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World Tuberculosis (TB) Day 2024: Clinical and Public Health Approaches to Pediatric TB

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PHO Rounds: World TB Day 2024

Land Acknowledgement

Disclosures

- Ms. Saunders does not have any conflicts of interest to disclose
- Dr. Kitai does not have any conflicts of interest to disclose
- Ms. Joshi does not have any conflicts of interest to disclose

Learning Objectives

By the end of this session participants will be able to:

- Describe the recent epidemiology of TB in Ontario including in children aged 0-15 years;
- Identify aspects of the clinical presentation, diagnosis, and management unique to pediatric TB;
- Identify key aspects of public health management unique to pediatric TB, including source case finding and contact investigations;
- Consider how collaboration between local public health organizations and clinicians can support TB case and contact investigations involving children.

Outline

- Provincial trends in the epidemiology of pediatric TB
- Clinical presentation, diagnosis, and management of pediatric TB
- Public health management of pediatric TB, including source case and contact investigations
- Discussion

Polling Question #1

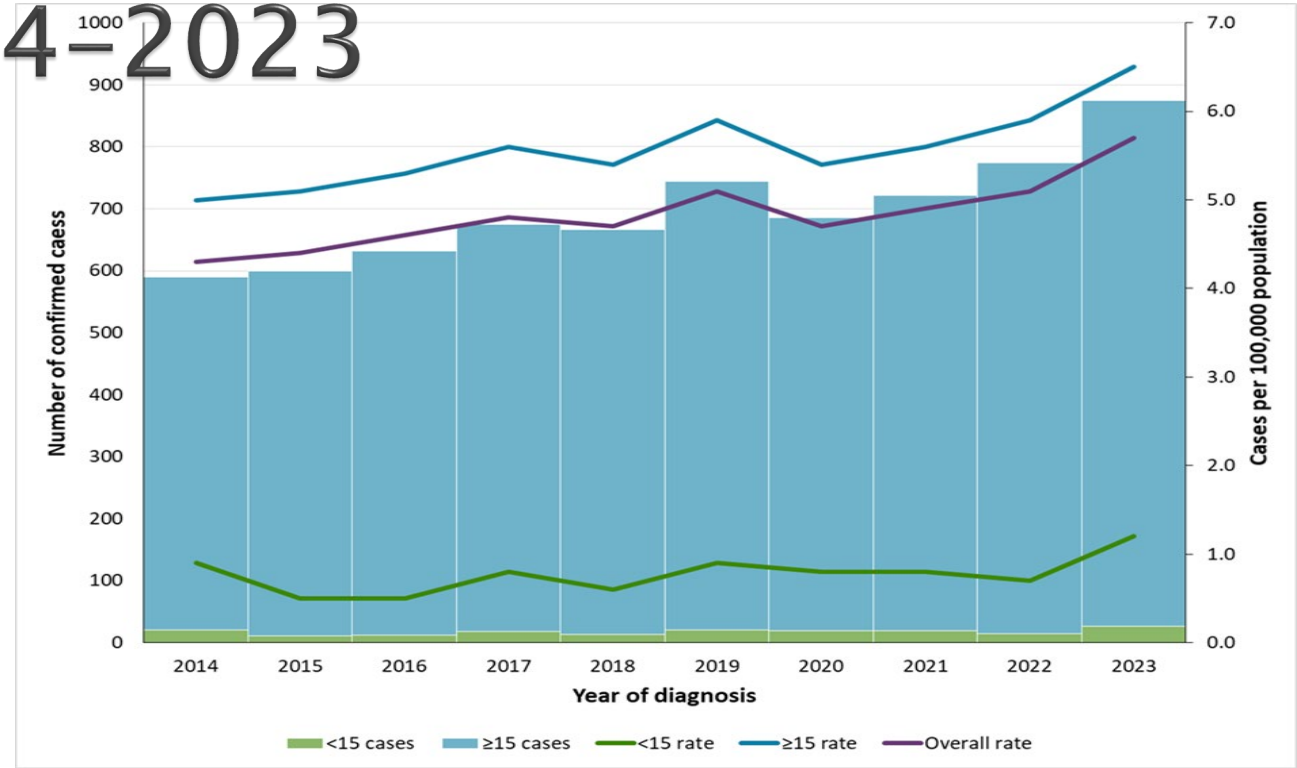
True or False?

In Canada, most cases of childhood TB occur in children who were born in high TB incidence countries?

Epidemiology of Childhood TB (<15 Years of Age)

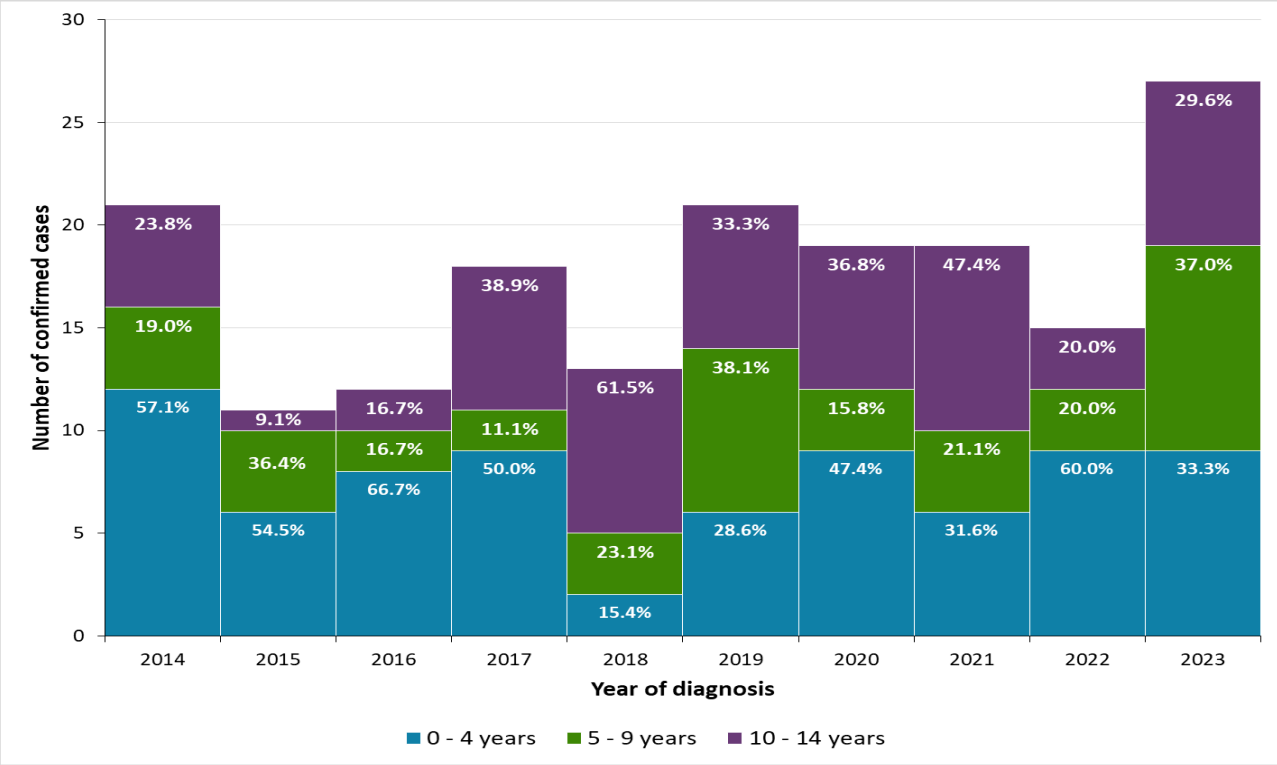
- Children <15 years accounted for ~12% of the estimated global TB burden in 2022[1]
  - In Canada and other low TB burden countries this proportion is <5%[2,3]
- In Canada and the United States (US), most childhood TB cases occur among those born in Canada/US to parent(s) who were born outside of Canada/US[3,4]
  - Of those born in Canada/US, there is a disproportionate burden among children most affected by the social determinants of health (e.g., poverty, Indigeneity)[3–5]
- Travel to high-TB incidence countries has also been identified as a risk factor for the acquisition of TB in children born in Canada and the US[5,6]

Incidence of Active TB by Age Group and Year of Diagnosis: 2014-2023



Data source: Ontario. Ministry of Health. integrated Public Health Information System (iPHIS). [Extracted 2024 Mar 6]

Proportion of Active TB Cases <15 Years by Age Group and Year of Diag



Data source: Ontario. Ministry of Health. integrated Public Health Information System (iPHIS). [Extracted 2024 Mar 6]

TB Cases by Provincial Region and Age Group: 2014–2023

Provincial region	Cases <15 years n (%)	Cases ≥15 years n (%)	Total cases n (%)
Central East	43 (1.9)	2,269 (98.1)	2,312 (100.0)
Central West*	21 (3.0)	676 (97.0)	697 (100.0)
Eastern*	32 (5.4)	558 (94.6)	590 (100.0)
North West*	11 (14.1)	67 (85.9)	78 (100.0)
North East*	9 (9.5)	86 (90.5)	95 (100.0)
South West	8 (2.9)	265 (97.1)	273 (100.0)
Toronto (reference)	53 (1.8)	2,869 (98.2)	2,922 (100.0)
Ontario	**177 (2.5)**	**6,790 (97.5)**	**6,967 (100.0)**

*significant at $p<0.05$

Data source: Ontario. Ministry of Health. integrated Public Health Information System (iPHIS). [Extracted 2024 Mar 6]

TB Cases by Origin of Birth and Age Group: Ontario, 2014–2023

Origin of birth	Cases <15 years n (%)	Cases ≥15 years n (%)	Total cases n (%)
Born outside Canada*	52 (29.4)	6,111 (90.0)	6,163 (88.5)
Born in Canada*	115 (65.0)	429 (6.3)	544 (7.8)
Indigenous*	13/115 (11.3)	119/429 (27.7)	132/544 (24.3)
Unknown/missing	10 (5.6)	250 (3.7)	260 (3.7)
Total	**177 (100.0)**	**6,790 (100.0)**	**6,967 (100.0)**

*significant at $p<0.05$

Data source: Ontario. Ministry of Health. integrated Public Health Information System (iPHIS). [Extracted 2024 Mar 6]

TB Cases by Disease Type and Age Group: 2014–2023

Figure 1: Proportion of cases by disease type and age group

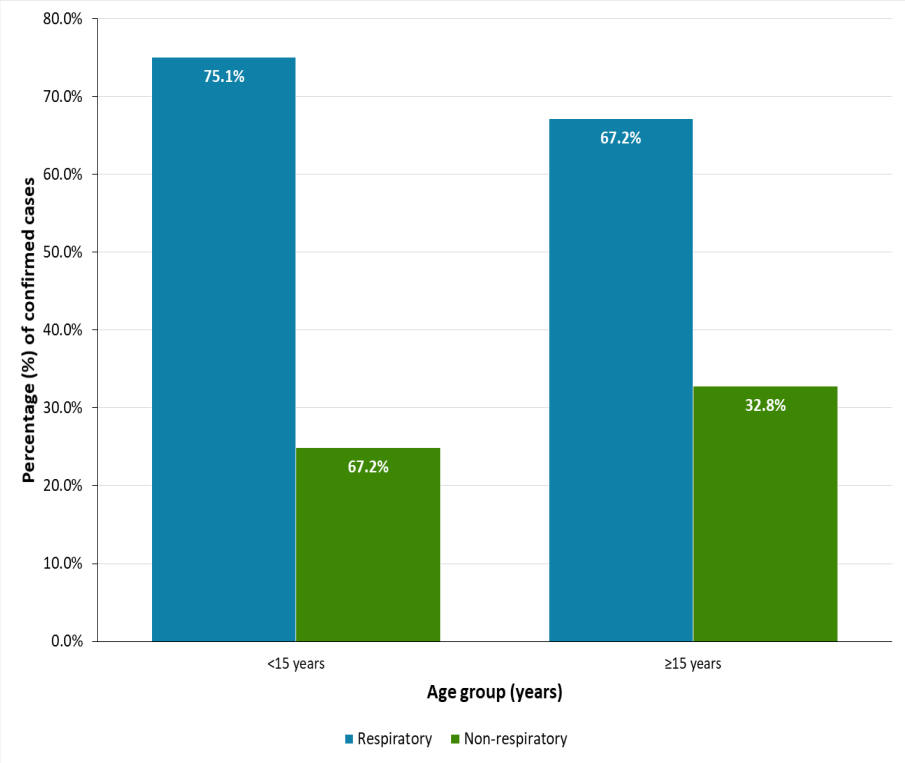
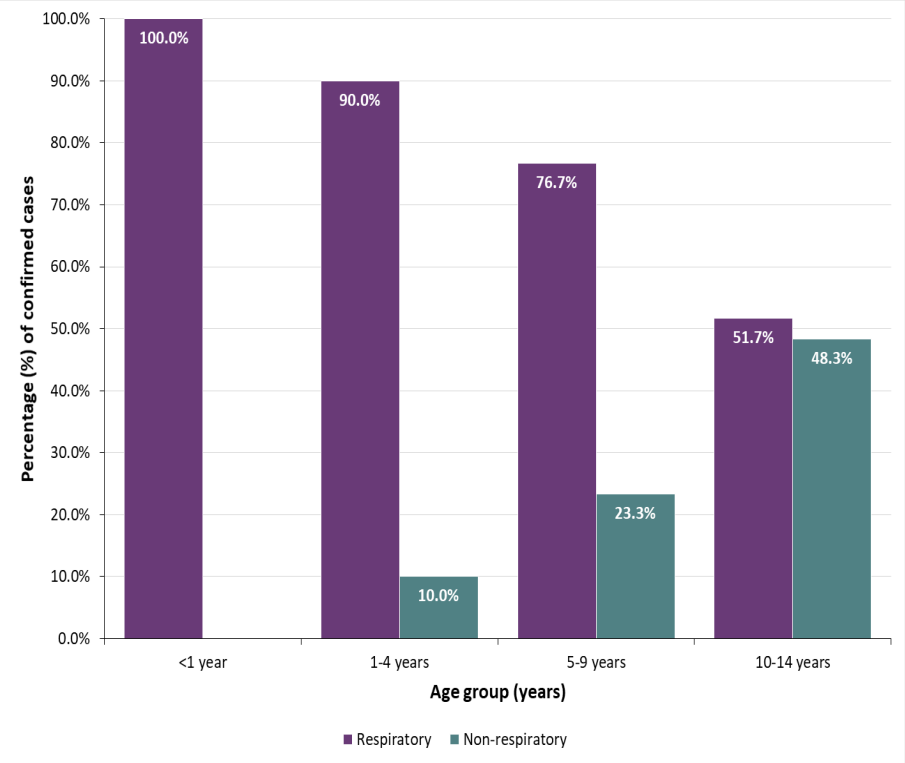


Figure 2: Proportion of cases by disease type: <15 years only



Data source: Ontario. Ministry of Health. integrated Public Health Information System (iPHIS). [Extracted 2024 Mar 6]

Key Messages: Epidemiology of Childhood TB in Ontario: 2014-2023

- In Ontario, children <15 years accounted for, on average, 2.4% (149/6,090) of the annual burden of TB between 2014-2022; this proportion increased to 3.1% (27/875) in 2023
- Compared to those ≥15 years, a higher proportion of childhood TB cases were born in Canada (65% vs. 6.3%, $p<0.00001$)
- Childhood TB cases were more likely to have respiratory disease compared to those ≥15 years (75.1% vs. 67.2%, $p<0.05$)
  - For those <15 years, the proportion of cases with respiratory disease decreased with increasing age
- Of childhood TB cases with risk factor data available, 50/162 (30.9%) lived and/or traveled to an endemic country

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1. World Health Organization. Global tuberculosis report 2023 [Internet]. Geneva: World Health Organization; 2023 [cited 2024 Mar 8]. Available at: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023
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3. Cowger TL, Wortham JM, Burton DC. Epidemiology of tuberculosis (TB) among children and adolescents in the United States, 2007-2017: an analysis of national surveillance data. Lancet Public Health.2019;4(10):e506-e516. Available at https://doi.org/10.1016/S2468-2667(19)30134-3
4. Kitai I, Morris SK, Kordy F, Lam R. Diagnosis and management of pediatric tuberculosis in Canada. CMAJ. 2017;189(1):e11-e16. Available at: https://doi.org/10.1503/cmaj.151212
5. Ali M, El Hafid M, Farrar DS, Kourdi H, Rea E, Waters V, et al. Travel-acquired paediatric tuberculosis in the greater Toronto area, Canada, 2002-2018. Eur Respir J. (in press)
6. Rayment JH, Guthrie JL, Lam K, Whelan M, Lee B, Kitai I. Culture-positive pediatric tuberculosis in Toronto, Ontario: sources of infection and relationship of birthplace and mycobacterial lineage to phenotype. Pediatr Infect Dis J. 2016;35(1):13-8. Available at: https://doi.org.10.1097/INF.0000000000000915

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Pediatric Tuberculosis: Clinical features

Ian Kitai
TB Specialist
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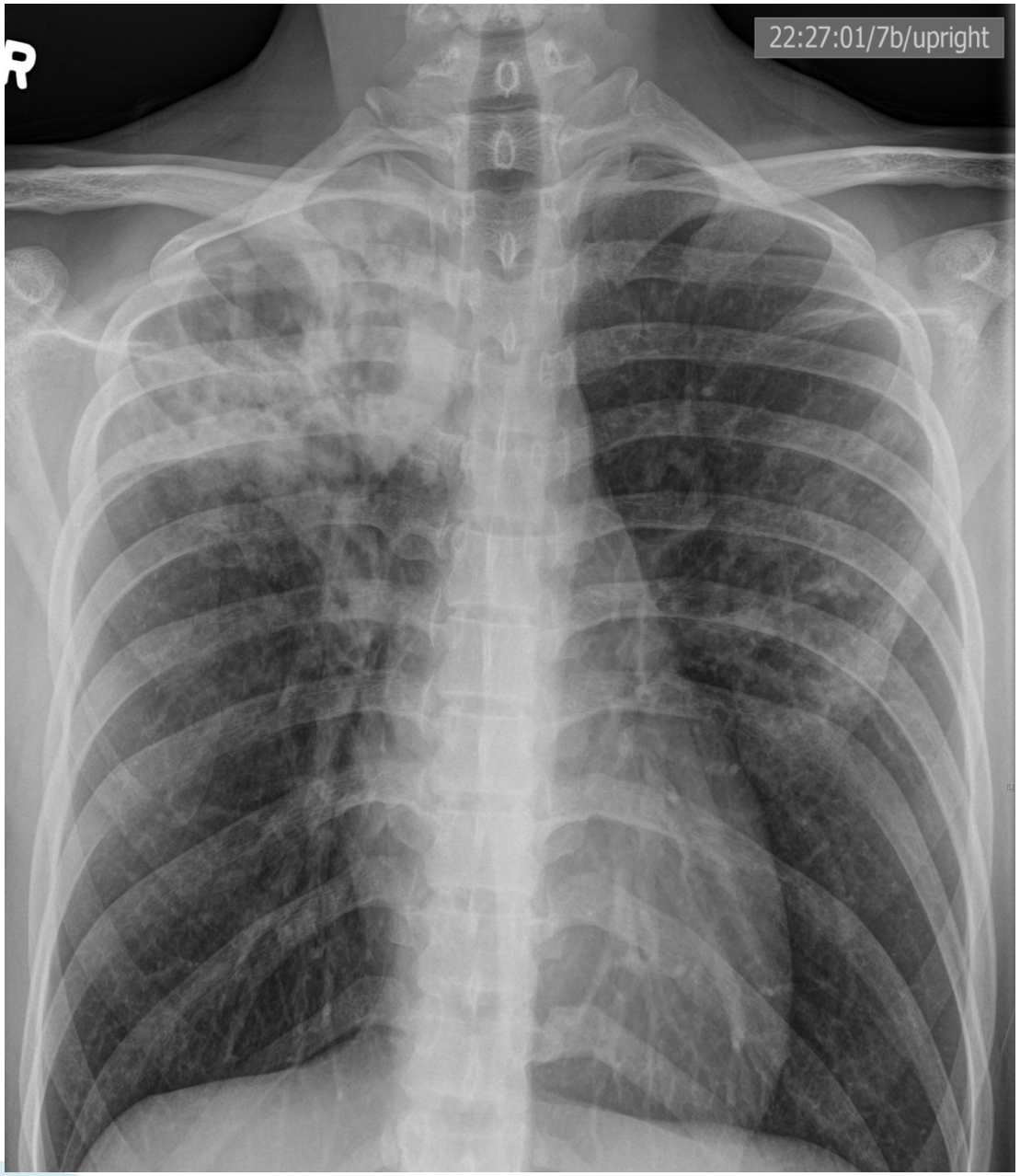
- Patient details have been altered to help preserve confidentiality.

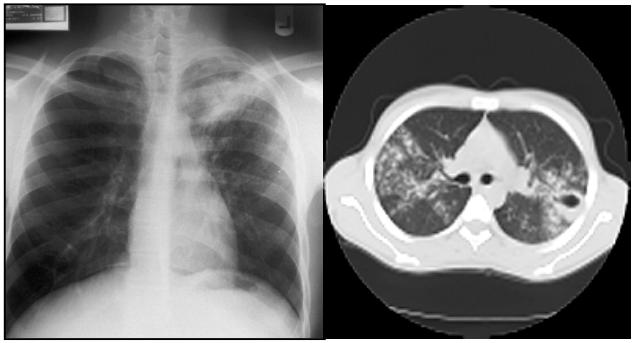
- **Childhood TB – Age <15 years**
- **Pediatric TB- Age <17 years**

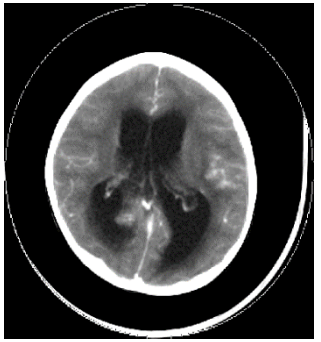
Outline:

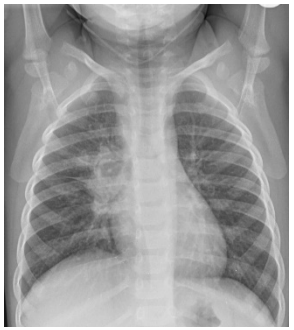
- Childhood TB and Adult TB- contrast
- Age related presentation of TB and immunologic correlates
- Diagnostics in Young Children
- TB in adolescents- clinical features
- Missed opportunities for diagnosis

Adolescent with cough



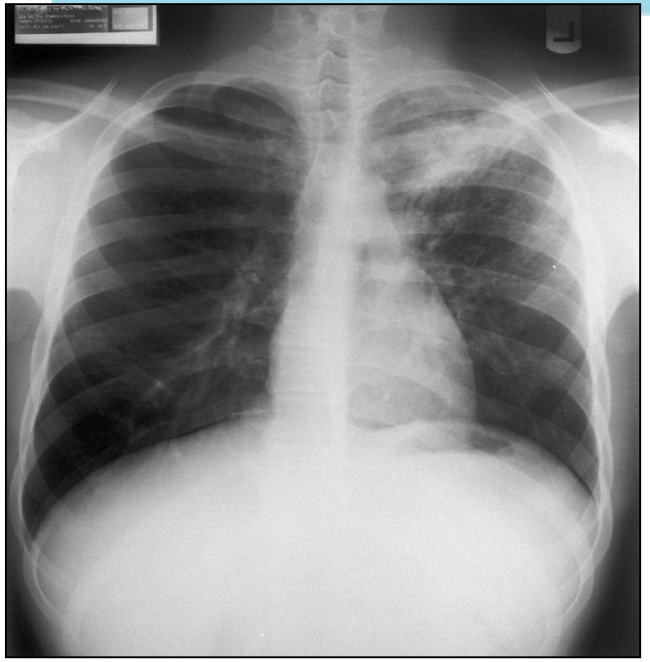






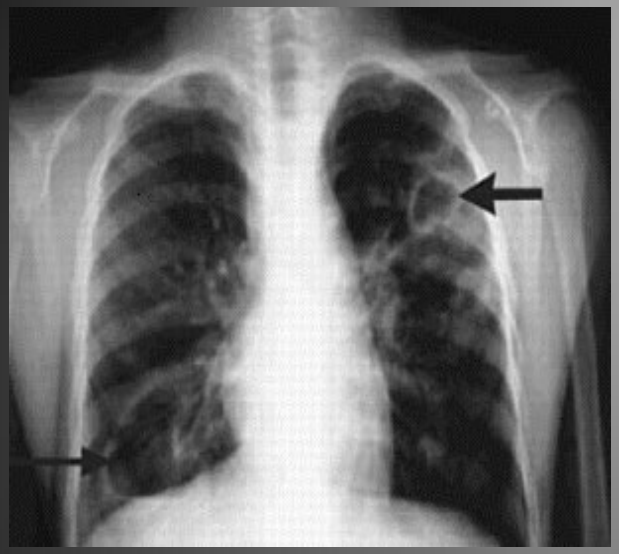
Adult TB	Childhood TB (<15)
Typical symptoms	Nonspecific symptoms
Often Pulmonary	Often Extrapulmonary
MULTIBACILLARY Sputum easy to obtain Often culture positive Often smear- positive	PAUCIBACILLARY Cultures difficult Often culture negative Very often smear negative
SMEARS AND CULTURES CONVERT TO NEGATIVE	**REPEAT SPECIMENS DIFFICULT AND UNRELIABLE**

TB:Who Infects Others ?

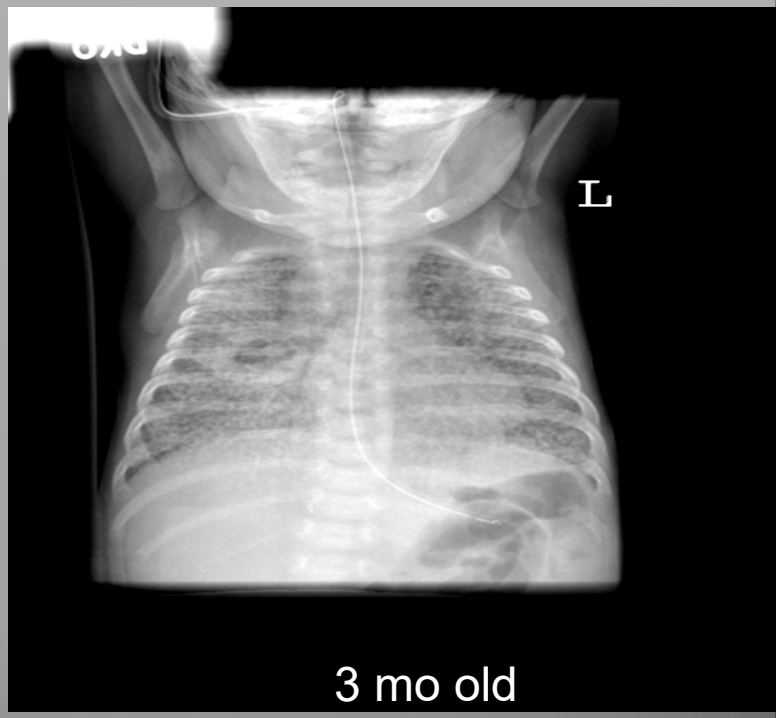


1. Close contacts with multibacillary and cavitary disease and cough-ADULTS or ADOLESCENTS. Smear positive=more infectious
2. Less often: smear negative culture positive patients

Children generally not infectious- some exceptions



- 9 yr old.- Infected ¾ household
- 16/24 classroom contacts
- Curtis et al N Engl J Med 1999 Nov3411491-



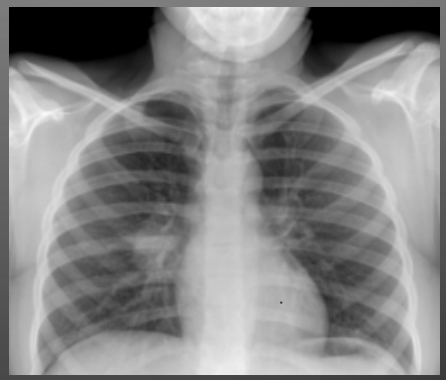
3 mo old

Infected 2 HCW's

Parents

Both children had multibacillary disease with cavities

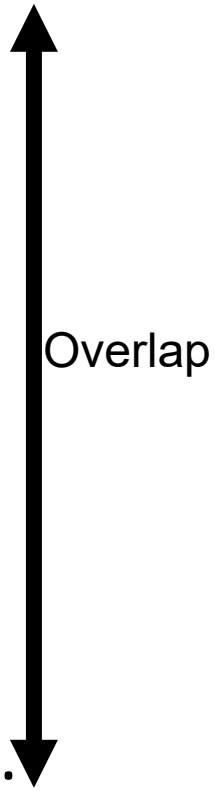
Risk generally from adults accompanying child



Not infectious

TB in childhood. Presentation

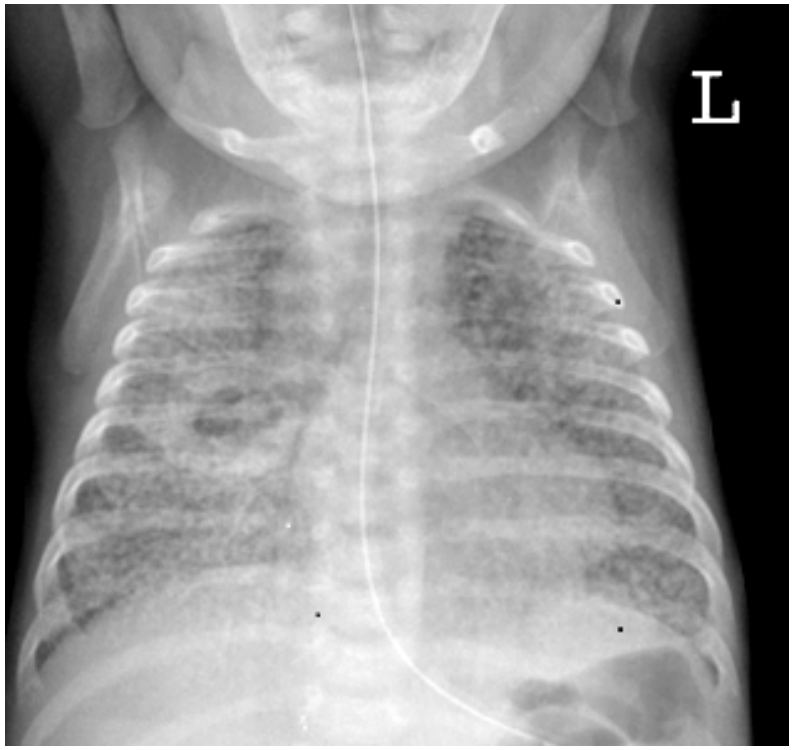
- Very young <5, esp. < 1
  - Miliary , pulmonary, extrapulmonary, TB meningitis
- Young child
  - Primary complex and its complications
- Older child and adolescent
  - Pulmonary and extrapulmonary- protean.



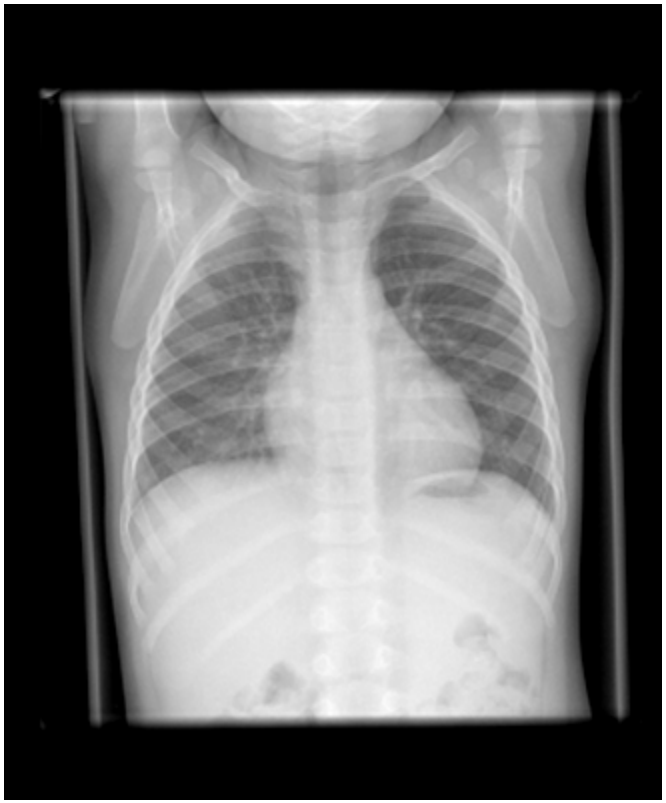
Crockett M, Clinical Infectious Disease 2004: 39:1719-23

TB in the very young

- 3 month old
- Hx pertussis like cough
- Fever
- Canadian Born
- Unwell
- Hemophagocytosis
- ICU admission



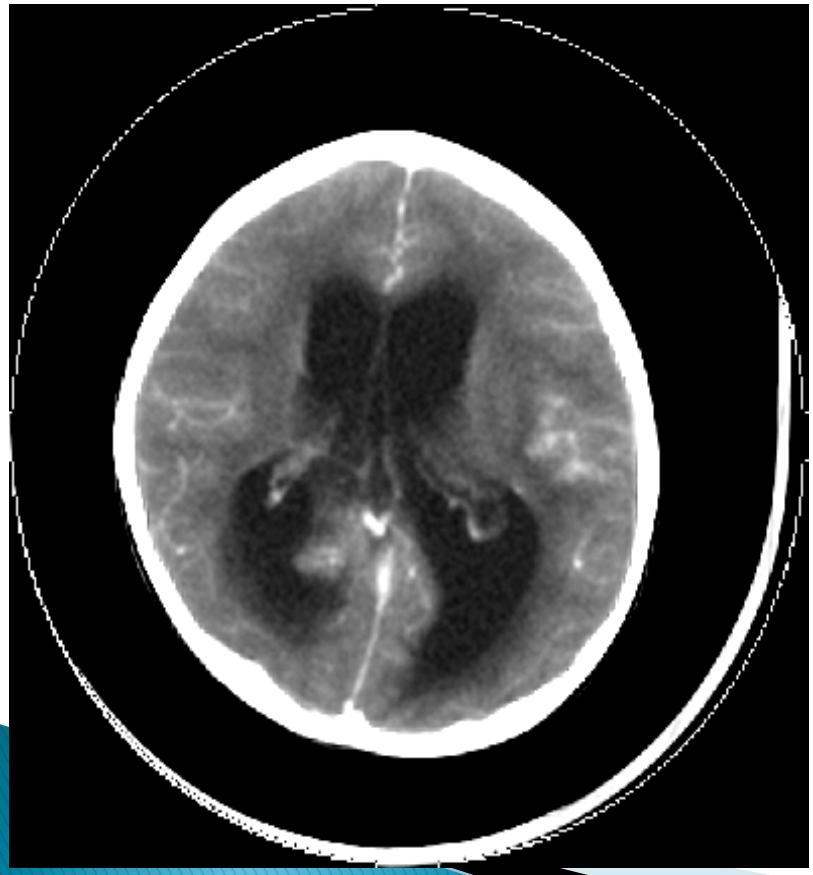
TB in very young



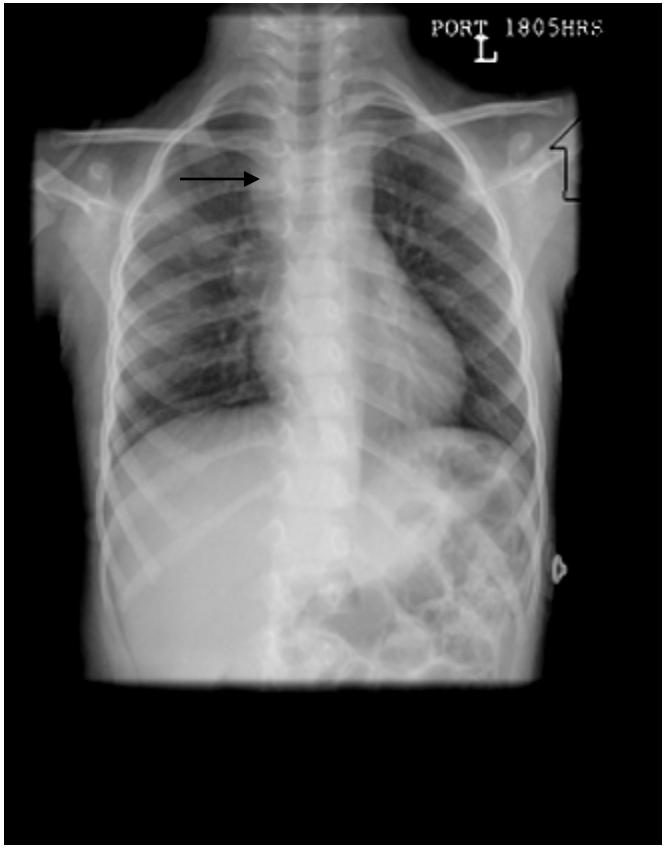
- After 1 years therapy
- Immune competent
- Major risk factor for disseminated and severe disease-
- YOUNG AGE

TB in the young

3 year old



- 6 WEEKS FEVER LETHAGY WT LOSS
- Coma



TB Meningitis: meta analysis

- Outcome relates to stage
- Most present in stage 3 – severe deficits at presentation

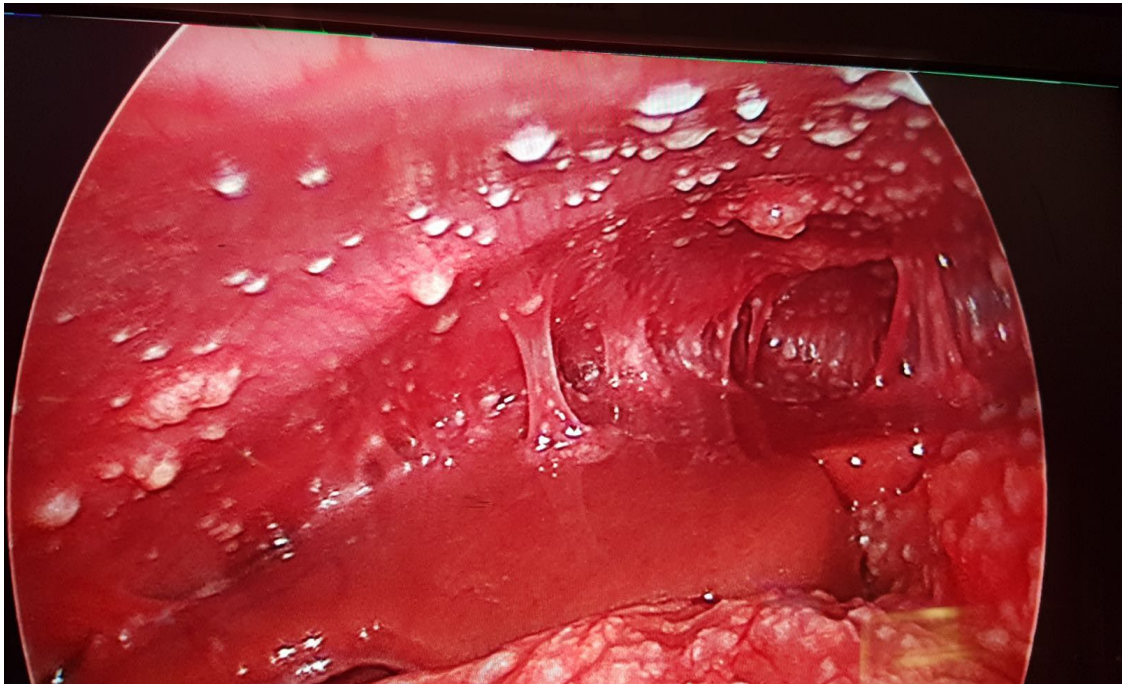
For all:

- 19% mortality
- 55% significant neurologic sequelae.
- Hydrocephalus at presentation common.

Treatment outcomes of childhood tuberculous meningitis: a systematic review and meta-analysis

Silvia S Chiang, Faiz Ahmad Khan*, Meredith B Milstein, Arielle W Tolman, Andrea Benedetti, Jeffrey R Starke, Mercedes C Becerra*

3 year old –acute abdomen



Young children get sick from TB

Childhood TB sentinel event Implies source case and transmission

Lots of childhood TB implies ongoing transmission in the community.

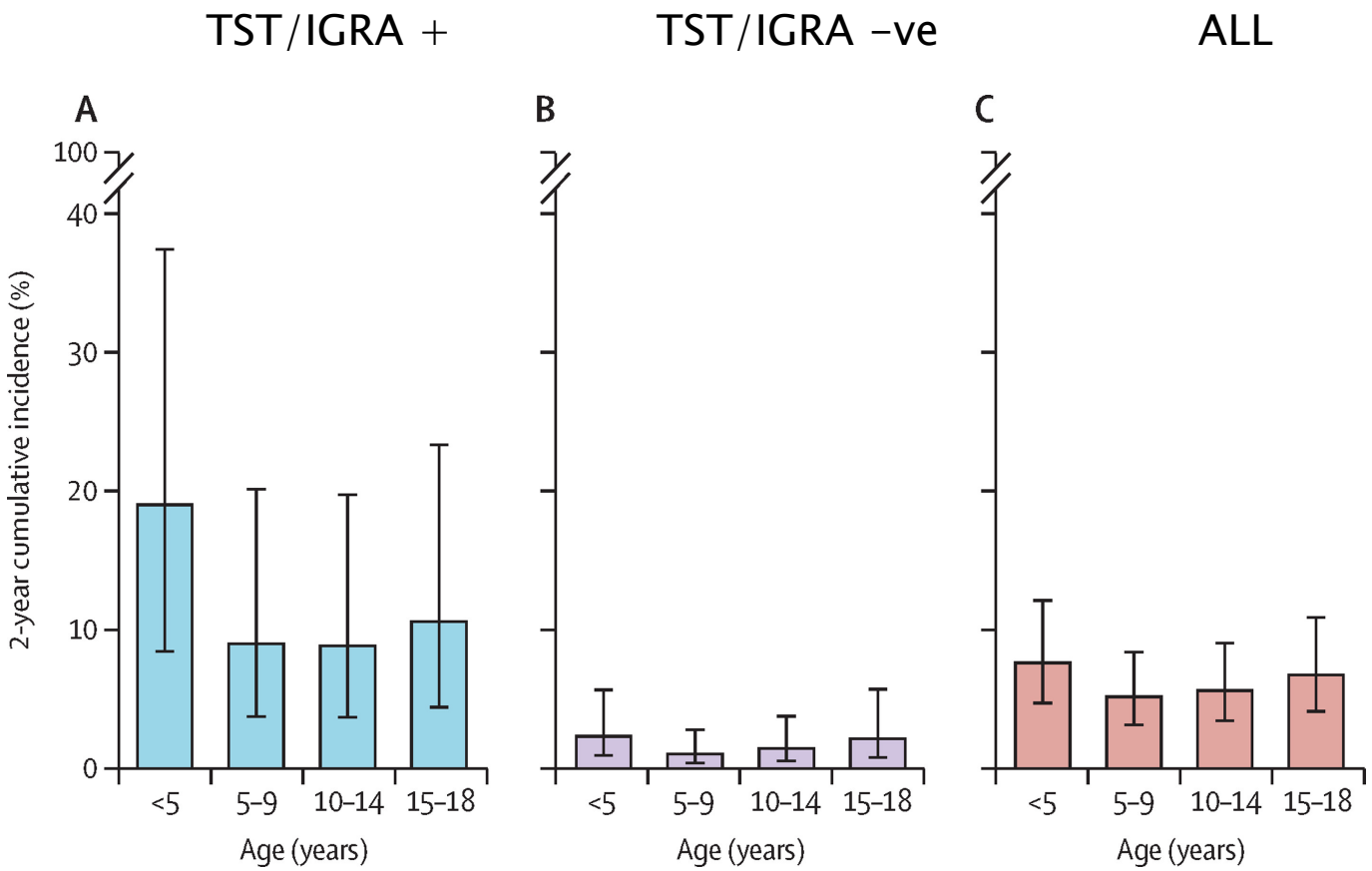
Teams and systems are needed to prevent TB

Age-Specific Risk for Disease Development after Untreated Primary Infection*

Age at Primary Infection	Manifestations of Disease	Risk of Disease (%)
< 12 months	No disease	50
	Pulmonary disease	30-40
	TB meningitis /miliary	**10-20**
12 -23 months	No disease	70-80
	Pulmonary disease	10-20
	TB meningitis or miliary disease	**2-5**
2-4 years	No disease	95
	Pulmonary disease	5
	TB meningitis or miliary disease	**0.5**
5-10 years	No disease	98
	Pulmonary disease	2
	TB meningitis /miliary disease	**< 0.5**
> 10 years	No disease	80-90
	Pulmonary disease	10-20
	TB meningitis or miliary disease	< 0.5

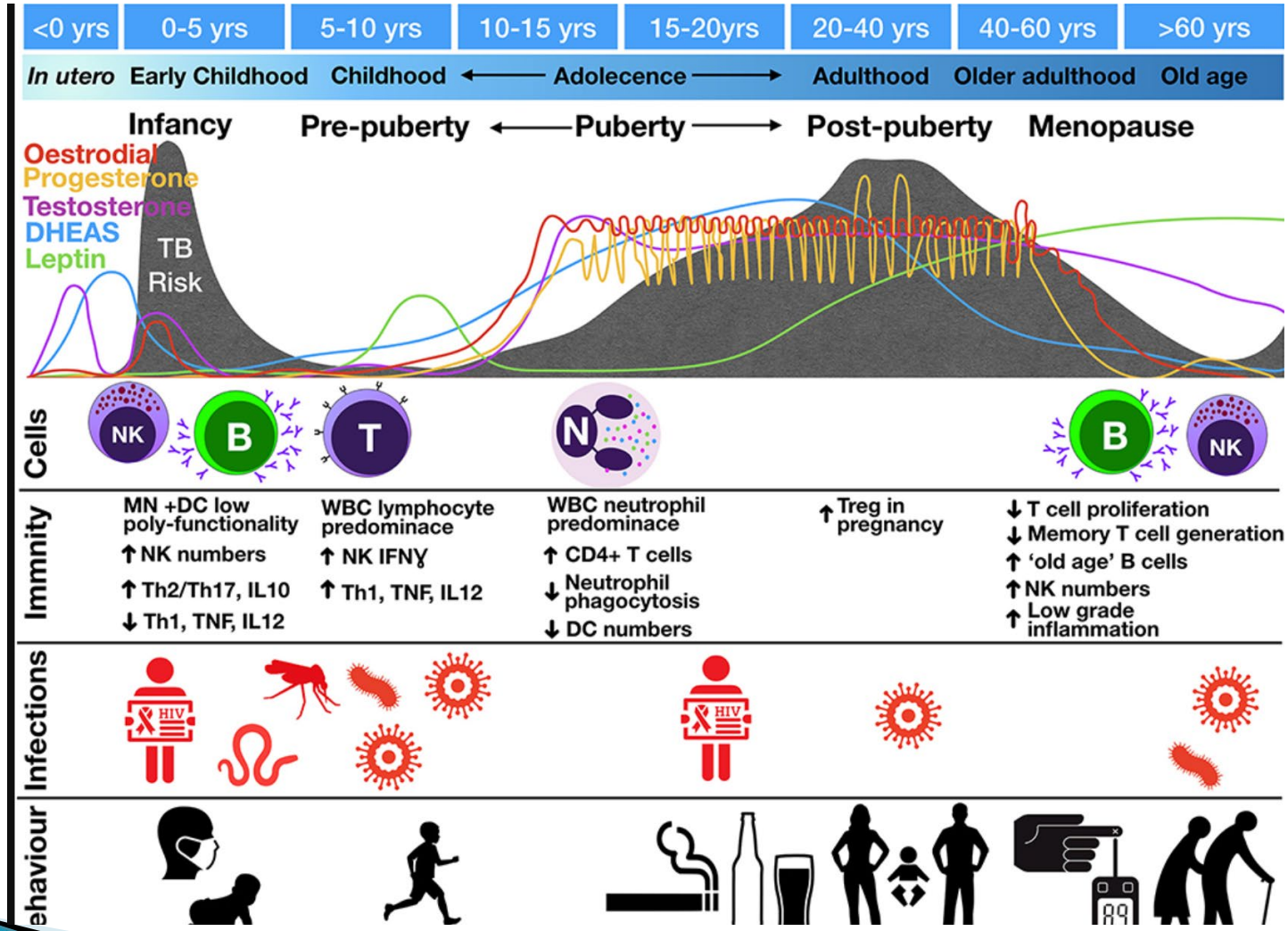
Marais BJ, et al. The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era. *Int J Tuberc Lung Dis* 2004;8(4):392-402.

2year cumulative incidence of TB disease- contacts Martinez Lancet 2020- IPD metanalysis of contacts



The risk of tuberculosis in children after close exposure: a systematic review and individual-participant data

Risk in very young- immune related



Seddon J et al
Frontiers in immunology 2018

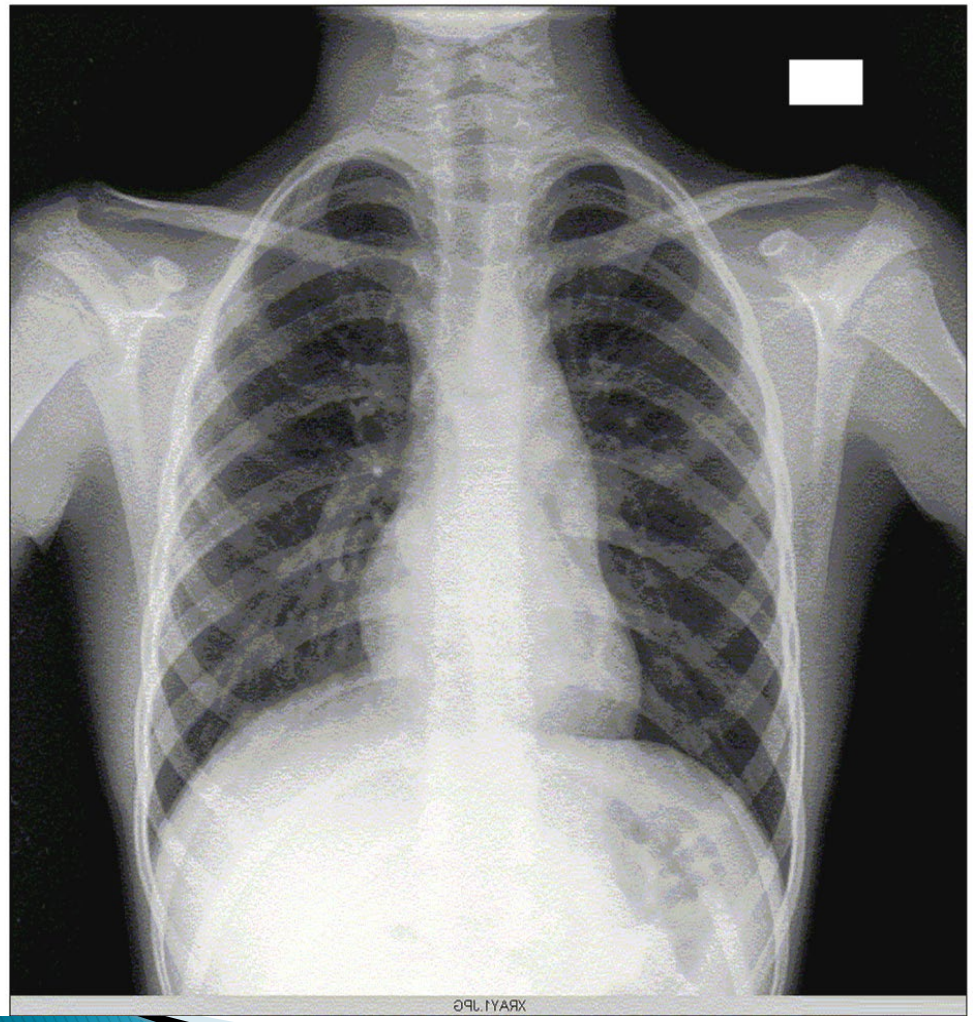
Management of Contacts—Most NB task in childhood TB

- **TST and IGRA in all- and Cxr.**
- **If TST/IGRA +ve and no disease-Rx for LTBI**
- **Takes up to 8-12 weeks after break in contact to develop positive TST /IGRA**

"the window".

If first TST/IGRA -ve and still within the window **Rx children <5 as for LTBI until the second test result - "window prophyalxis"** because severe disease may develop during this window.

Childhood TB : Intrathoracic



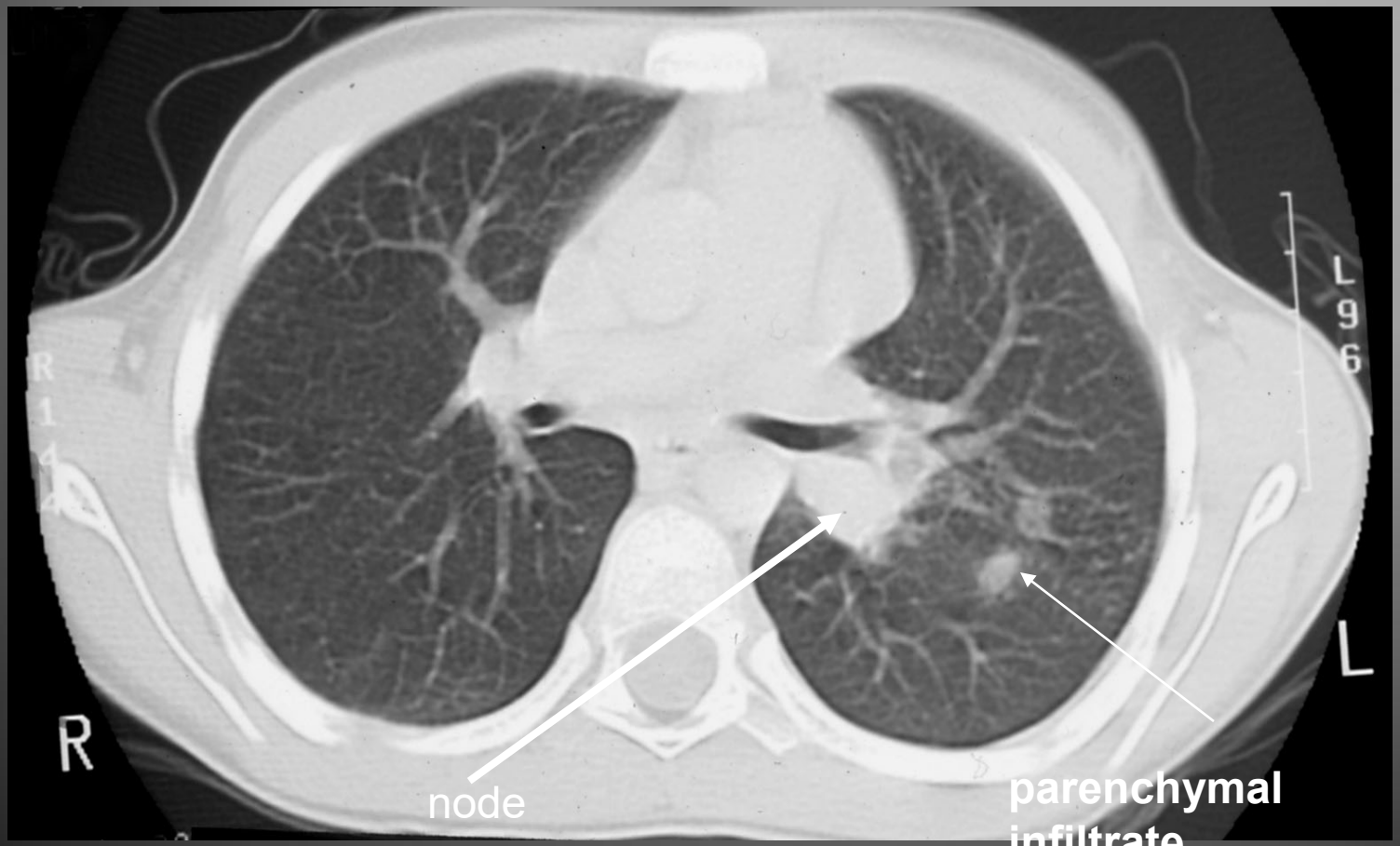
- 8
- Close contact
- CxR

" normal"

Mantoux 22mm

Asymptomatic

Primary TB: CT



Confirmed Tuberculosis

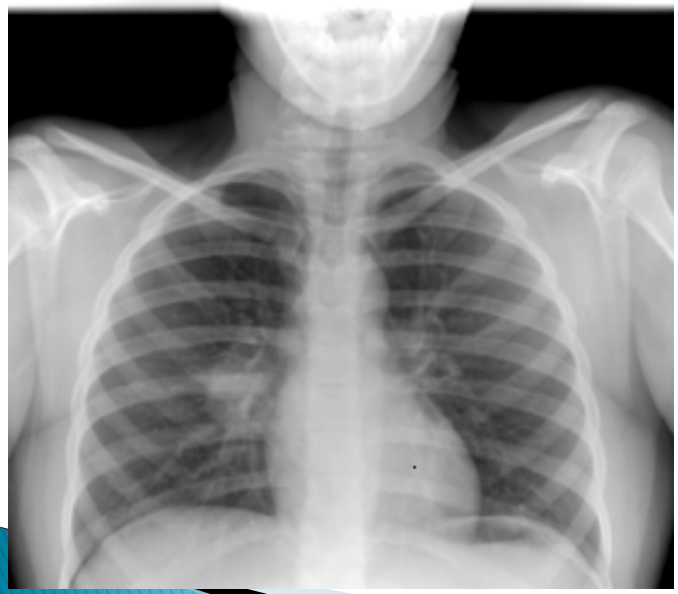
J Infect Dis. (2012)

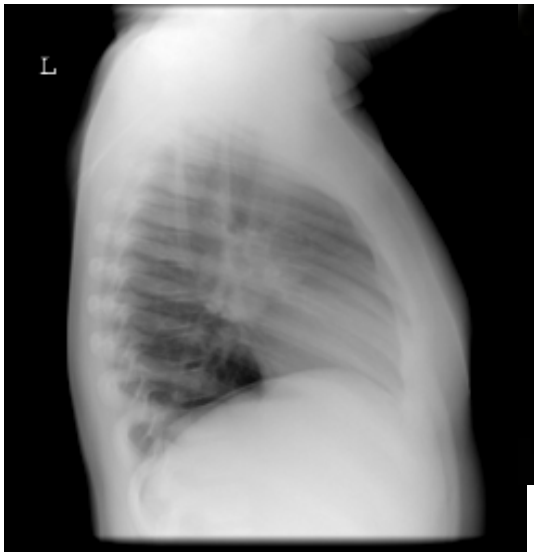
> 1 of the signs and symptoms suggestive of TB
(But some of our patients are aymptomatic)

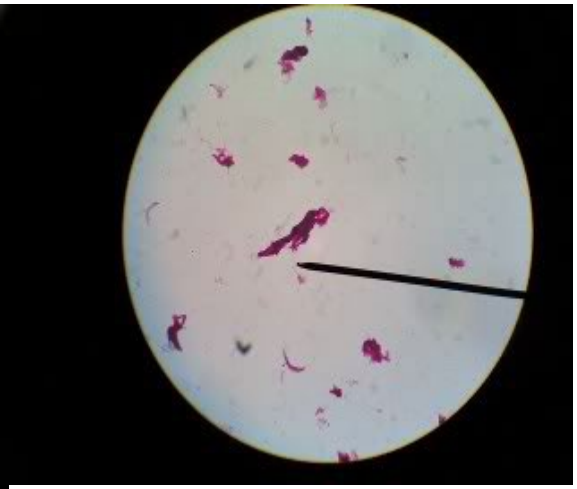
and

2. Microbiological confirmation

Intrathoracic lymphadenopathy is a hallmark of childhood TB







Unconfirmed Tuberculosis

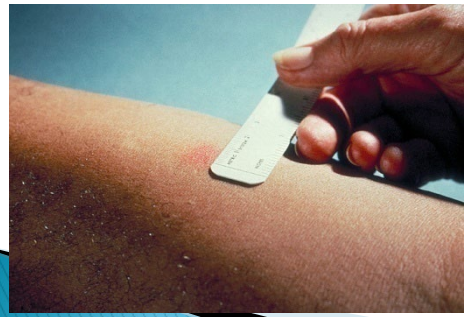
1 of the signs and symptoms suggestive of tuberculosis

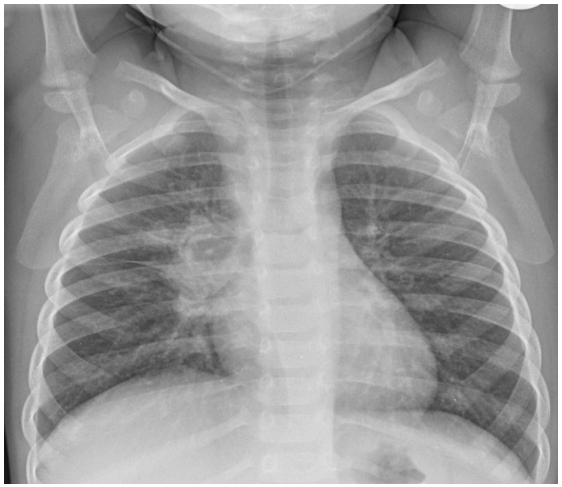
AND

CxR consistent

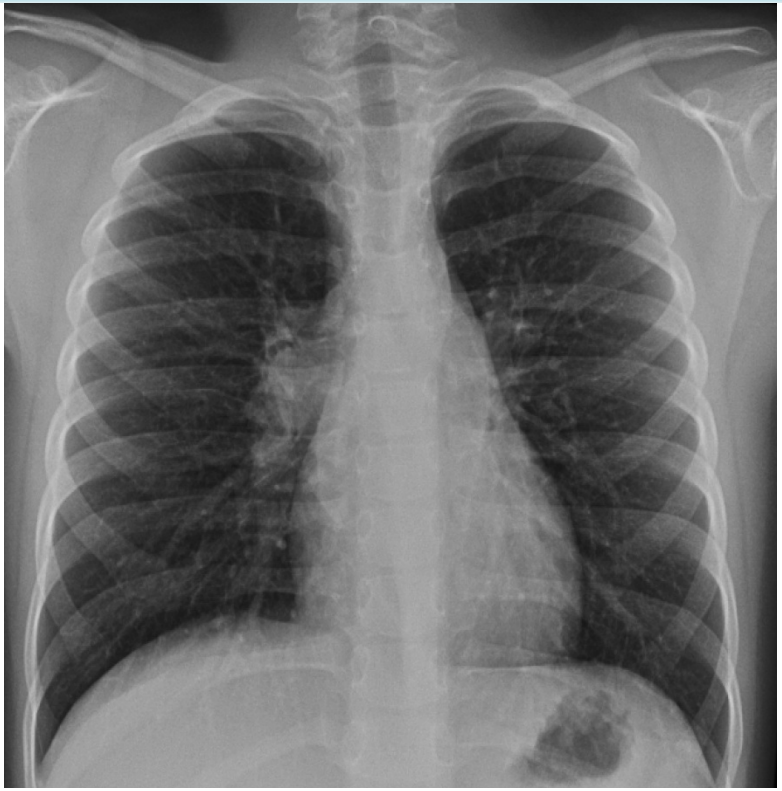
AND ≥ One of

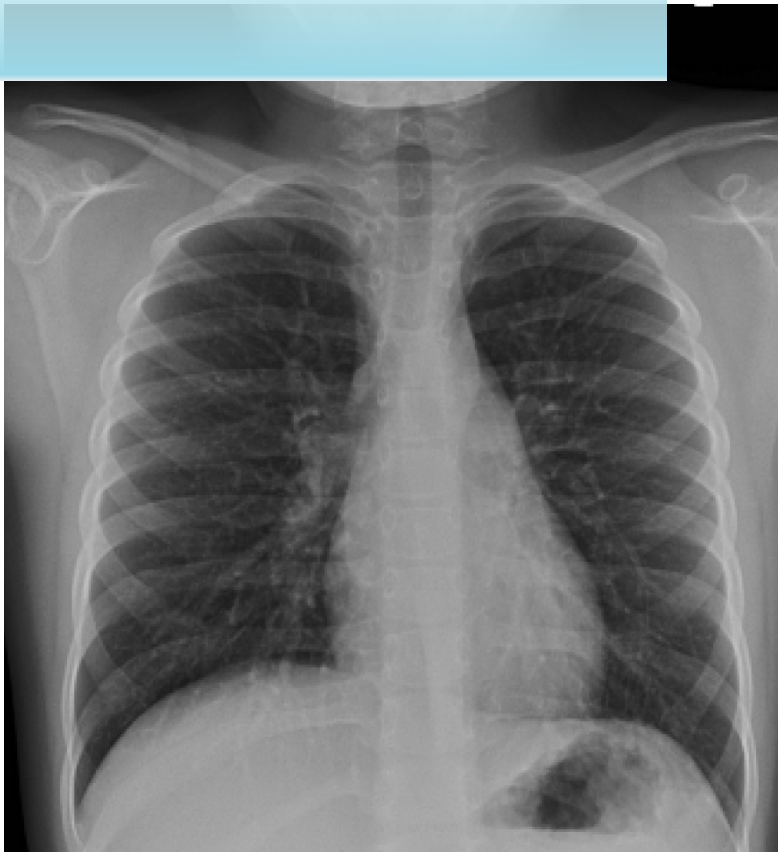
- +ve clinical response to antiTB Rx
- Documented exposure
- Immunological evidence





Disease or Not Disease? TST =14mm

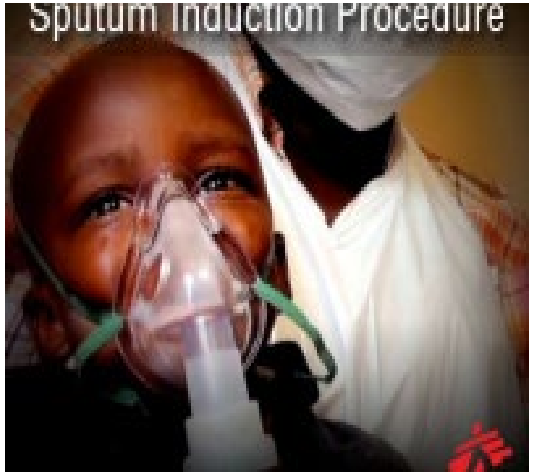


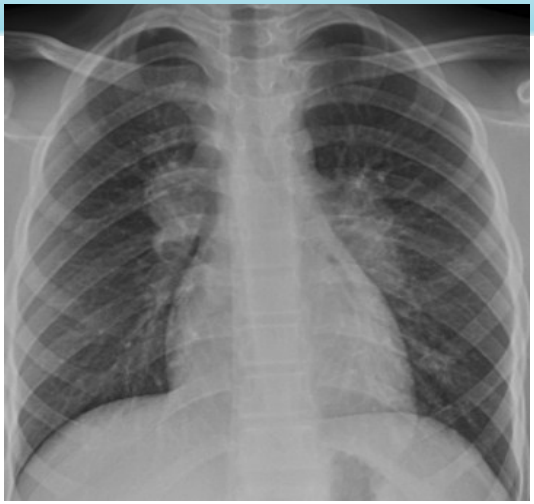


Before and After 3 months of therapy?

During URI and 2 months later?

Diagnosis : Induced sputum ± NP aspiration





Advantages:

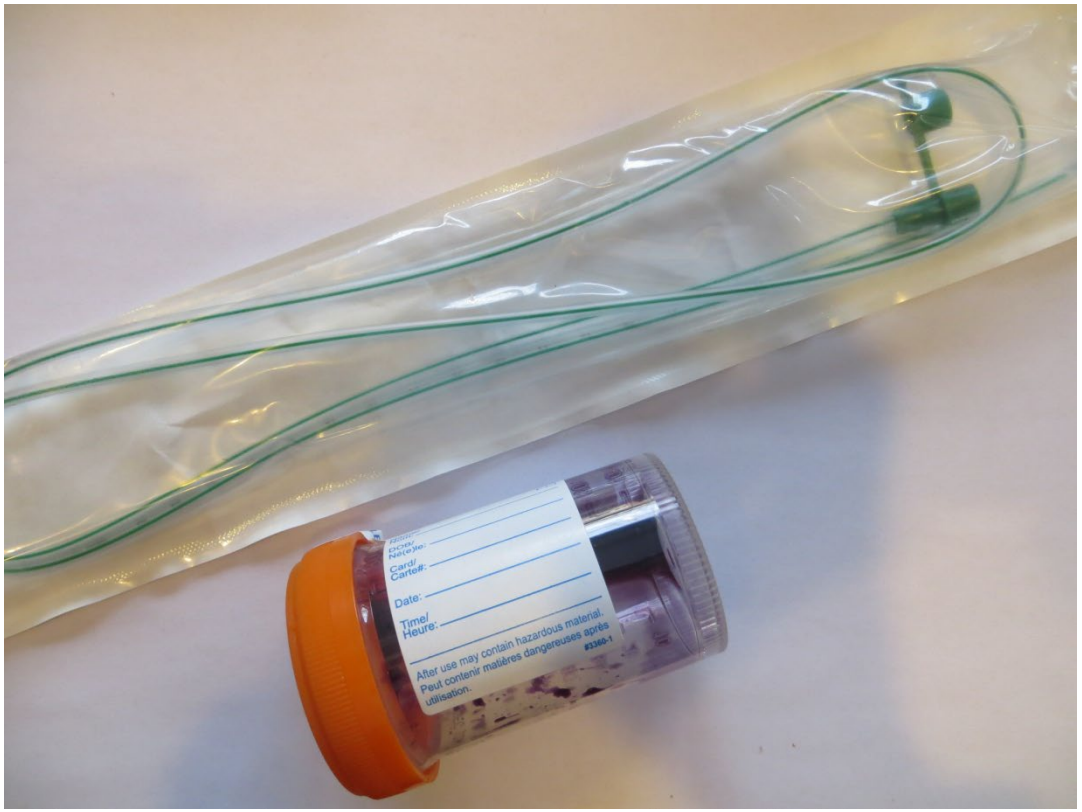
- 2-3 hr fast
- No admission
- No NG
- No killing of orgs. by gastric acid
- Older child expectorates

Disadvantages

- Special training and equipment
- Isolation
- Bronchospasm, traumatic

Gastric Aspirates

Anne Loeffler Video very helpful.



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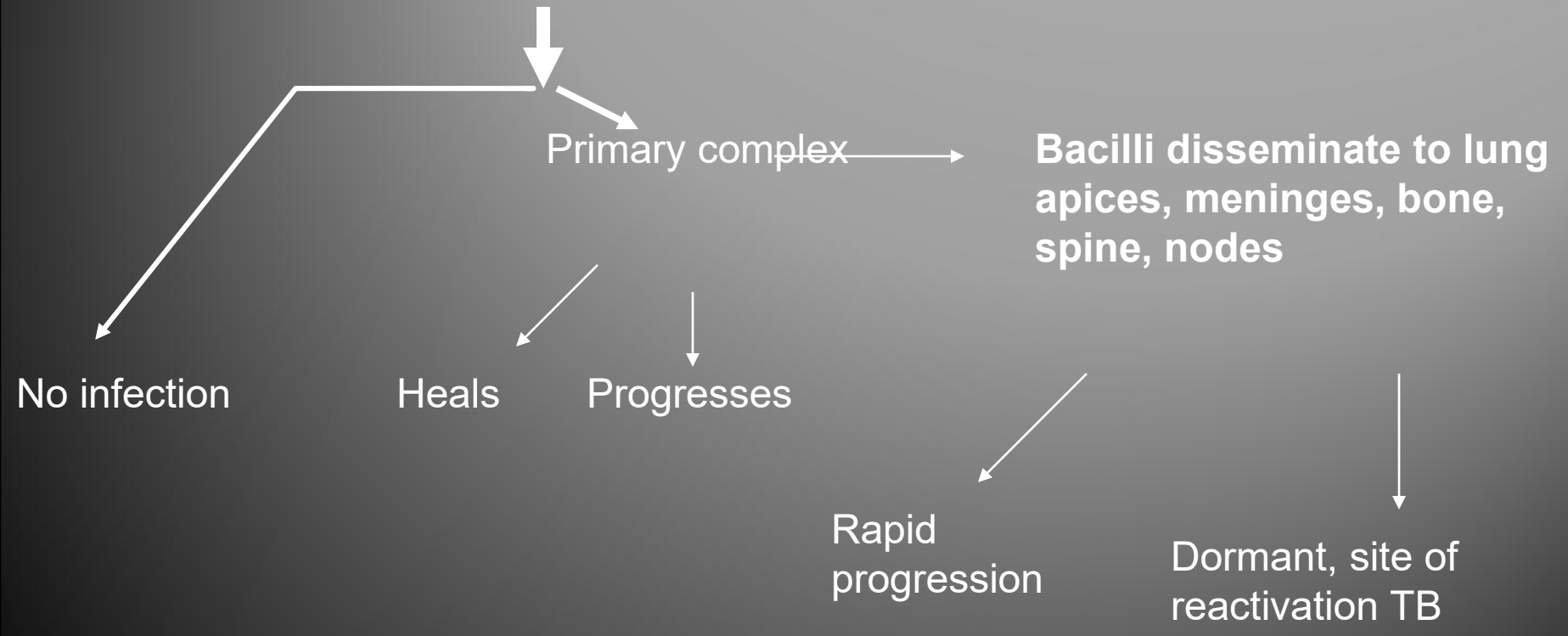
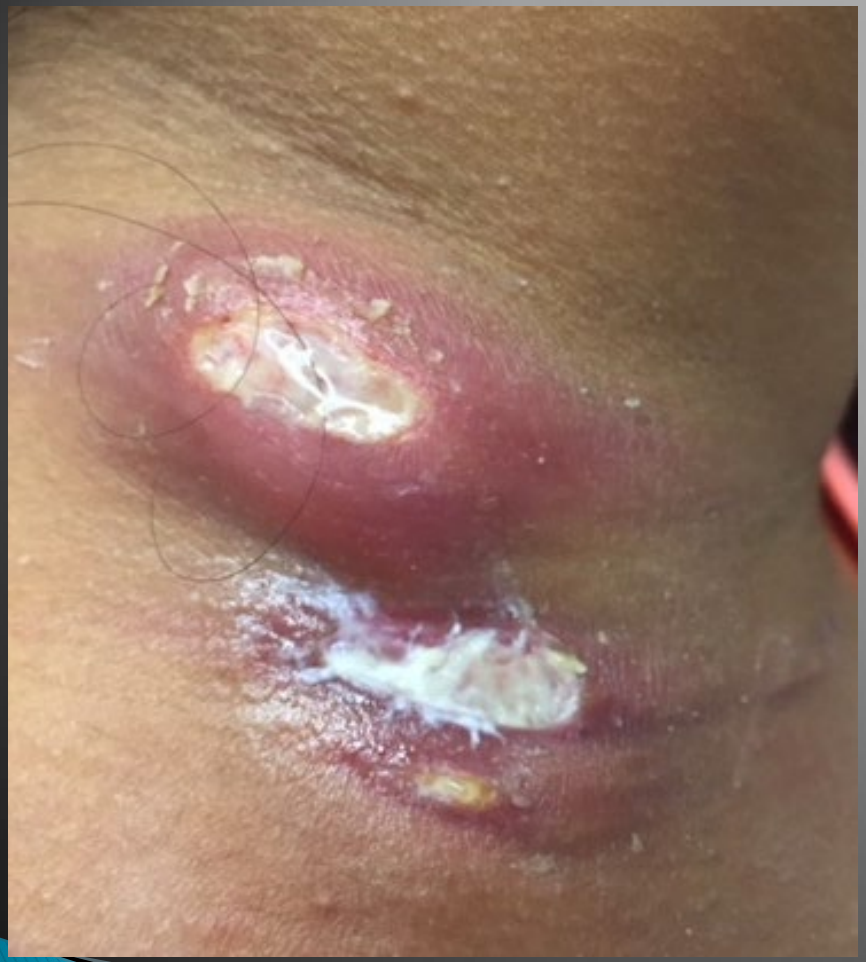
TB IN CHILDHOOD: PATHOGENESIS

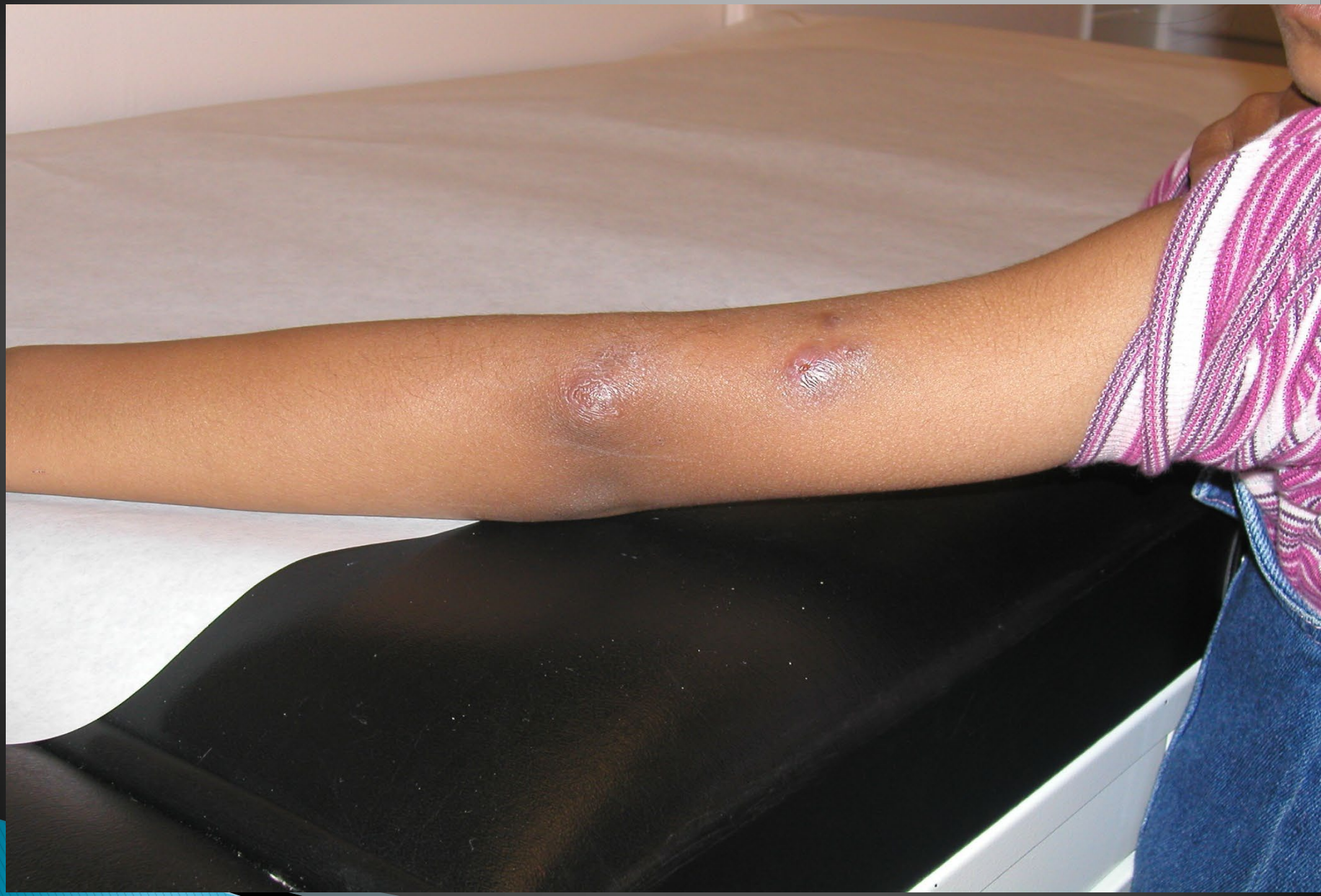
EXPOSURE

Child exposed to bacilli from adult or adolescent

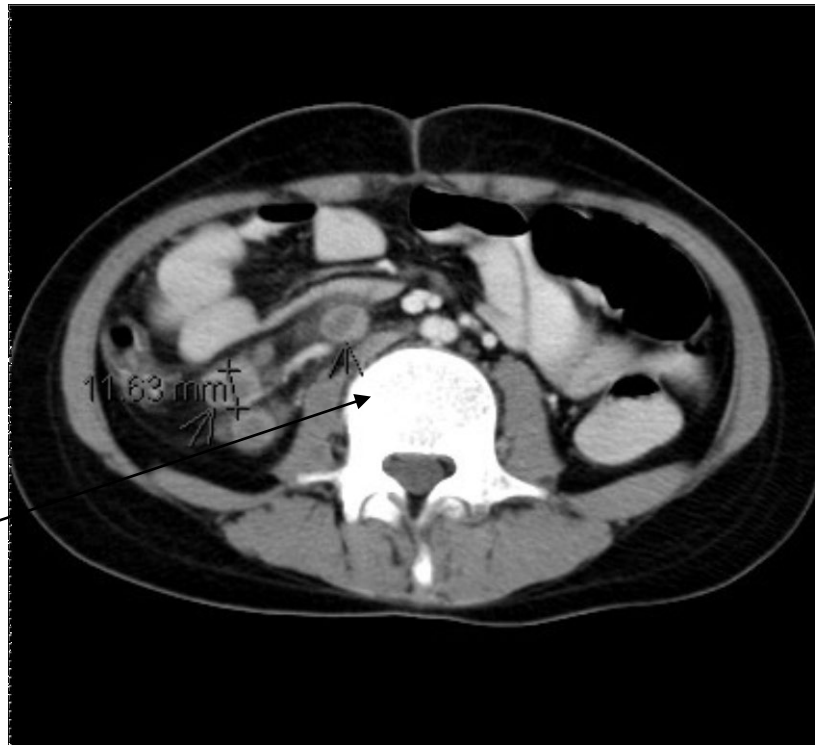


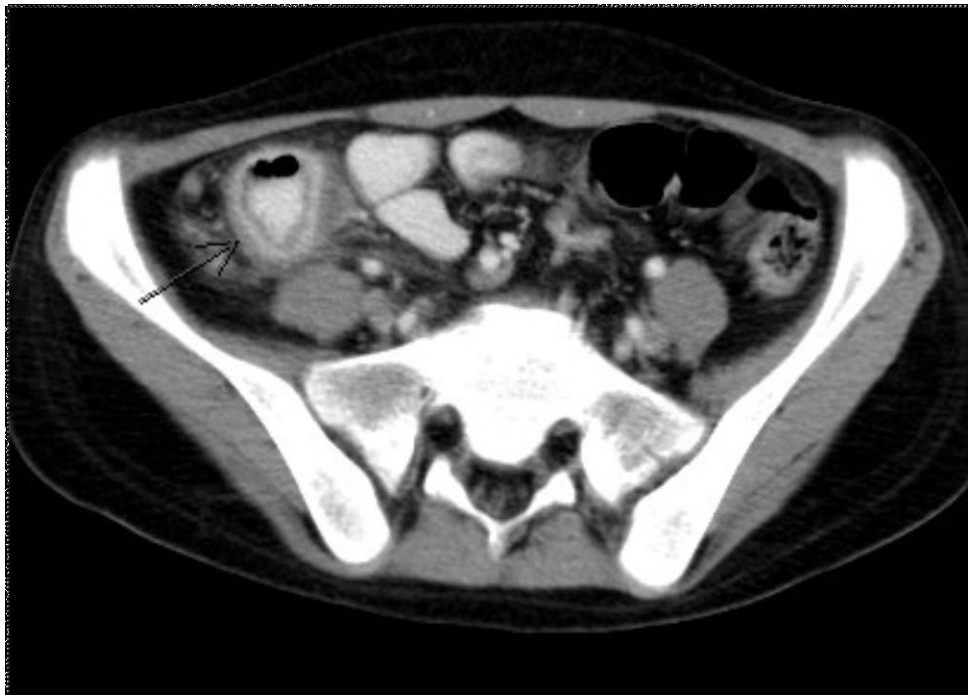
Lymphadenitis- usually >12yrs old



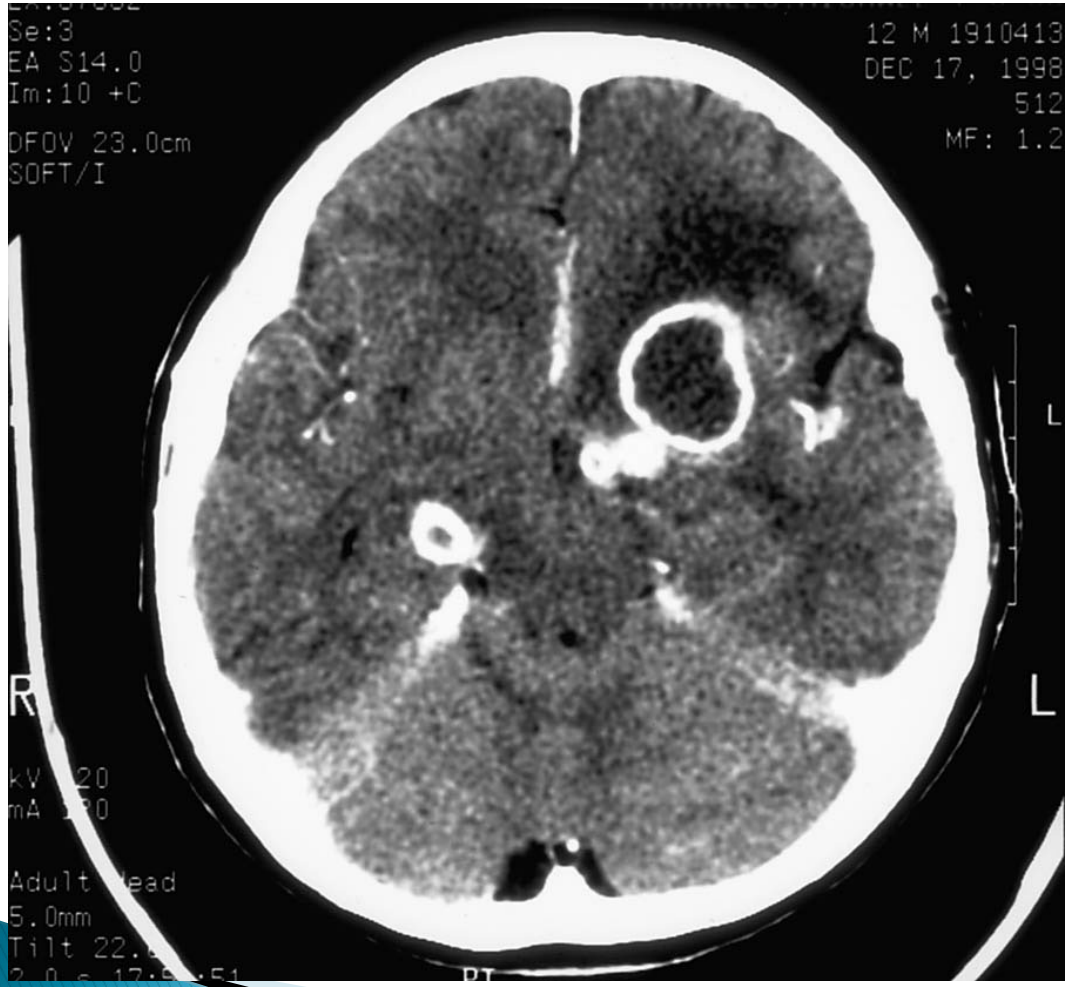


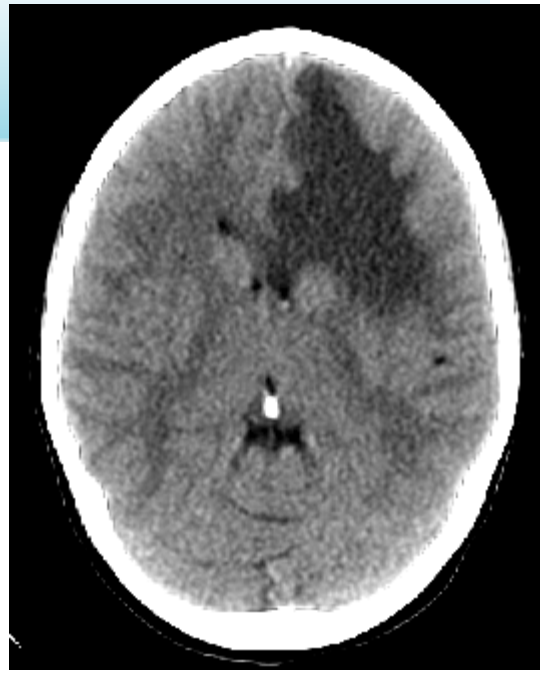
Weight loss, fever, thickened terminal ileum 16 year old

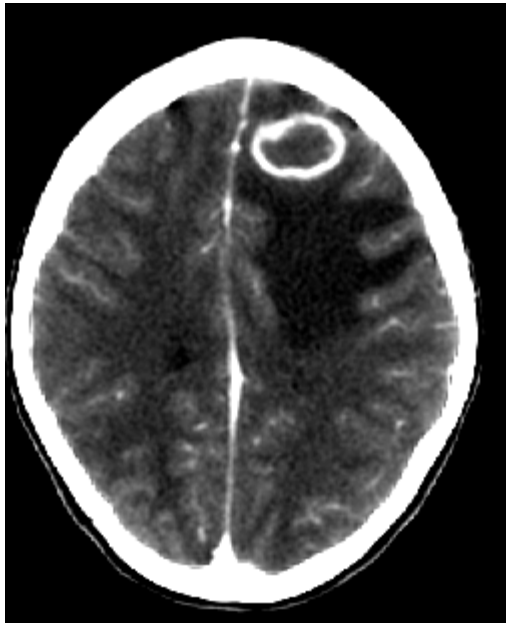




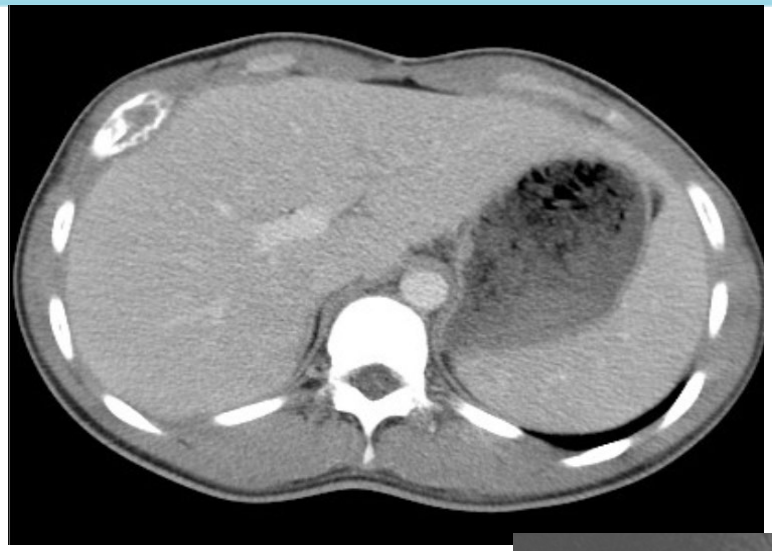
TB Disease

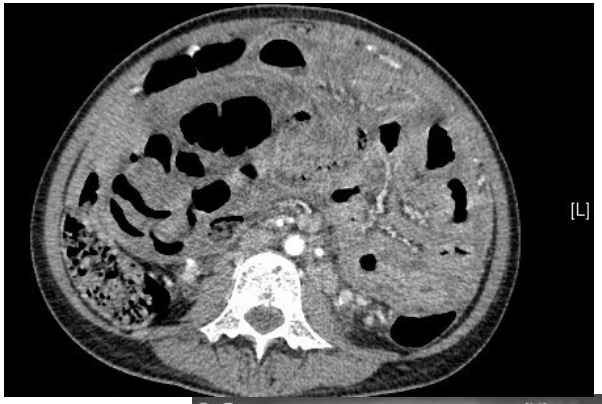

Se:3
EA S14.0
Im:10 +C
DFOV 23.0cm
SOFT/I
12 M 1910413
DEC 17, 1998
512
MF: 1.2
L
R
L
Adult Head
5.0mm
Tilt 22.

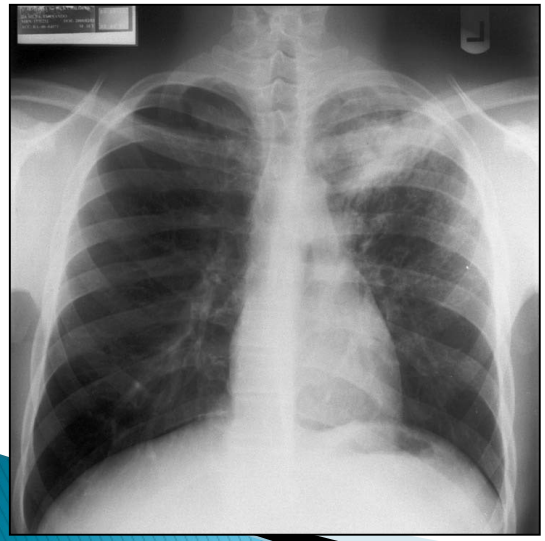


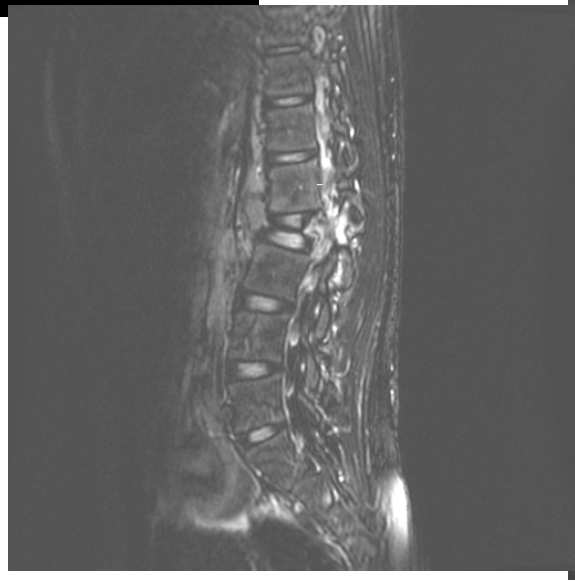


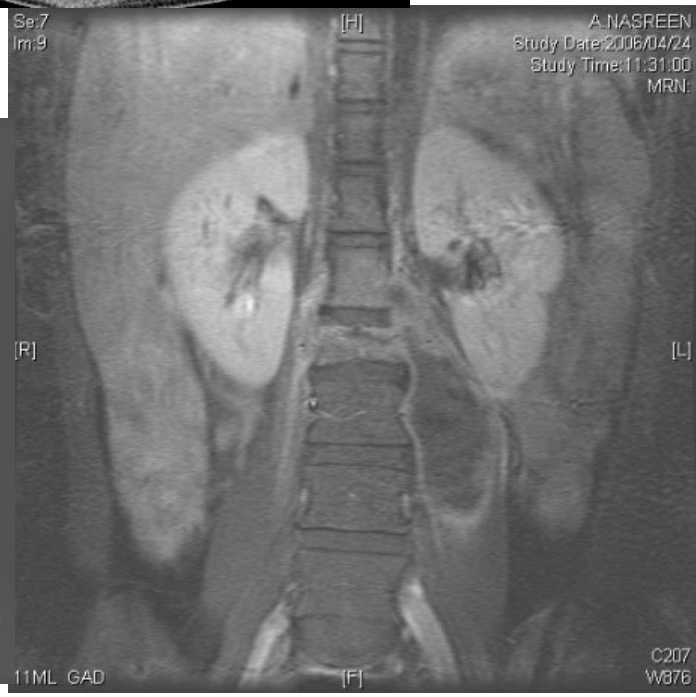
TB in adolescents-protean





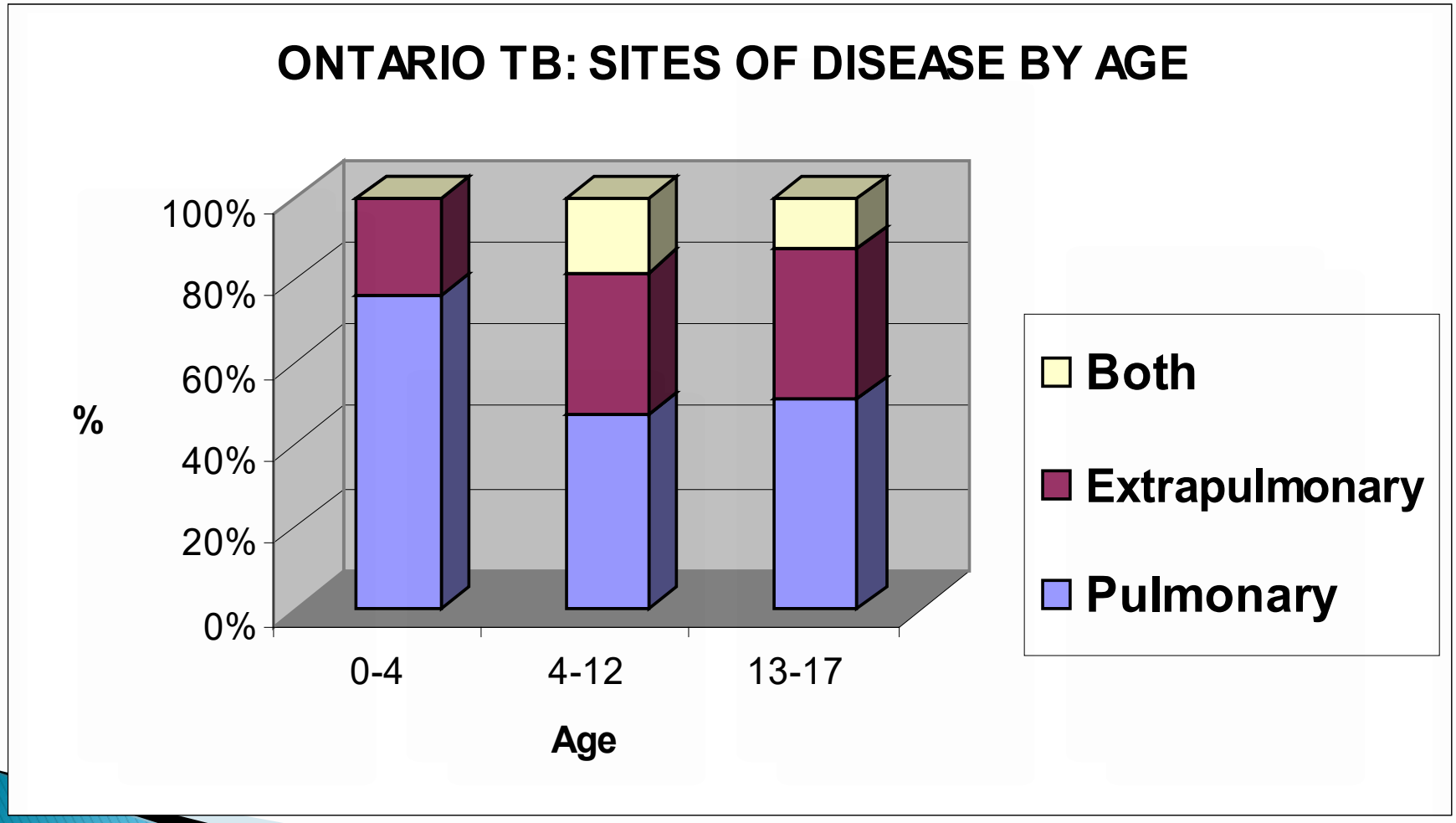






Phongsamart W Pediatr Infect Dis J 2009; 28:416-9

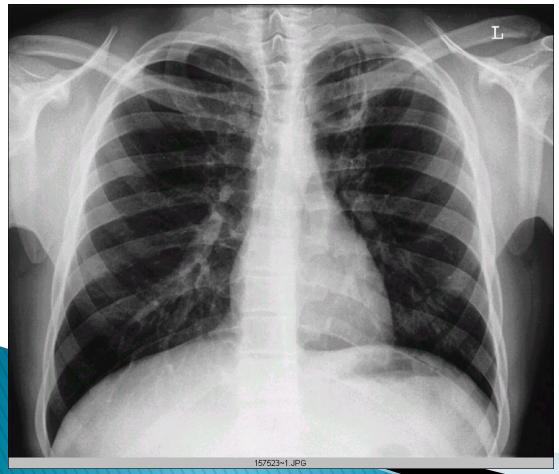
Population based study 1999-2002.

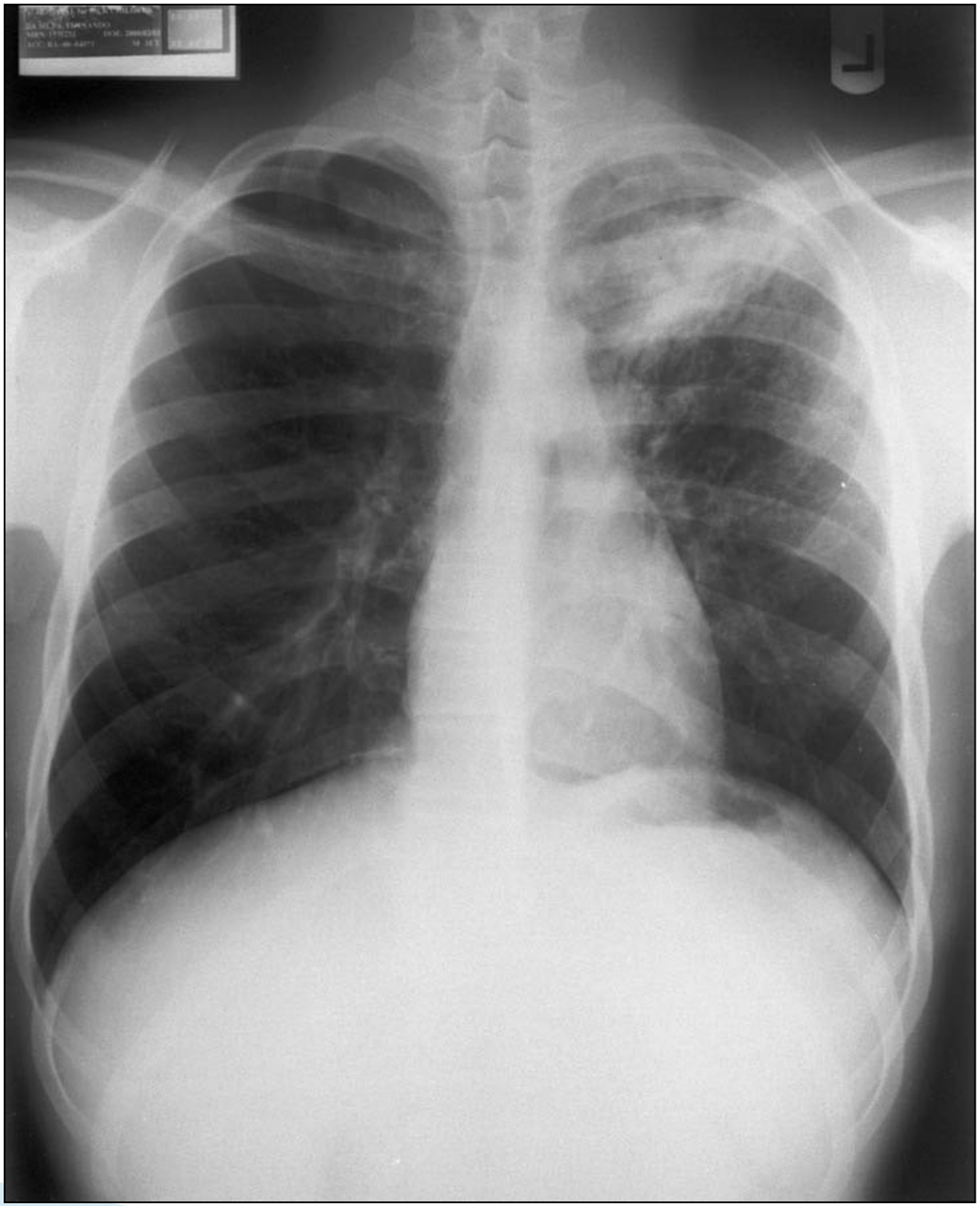


TB DISEASE "typical"

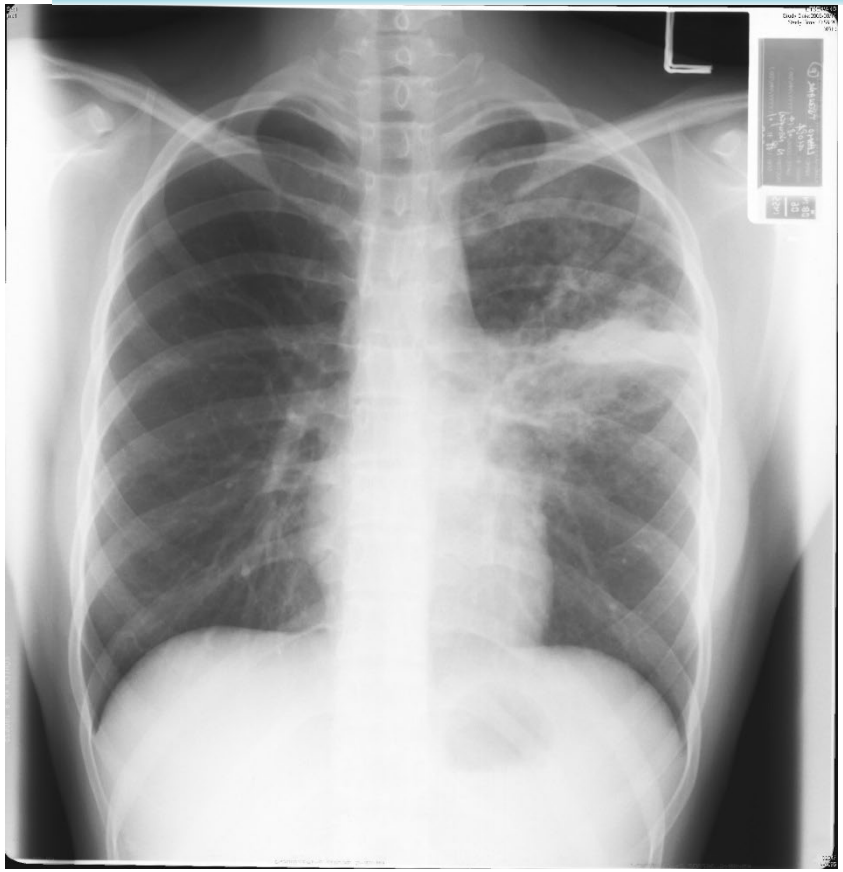
- 16 yr old
- Cough , Fever
- Nightsweats

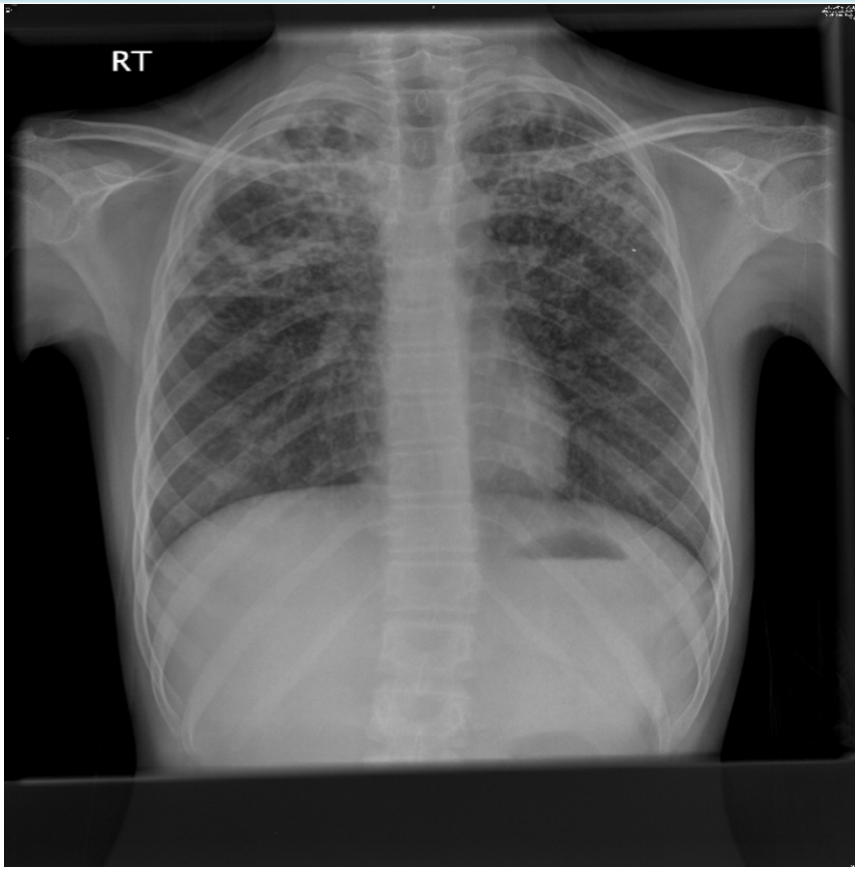
- Smear +ve for 3months on Rx





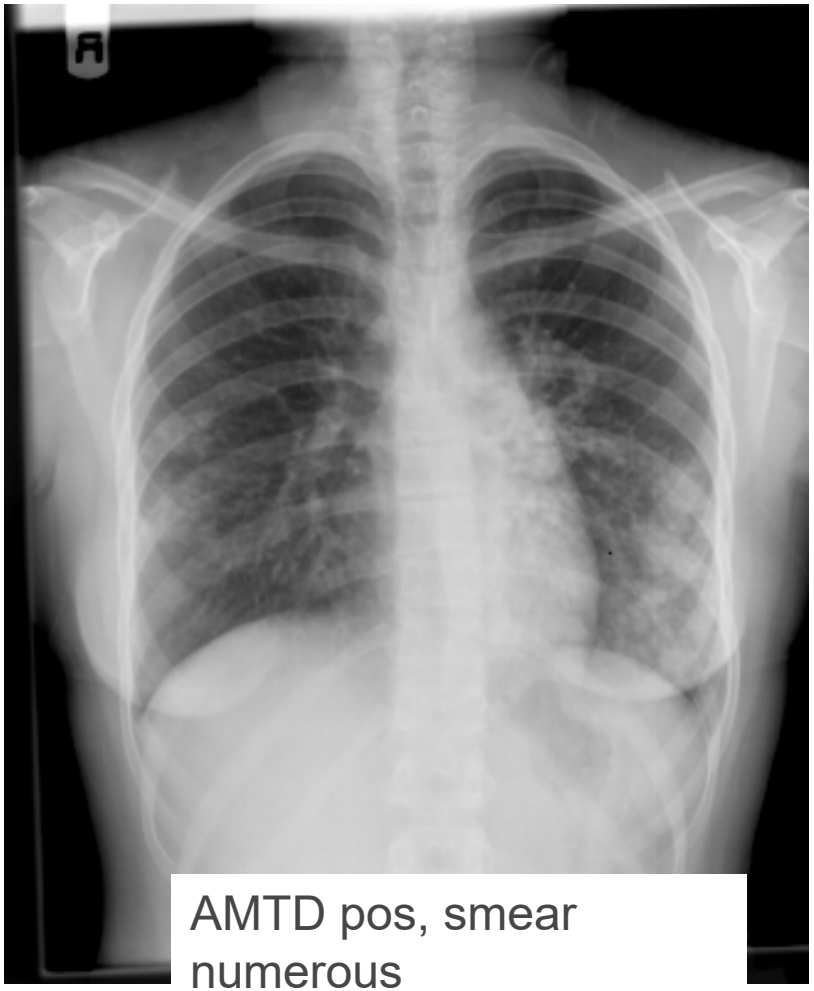
Pulmonary disease adolescents:
Upper lobe, posterior segment lower lobe…





In ED: >10 days fever >13 days of cough good discrimination of TB from pneumonia (Al Dubisi OFID 2021)

But can be any lobe…



AMTD pos, smear numerous

- Cough for 3 months
- Saw family MD at onset
- 3 courses of antibiotics
- Then sputum

TB in adolescence

- Late diagnosis– lack of clinical suspicion
- Median 5.5 months—multiple physician visits (Kam)
- Protean with extrapulmonary disease.
- Recent immigrants <5 years, sometimes sooner
- Mood disorders common
- School investigations and return are problems
- Compliance issues
- Social work support NB,

Kam et al PIDJ 2007; Pongsamart PIDJ 2009
Cruz et al PIDJ 2013

PULMONARY DISEASE IN THE OLDER CHILD AND ADOLESCENT

- May present as
  - **Unresolving pneumonia**
  - **Pleural effusion +/- small parenchymal infiltrate**
  - **Upper lobe airway disease**
  - **Lower lobe- any lobe- airway disease**
  - **Cavitary and non cavitary disease**
  - SPUTUM SMEAR AND CULTURE STILL CRITICAL
  - Duration of symptoms >12 days and UL disease help discriminate from pneumonia in ED (Al Dubisi OFID 2021)

Missed opportunities for early diagnosis of paediatric TB in Canada

- Failure to consider epidemiologic history
- Failure to obtain sputum for TB culture
- Failure to send biopsy specimens for TB culture.
- Not considering TB because the TST/IGRA is negative.
- Expecting pulmonary disease

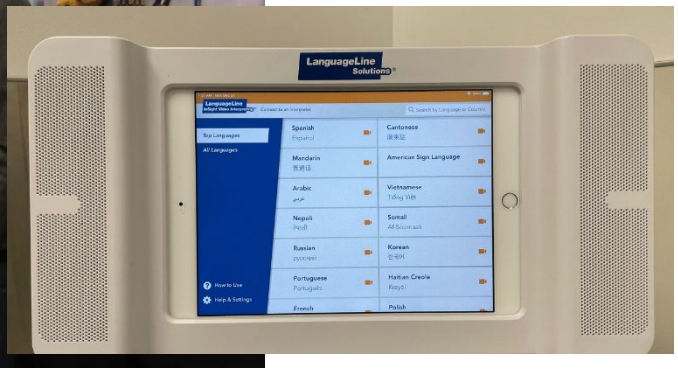
Missed opportunities for early diagnosis of paediatric TB in Canada

Failure to consider TB in the following circumstances:

- Poorly responding pneumonia
- Pleural effusion with or without parenchymal change
- Hydrocephalus and meningitis with negative bacterial cultures.
- Prolonged fever in the returning traveller

Who should assess and manage? Team: Essential

- **Critical mass**
- **Ensure treatment completion**
- **Counsel and monitor for toxicity**
- **Deal with comorbidities and social issues**



Peel Region
working with you

Pediatric TB:

Public Health Management

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Disclosures

- I have no conflicts of interest to declare.

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Polling Question

Children are most often diagnosed with TB through:

1. Signs and symptoms consistent with TB
2. Immigration medical exams
3. Contact investigations
4. Routine check-ups

Principles

1. Children are more vulnerable to both infection and development of active disease
2. Most children with TB are diagnosed via contact follow-up
3. An ounce of prevention is worth a pound of cure
4. Pediatric cases and contacts require extra support from Public Health
5. Screening, diagnosis and treatment of children works best when PHUs and clinicians work as a team

Older Child/Adolescent Case

Case Management

- Can be infectious – isolation required for respiratory TB
- Ideally treated by a pediatric TB specialist
- Supportive therapy including DOT up to 5 days per week

Contact Management

- Contact investigation as per established guidelines

Young/Very Young Child Case

Case Management

- <10 years old generally not considered infectious – no isolation
- Must be treated by pediatric specialist
- Supportive therapy including DOT 5 days per week

Contact Management

- Contact investigation generally not required <10 years old unless significant disease
- Source-case investigation for <5years old

Pediatric Contacts

- Contacts <5 years old
  - Lower threshold for hours of exposure
  - Screening involves CXR regardless of TST result
  - Recommend specialist referral, and Window Prophylaxis to protect against infection and progression to disease
  - Can receive DOPT

- Contacts >5 years old
  - Same as adult

Case Study #1 – Delayed Screening

- Index case 30yo male, AFB 4+, cavitary CXR – high infectivity
- Identified 10 Household contacts, including 7 kids age 10m-6yo
- Both families resistant to contact screening and some out of country
- Case Manager offered significant counselling, TSTs and arranged specialist appointments
- No contacts screened

- 6 months later 3yo developed respiratory illness
- Mother requests TST – positive, but CXR not done for 1 month
- CXR abnormal and TST reported by family physician
- Referred to SickKids, diagnosed with active TB
- Siblings of case referred to SickKids – both diagnosed with LTBI
- Children <5yo in household #2 screened – infant screened negative, 3yo LTBI, 4yo

Case Study #2 – Nursery School Exposure

Index Case:

- Asymptomatic, abnormal CXR on IME
- Expectorated sputum smear and culture negative x3
- Induced sputum x2 – one sample AFB “few”, one negative, both culture +ve MTB, pan-sensitive
- CXR Ill-defined opacities in bilateral upper lobes
- Low infectiv

- Recent graduate of ECE program, working as ECE in Montessori school
  - no clinical placements during POI
- Spent enough time during POI with students in toddler room at school
  - 15 children ages 18m – 3yo
- Recommendations – initial and repeat TST, plus CXR and referral to specialist for window prophylaxis

Screening – 2 Options

1. On-site clinic
   - PRO: Better chance that contacts will be screened appropriately, chance to speak with parents/guardians and to provide education
   - CON: Very young clients can be difficult to test, may require ++ resources and parental involvement, may cause panic at school

2. Families to arrange for screening themselves
   - PRO: Clients need to see physician anyway for CXR so means less appointments for clients/families, less disruptive to school
   - CON: Less control over screening – will be up to parents/guardians to take child in to be tested

Plan

- On site clinic at school for TST plant and read
- Collaboration with local pediatric respirologist to support follow-up and prescribe window prophylaxis
- Letters, consent form, fact sheet and information on booking appointment with identified specialist provided to school for delivery to parents

Results

- 11 children had initial screening at the clinic, 4 at their MD office
  - All negative
- 11 children had CXRs
- 11 children were seen by designated specialist
  - 1 had own specialist, 3 declined
- 8 children initially accepted window prophylaxis (WP)
  - Only two started and completed WP
- All completed repeat TST – All Negative

Questions?

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