy, chemotherapy, tumor necrosis factor (TNF-alpha) antagonists

Red Book 2018

Changes in TB Diagnosis Tools in Children: IGRAs and the 2018 "RED BOOK"

- IGRAs recommended in immunocompetent children **≥2 years of age** [previously ≥5 years of age] in all situations where a TST would be used
  - Particularly useful for children who have received BCG vaccination
  - Use with caution in immunocompromised children

- TST was acceptable for all age groups and remains the preferred test for those <2 years of age

- In evaluating children for TB disease neither IGRAs nor the TST are perfect; always need clinical judgement

Red Book 2018

Treatment of Tuberculosis Infection in Children: 2018 Red Book and CDC

- Isoniazid + rifapentine (3HP)*
- Rifampin (4R)
- Isoniazid (9H)

*Red Book does not state a preference but says that some experts think 3HP is the preferred regimen

Borisov A, et al, MMWR 2018

LTBI treatment: 3HP for children

- As effective as 9H, shorter course, higher completion rates, safe, DOT or SAT, greater pill burden
- Children ≥12 years of age: Recommended as equal alternative to 9 months of INH
- Children 2-11 years of age: Recommended as equal alternative to 9 months of INH
- Children <2 years of age:
  - INH-RPT: Not recommended: Lack of safety and pharmacokinetic data in this age group

Villarino E, et al JAMA Pediatr 2015; Borisov A, et al, MMWR 2018

Dosing: 3HP

- INH (100 and 300 mg tabs):
  - Children age 2-11 years: 25 mg/kg/dose [900 mg]
  - Children older than 12 years of age: 15 mg/kg/dose [900 mg]

- Rifapentine (150 mg tabs):

Weight (kgs)	Dose (mg)	Maximum (mg)
10-14	300	
14.1-25	450	
25.1-32	600	
32.1-49.9	750	
>50	900	900

Treatment of Latent Tuberculosis Infection

- Rifampin for 15-20 mg/kg/day (max. 600 mg) po daily for 4 months (prior recommended dose 10-15 mg/kg)
  - Acceptable regimen for LTBI treatment
  - As effective as 9H, shorter course, better adherence, higher dose safe
  - INH not tolerated; index patient isolate INH-resistant
- Cruz & Starke, (IJTLD 2014): Rifampin 10-15 mg/kg/day (max. 600 mg) po daily for 4 months: Safe, completion rates similar to 9H by DOPT
- Gaensbauer (PIDJ 2018): No treatment failures: 395 children; well-tolerated; high completion rates
- Diallo (NEJM 2018): Rifampin 10-20 mg/kg/day for 4 months: Effective and safe as 9H

Treatment of Latent Tuberculosis Infection

- INH 10-15 mg/kg (max., 300 mg) PO daily for 270 doses
  - Efficacy approaches 100%; prevents TB meningitis
  - Poor completion rates due to treatment length
- 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:
  - 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, except:
    - Concurrent liver disease
    - Pregnancy or first 12 weeks postpartum
    - Concurrently on other hepatotoxic medications
    - Clinical evidence of heptatoxic effects

Summary of contact investigations and LTBI diagnosis and treatment in the U.S.:

- Contact investigations use the concentric circle model and target high priority/high risk contacts first
- Programs need to improve the number of contacts evaluated, started on and completing LTBI treatment
- Diagnosis and treatment of LTBI is critical to control and elimination of TB in the U.S.
- Short course treatment regimens (3HP and 4R) for LTBI are safe and effective in children and should lead to increased treatment completion rates which lead to:
  - A decrease in active disease among children following recent infection
  - A reduction of the reservoir of LTBI from which reactivation disease may develop in the future

Tuberculosis Exposure in Children <4 years of age and "**Window Prophylaxis**"

- History, PE, TST/IGRA, CXR are done
  - CXR is done regardless of TST/IGRA result
- IF the child is:
  - Asymptomatic and physical examination is normal
  - TST is negative (<5 mm) or IGRA negative
  - Chest X-ray is normal
- AND IF <4 years of age START: Isoniazid (INH) 10 mg/kg (max., 300 mg) PO once daily
- TST/IGRA repeated 8-10 weeks after contact broken with infectious adult:
  - If TST/IGRA (-), discontinue INH
  - If TST/IGRA (+), re-evaluate child and treat accordingly

Targeted TB Testing Risk-Assessment Questionnaire

- Has a family member or contact had TB disease?
- Has a family member had a positive TB 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 significant time with the resident population?

Red Book 2018

Percentage of Pediatric TB Cases by Age Group, 1993–2016