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Pediatric TB Cases

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Curry International TB Center

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Reasons children are evaluated for TB

- Contact investigation
  - Children are a priority during evaluation of an adult / adolescent with contagious TB disease
  - Associate investigation is when a sibling is found to have TB (likely exposed to the same adults)
- Symptoms
  - Often non-specific (and children often have no identified symptoms)
- Screening
  - School / day care entry
  - Immigration

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13 month old Afghani refugee

- What questions do you ask a family when you're screening for TB in a young child?

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13 month old Afghani refugee

- What questions do you ask a family when you’re screening for TB?

- Refugee screening visit reports no signs or symptoms of TB.

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13 month old Afghani refugee

- What questions do you ask a family when you’re screening for TB?

- Family not aware of any exposures
- All immediate family members are negative by IGRA

- This baby’s TST is 10 mm induration

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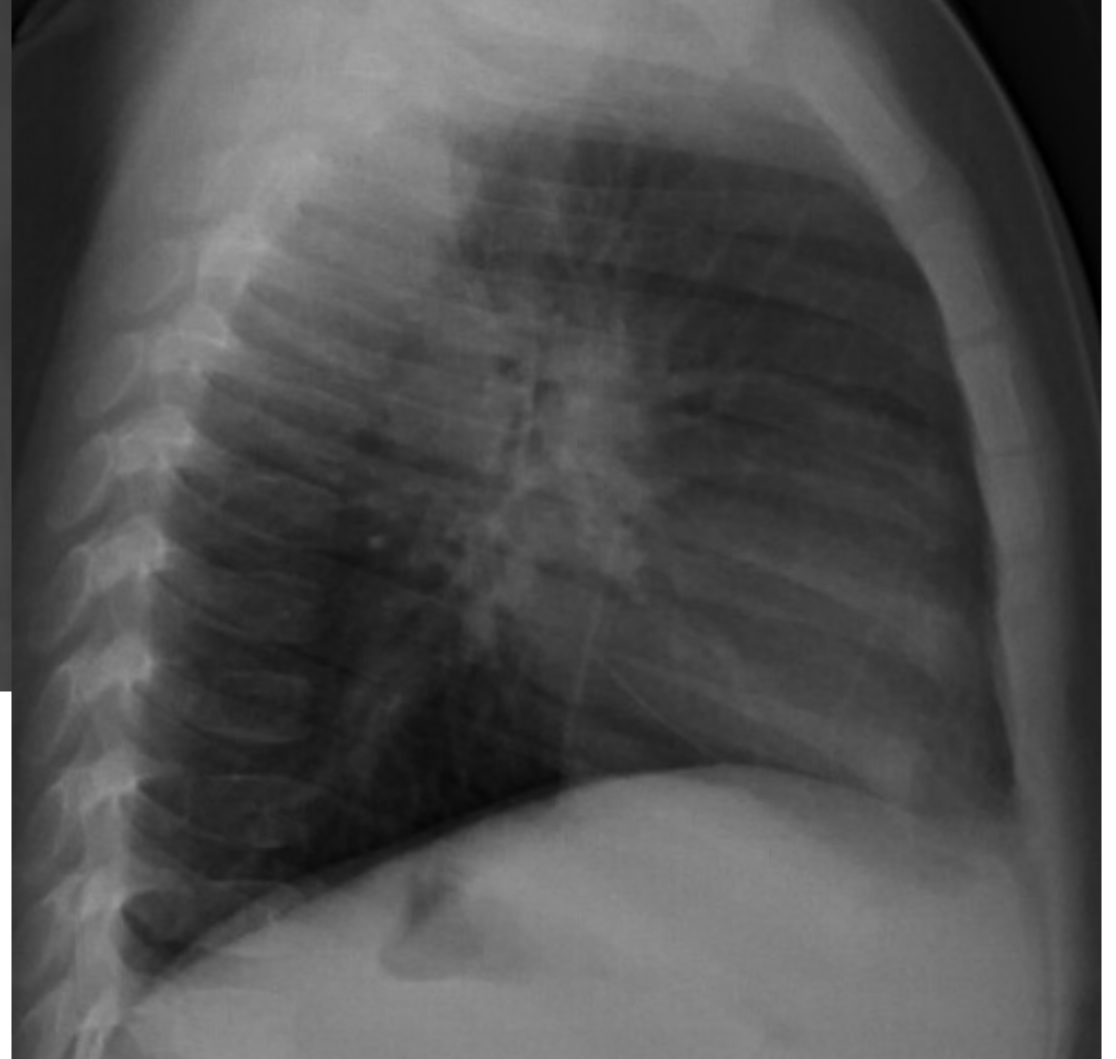

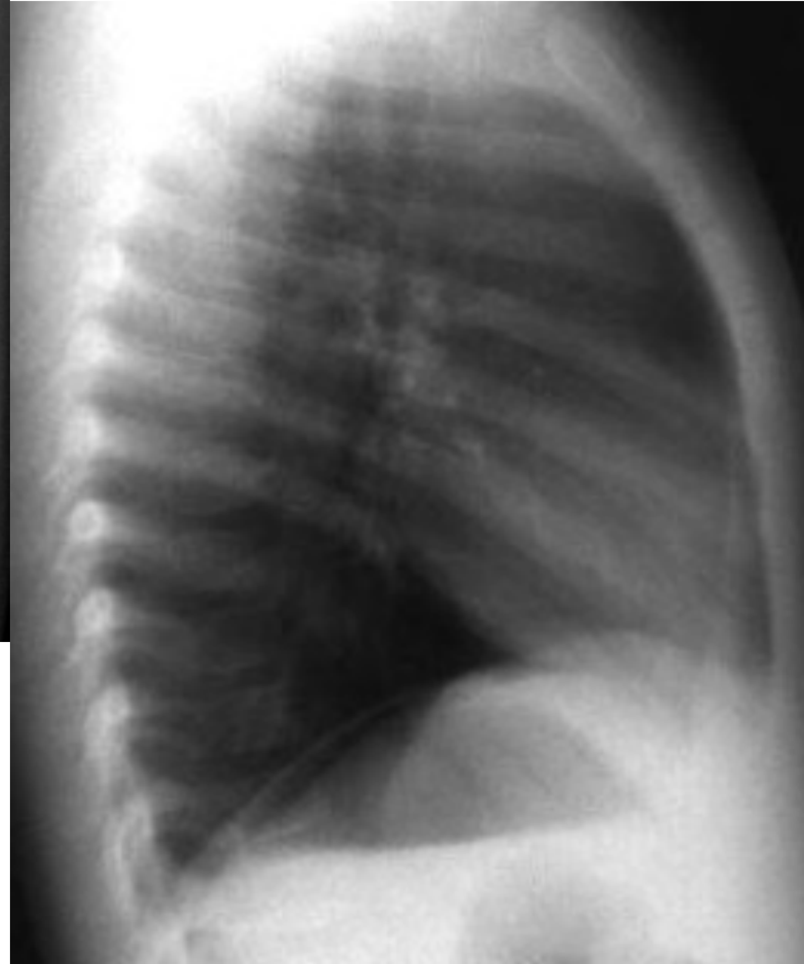

Normal toddler chest images

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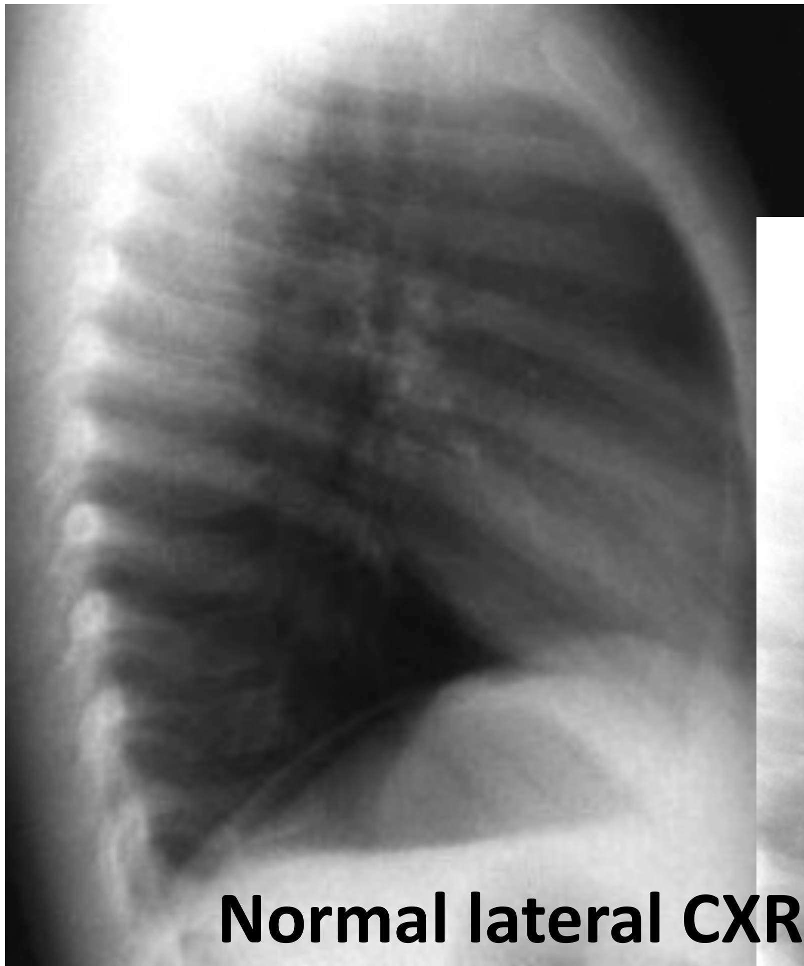
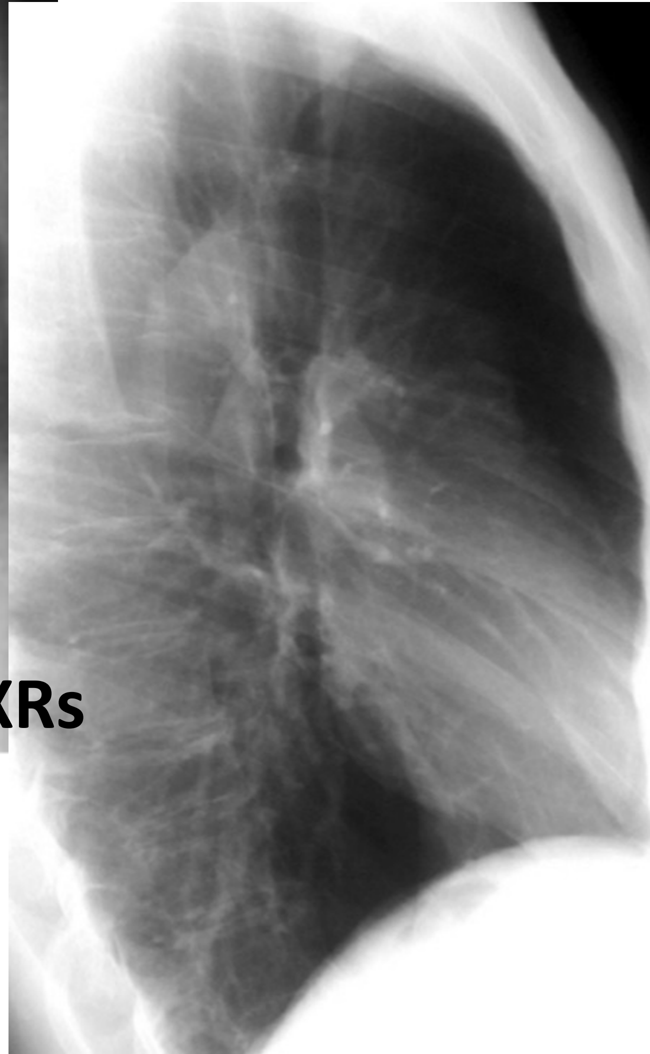
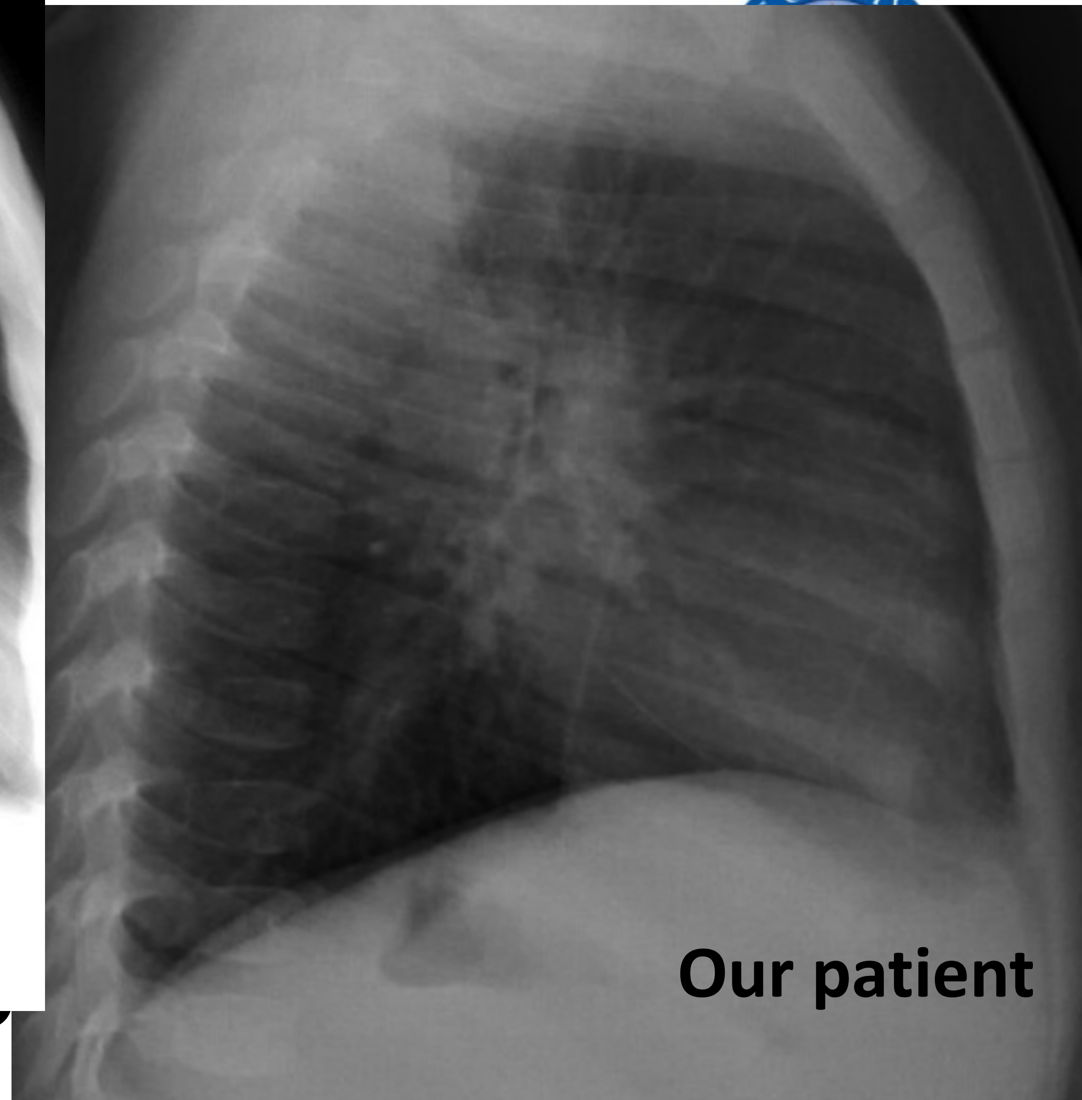




Normal lateral CXRs



Our patient

Consider all the factors

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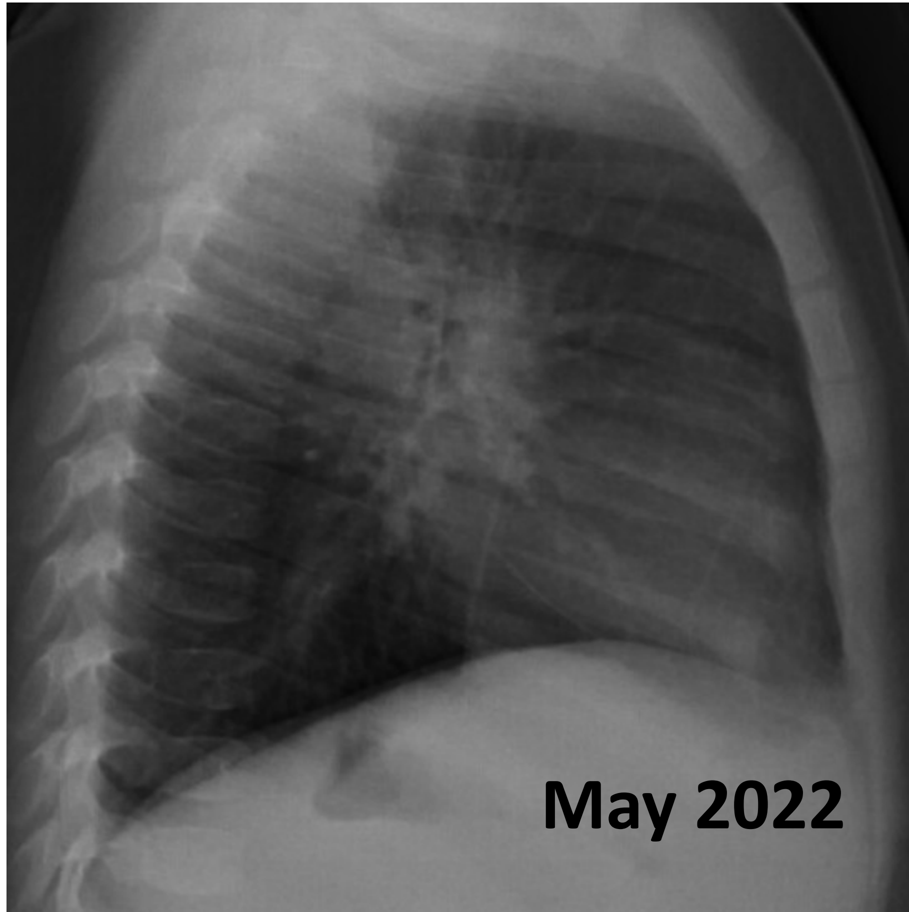
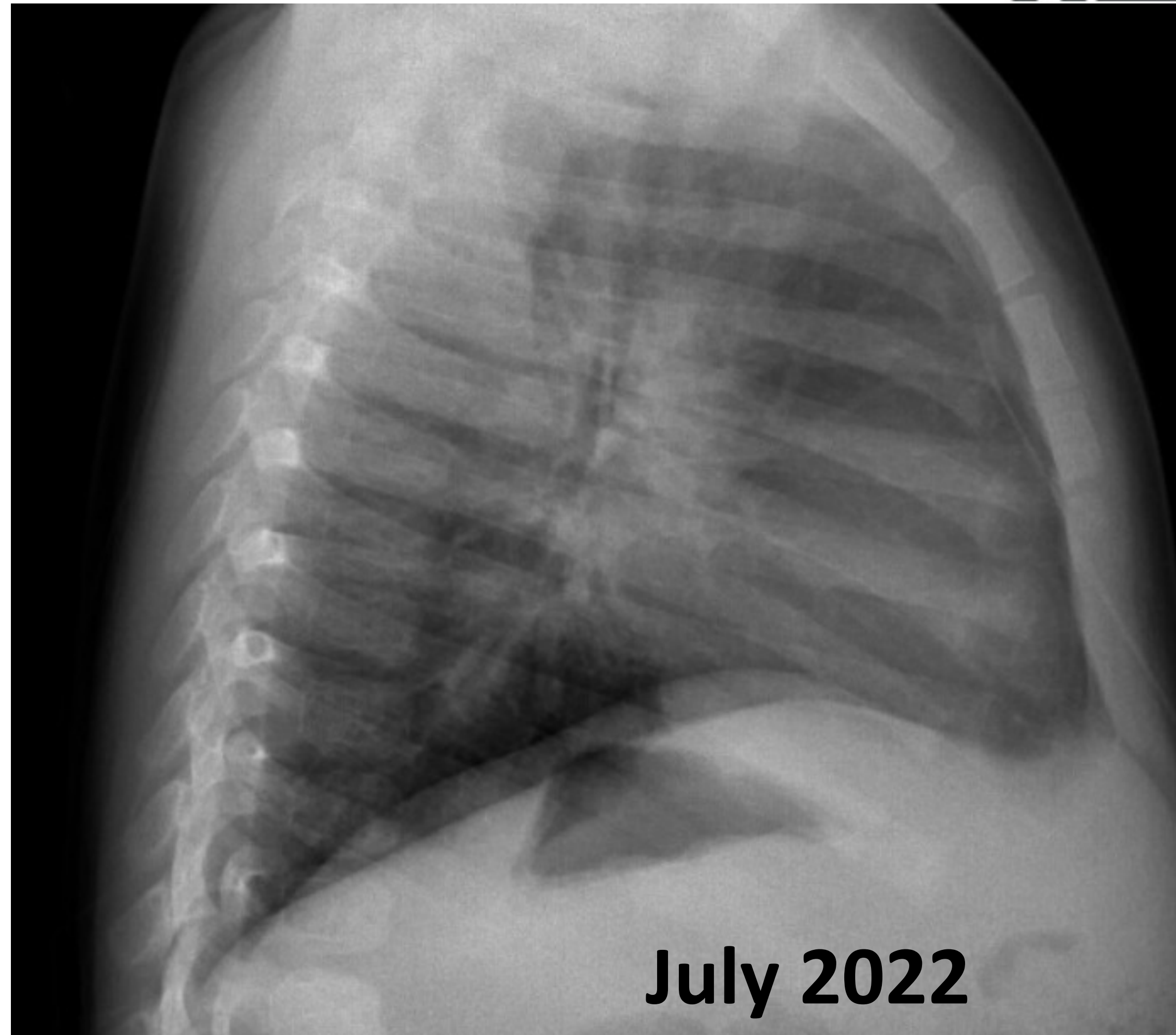
- TST or IGRA
- Exposure history
- Risk factors
  - Age / co-morbidities
- Symptoms
  - Obvious TB symptoms: cough, fever, weight loss, night sweats
  - Non-specific pediatric sx:
    - failure to gain weight
    - sluggish appetite
    - less energy / placid
    - delayed development

F/U CXR





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More detailed history – 16 mo

- They were in the military base in Wisconsin for about 6 months.
- About 6 months ago, he had 2 weeks of high unexplained fever.
- Doctors at the camp were unable to diagnose the process.
- He also had about a week of fever several months ago.
- This last week he is also had fever and cough.
- He sometimes sweats at night.
- He has had several days of decreasing playfulness lately. He is reasonably well grown, but has some modest developmental delay.
- The patient is starting to take a few steps. Says a couple words. Family feels that his fine motor control is not very good.

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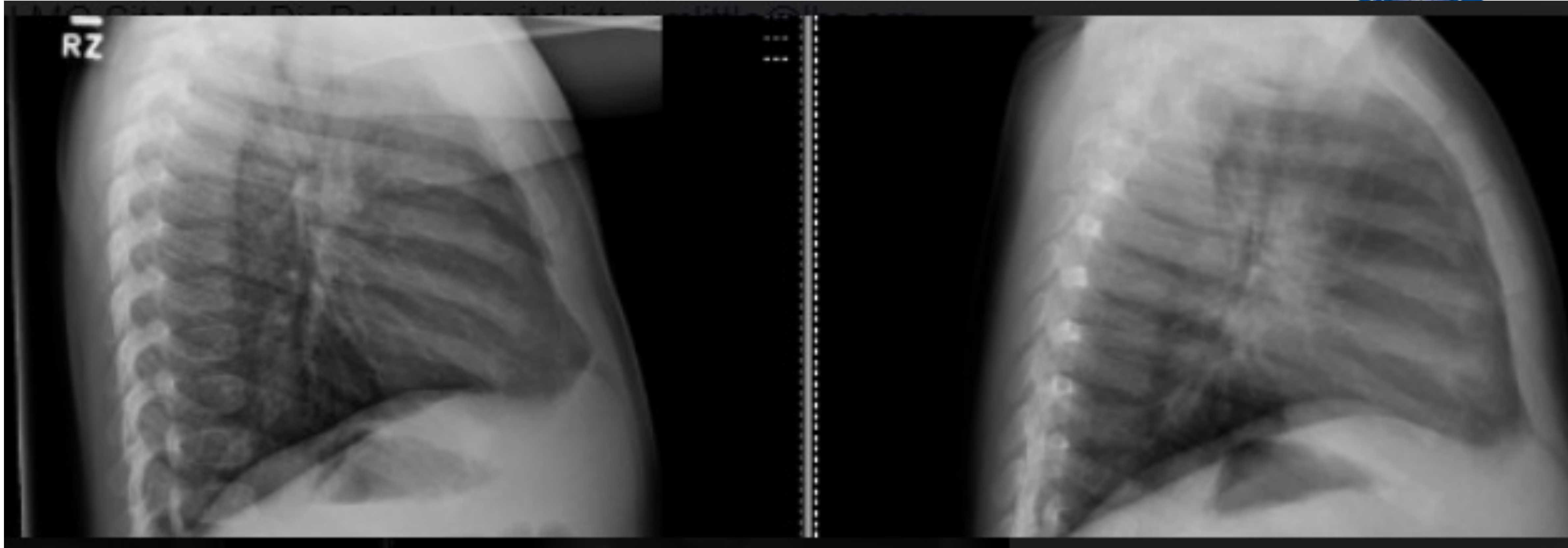

After therapy

Before therapy

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4 month old US born baby

- ~ 3 months of age, noted to have cough, progressing to poor PO intake, poor weight gain
- Referred to the ED

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What questions do you ask?

- More detailed symptoms
- Exposure history -
- TST / IGRA
- Imaging

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What questions do you ask?

- More detailed symptoms - 4 weeks of cough and intermittent fevers, work of breathing, wheezing
- Exposure history - family denies TB exposure.
  - Mom has had shoulder pain / Extremity numbness / tingling.
  - Mom immigrated from India 4 years prior.
  - She had gestational DM.
  - Reports losing weight in pregnancy
  - “baseline tachycardia”
- TST / IGRA - positive QFT
- Imaging

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Mom's CXR

- Right upper lobe patchy opacities in right suprahilar adenopathy.
- Chest CT: Tree-in-bud nodularity; Multiple enlarged right paratracheal lymph nodes
- MRI: effusion / enhancement of sternoclavicular joint
- Cortical irregularity and erosive change of clavicle

Baby evaluation

- Gastric aspirates and bronchoscopy are smear positive / Cx + / NAAT positive
- Baby was treated with INH / RIF / PZA / EMB
- Hospitalized serially for worsening respiratory symptoms
- Imaging showed increase lymph node size - treated for immune reconstitution with prednisone
- Serially hospitalizations due to respiratory distress / feeding difficulty / aspiration

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Four + months into therapy

- Despite:
  - Drug levels and dose adjustment
  - Courses of prednisone
  - Naso-duodenal tube feedings
  - Oxygen / CPAP at home

- Mass obstructing airway – required ENT resection
- Baby almost immediately was able to come off oxygen and have no work of breathing
- Finished therapy last week

Just another day on Curry Warmline duty

- Infection control nurse calls
- New mom with 13 day old baby was admitted after seizure at an outpatient visit
- Mom's evaluation shows CNS lesions, at least one bony lesion and opacities on CXR / possible miliary appearance on CT scan
- Question was whether the baby can visit the hospital with dad (mom in hospital x 9 days)

More information

- Mom did not yet have a diagnosis for her multifocal process
- She had immigrated from Africa about 4 years prior
- She was being evaluated for LTBI when she was found to be pregnant (chest radiograph deferred)

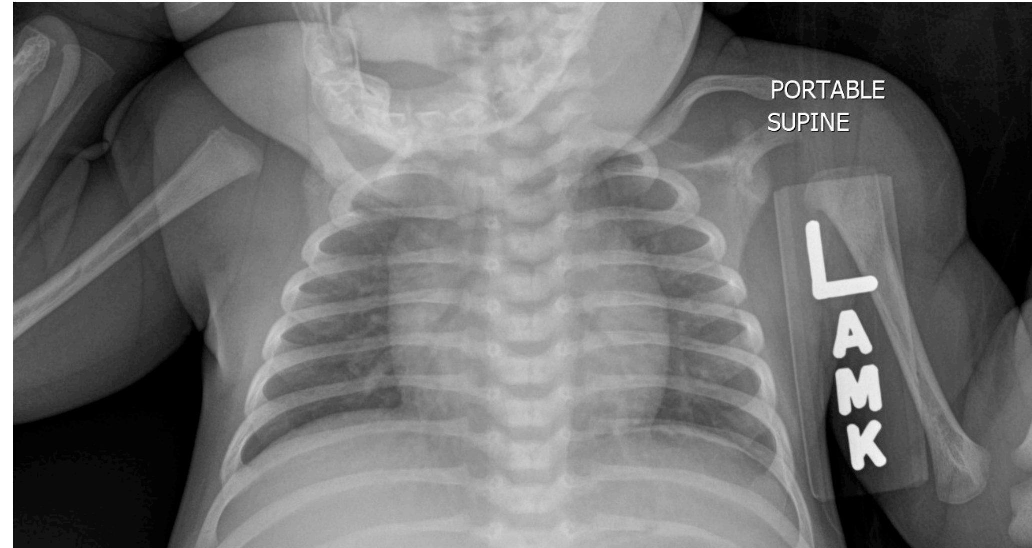
How would you respond ?

- Any advice for mom providers?
  - Look hard and start treatment for TB disease
- Any advice for baby providers?
  - Baby needs
    - » good physical exam
    - » 2 view chest radiograph
    - » Consideration of studies looking for TB
    - » TB treatment

Baby's course

- Despite long phone conversation with Peds ID attending, dad declined evaluation of the baby since TB diagnosis not confirmed for mom
- Several days later, dad sought care because baby hadn't stooled for 3 days
- In the ED, baby found to be febrile and fussy

Baby's course



- Otherwise normal infant physical exam
- WBC 11 K, 47% PMN, 39% lymph; Hgb 14, PLT 376
- CMP normal
- CSF 12 WBC, 83% lymph, glucose 48, protein 53, gram stain neg
- UA normal

Baby’s course

- Baby’s fever had initially resolved with antibiotics
- Antibiotics stopped as no evidence for bacterial infection
- Second fever to 39° noted and baby was sluggish

And then, this happened:

3/28/22 18 days of life

QUANTIFERON TB GOLD, BLOOD

Status: Final result Visible to patient: No (not released)

	Ref Range & Units	3wk ago
QUANTIFERON MITOGEN MINUS NIL	IU/mL	4.68
QUANTIFERON NIL	IU/mL	3.85

QUANTIFERON PLUS TB1 MINUS NIL	0.00 - 0.34 IU/mL	1.15 ^
QUANTIFERON PLUS TB2 MINUS NIL	0.00 - 0.34 IU/mL	1.70 ^

Baby's course

- Baby was treated with RIPE for concern for TB disease
- Mycobacterial blood culture subsequently grew *M. tuberculosis*

Perinatal Tuberculosis

- Like other infections of the newly born, TB can be
  - Congenital – acquired in utero
    - Hematogenous acquisition, often during maternal bacillemia
      - Primary or disseminated TB in mom most common
    - Tubercule can rupture into amniotic fluid and baby can swallow or “inhale” infected fluid into the lung
  - Natal – acquired during the birth process
    - Late swallowing or inhaling of amniotic fluid or urogenital secretions
  - Postnatal
    - Inhalation of tubercle bacilli when mom or another caregiver has contagious pulmonary / laryngeal TB

Congenital Tuberculosis

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Characteristics of congenital TB	Number or percent
Premature birth	70 / 170 (41%)
Average age of onset	20 days
Abnormal chest radiograph	133 / 170 (83 miliary / nodules)
Fatal case	68 / 169 (40%)
Postpartum maternal diagnosis	121 / 157 (71%)
Fever / respiratory distress	64% (both)
Hepatic and or splenic enlargement	66%
Lethargy / irritability / poor feeding	39%
Lymphadenopathy	34%
Skin lesions	17%
Ear discharge	14%

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6 month old US Born child

- Evaluated because her aunt's BF was diagnosed with 4+ smear positive TB
- Symptoms: weight gain has tapered off a bit and she has been fussy for the last few weeks.
- Only two people in the 9 person household did not have positive QFT / TST results.

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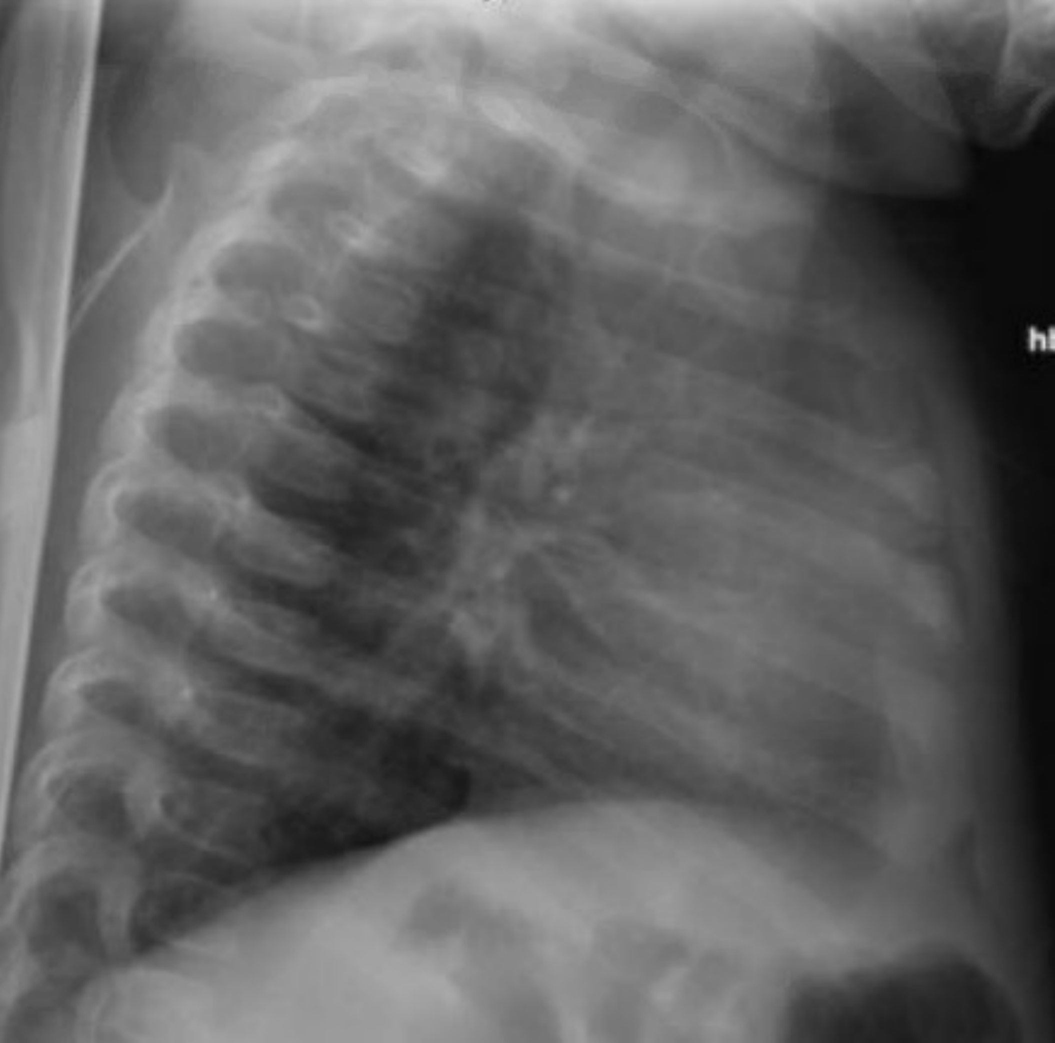

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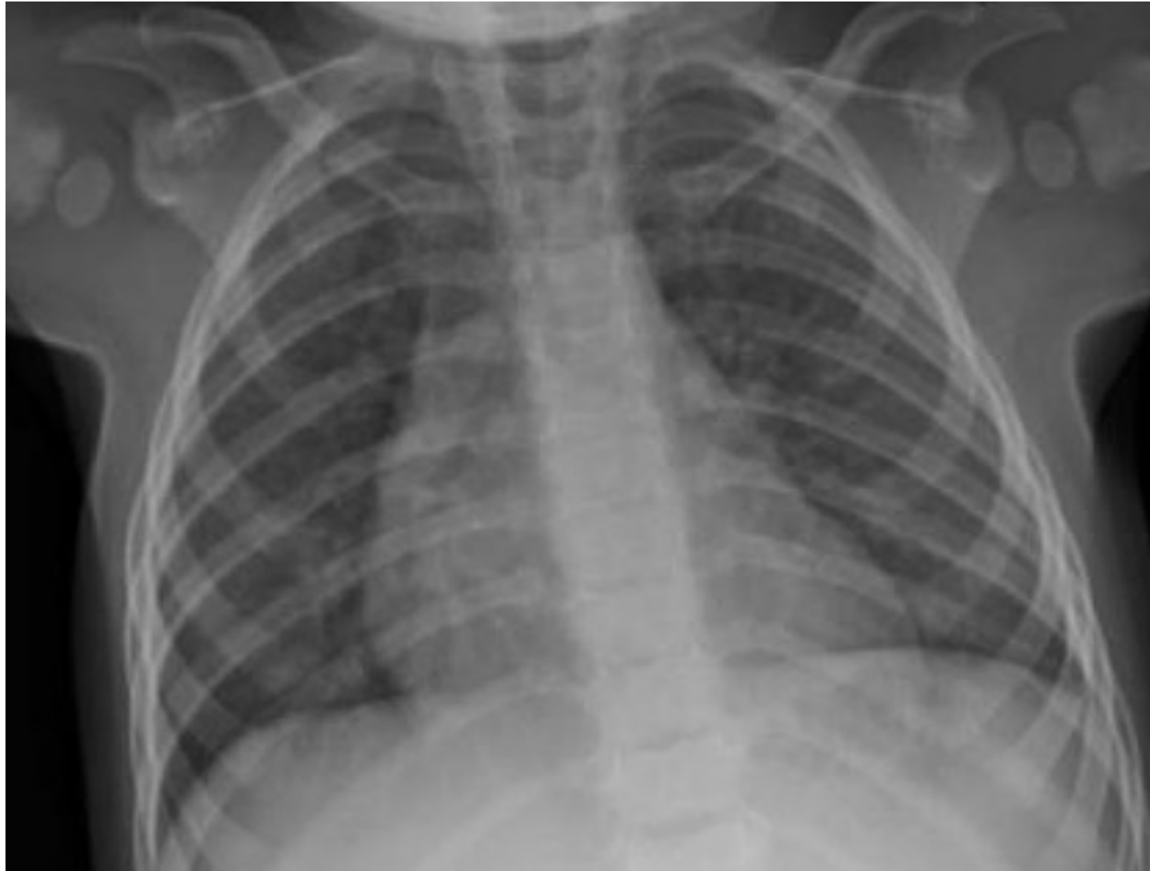
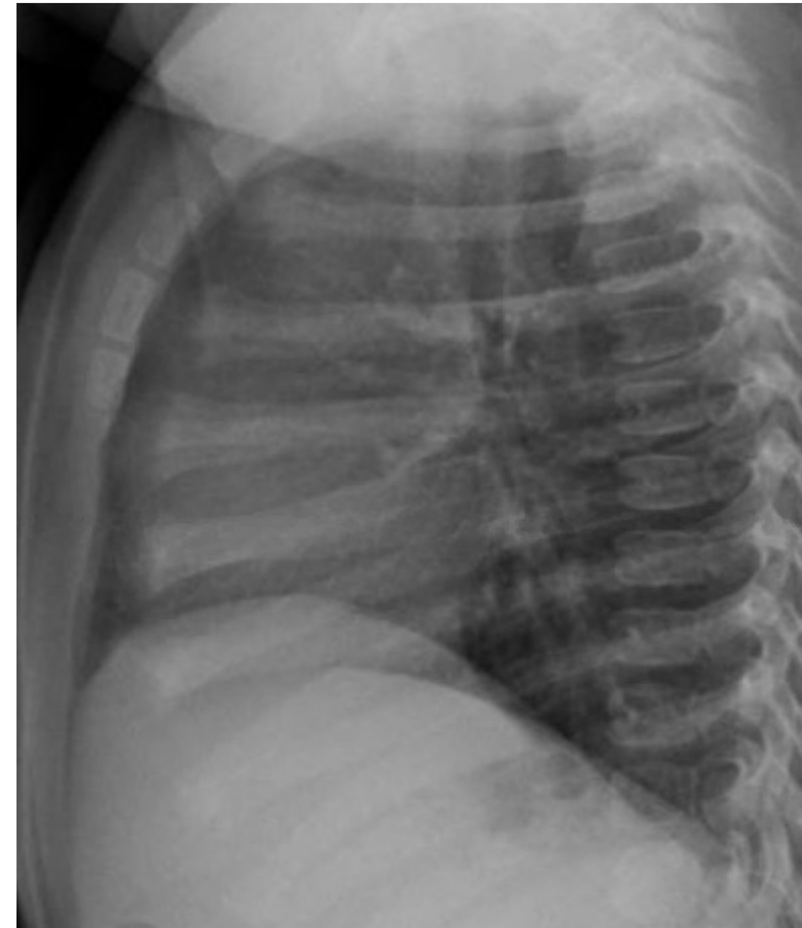
Several months into TB therapy





X ray had normalized - she was the first child we treated with the new four month regimen

ORIGINAL ARTICLE

Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

Anna Turkova, M.R.C.P.C.H., Genevieve H. Wills, M.Sc., Eric Wobudeya, M.Med., Chishala Chabala, M.Med., Megan Palmer, M.B., Ch.B., M.Med., Aarti Kinikar, M.D., Syed Hissar, M.D., M.P.H., Louise Choo, Ph.D., Philippa Musoke, Ph.D., Veronica Mulenga, M.Med., M.Sc., Vidya Mave, M.D., M.P.H.&T.M., Bency Joseph, M.B., B.S., M.P.H., et al., for the SHINE Trial Team*

March 10, 2022

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SHINE Trial comparing 4 vs 6 mo peds TB

- 1204 children diagnosed with non-severe (minimal) TB randomized (sm-)
  - 4 months total: INH, RIF, PZA +/- EMB x 2 months and INH & RIF x 2 months
  - 6 months total: INH, RIF, PZA +/- EMB x 2 months and INH & RIF x 4 months

- Median age 3.5 yrs
- 52% males
- 11% living with AIDS
- 14% bacteriologically confirmed

- 3% of each group had "unfavorable outcome"
- N = 8 treatment failure in 4 mo group. N = 4 treatment failure in 6 mo group –