



Meningitis Case - Taking Fire From All Directions

Lisa Armitige, MD, PhD

April 2, 2024

New Directions in TB
April 1 – 2, 2024
Houston, Texas

Lisa Armitige, MD, PhD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity





Meningitis Case - Taking Fire From All Directions

Lisa Armitige, MD, PhD

Professor of Medicine/Pediatrics
Division of Adult infectious diseases
UT HSC at Tyler

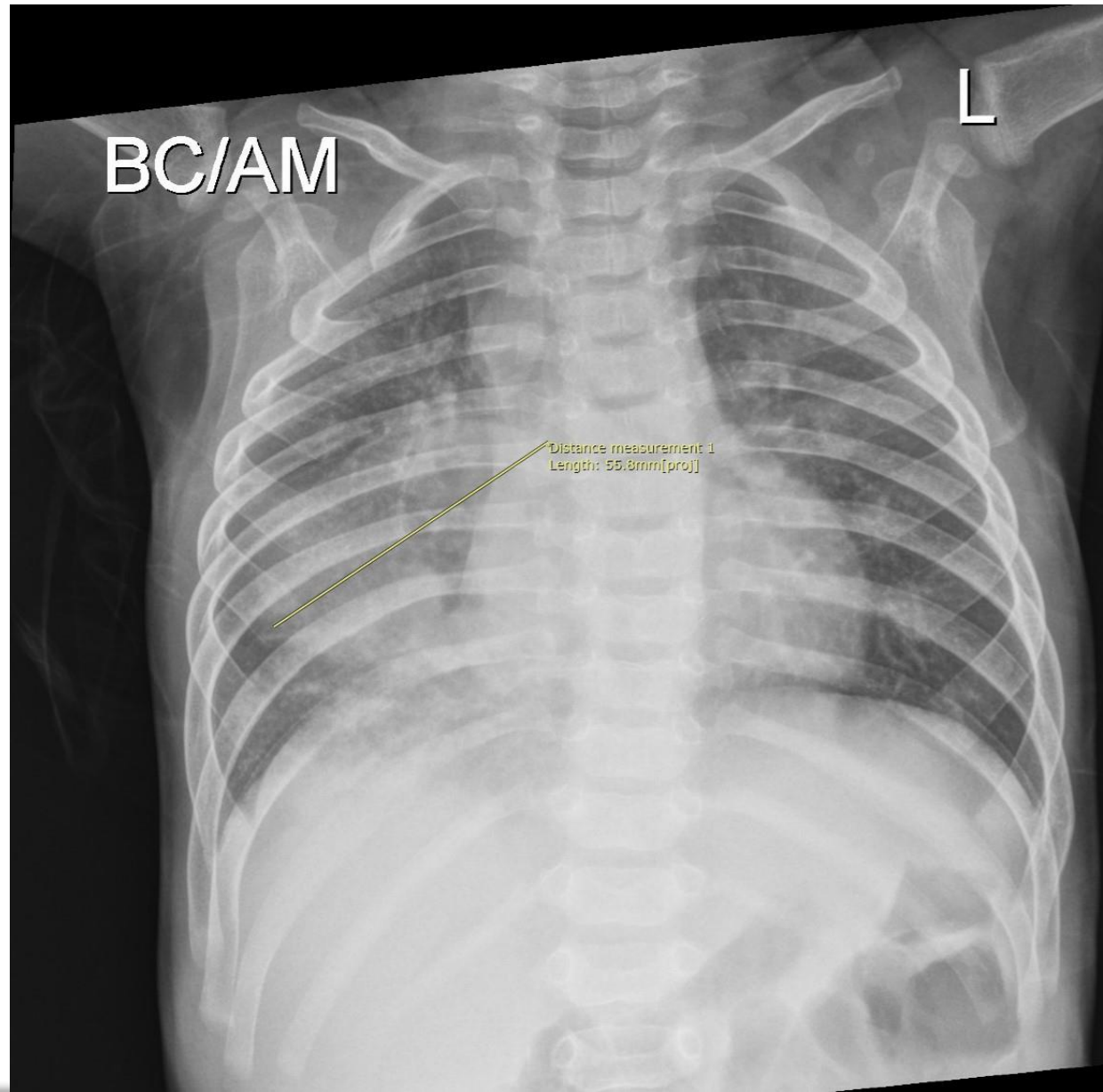
Co-Medical Director
Heartland National TB Center

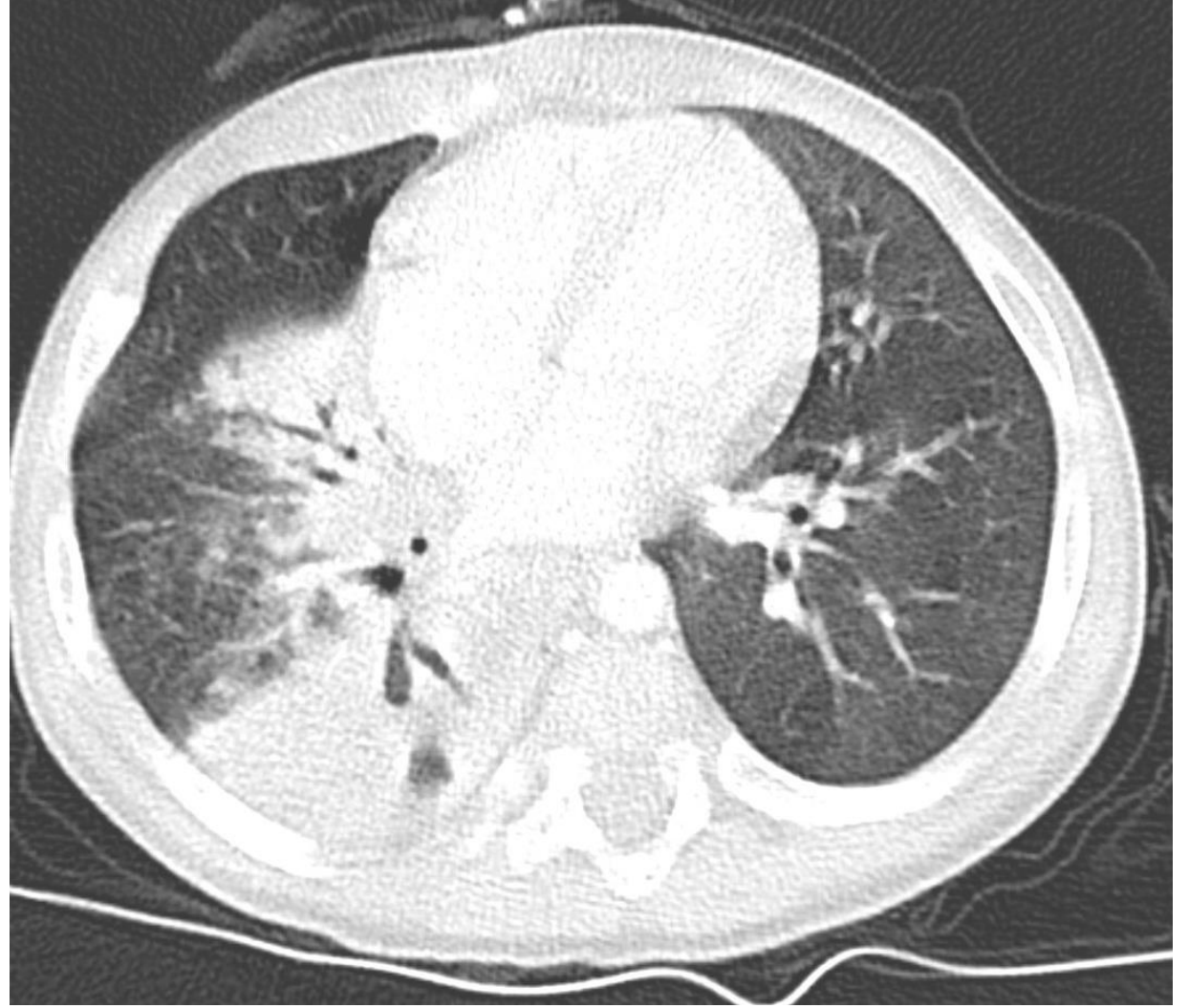
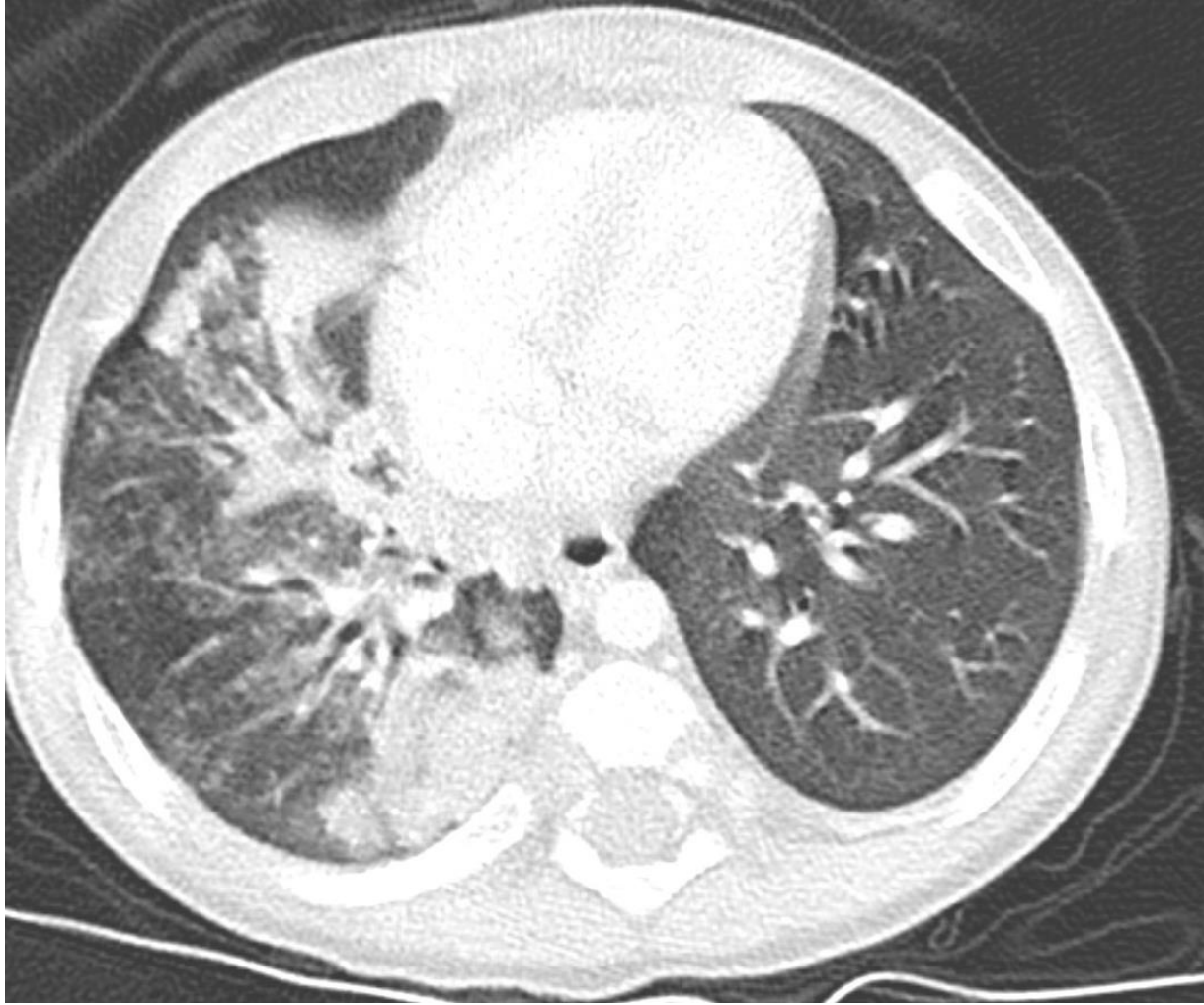
Little Dude with Big Problems

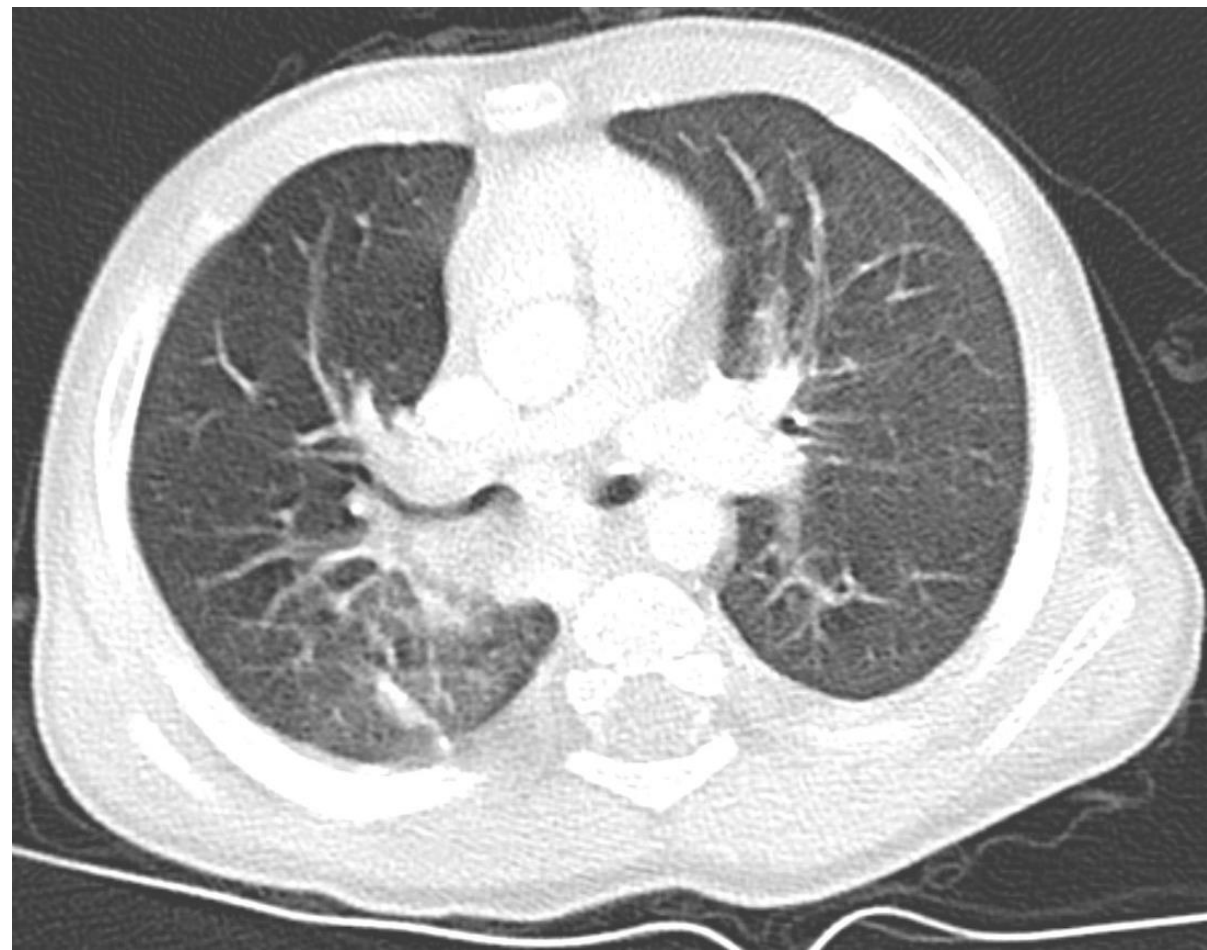
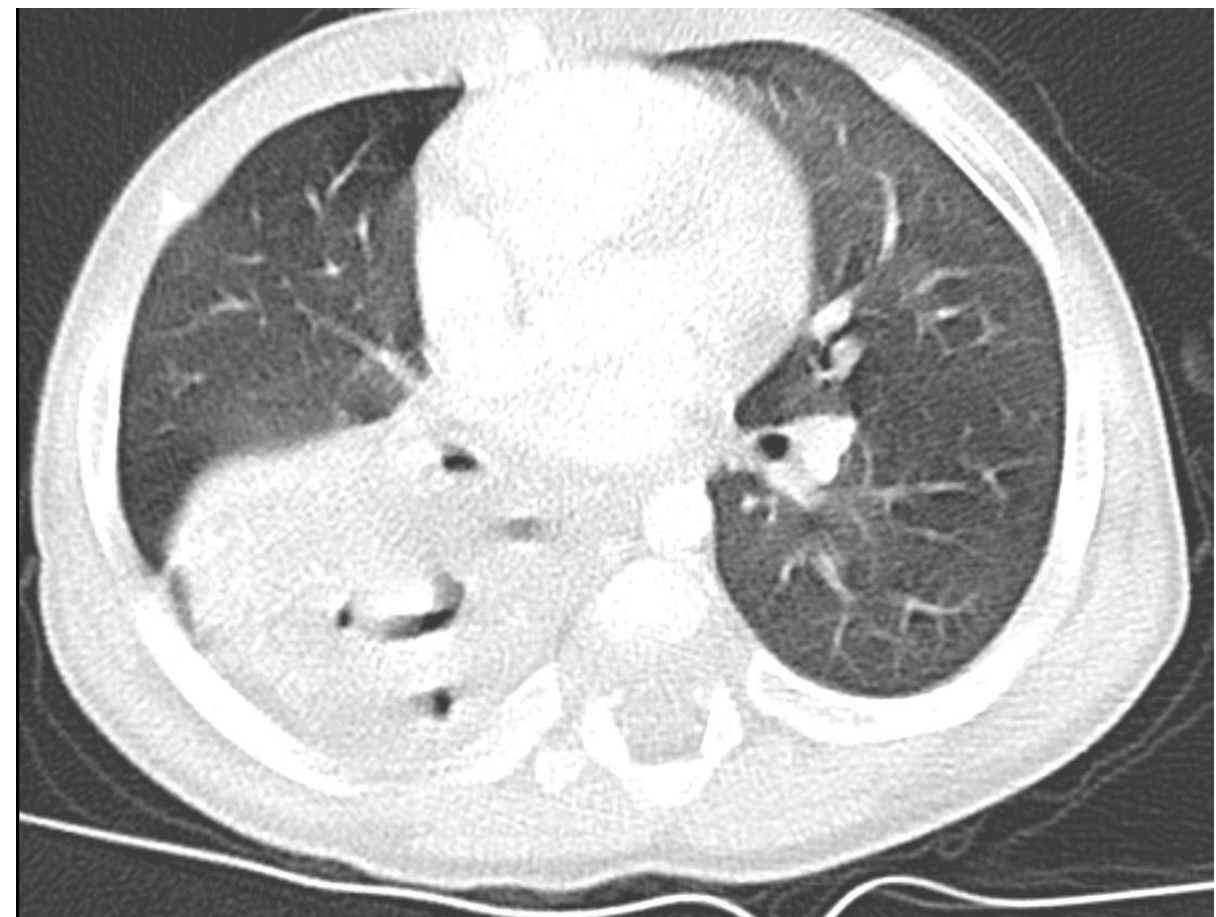
- Pt is an 8 ½ -month-old US born child
- He presented to the ER for
 - 2 weeks of fever,
 - 3 days of poor feeding, decreased urine output and associated lethargy/imbalance,
 - 2 days of watery diarrhea and vomiting the morning of admission
 - Associated cough/congestion
- Viral panel positive for parainfluenza and rhinoenterovirus
- CRP/procal wnl, ESR elevated
- BCx, Ucx negative



Admission CXR







TB workup

- QFT positive
- CSF glucose 30, CSF protein >460
- CSF WBC 679 (72% lymphs), CSF RBC 43,000
- MRI brain
 - Diffuse leptomenigeal enhancement with involvement of bilateral 5th, 7th, 8th CNs
 - Meningitis and ventriculitis
 - Hydrocephalus of lateral and third ventricles, mild dilatation of the 4th
 - No definitive infarct



Some History

- Mom took the baby to Mexico shortly after birth
- First 2 months of life were spent in Mexico
- Mom returned with the baby and sought care



Article

Report of 16 Years of the BCG Vaccine under the Expanded Program on Immunizations in Mexico (2006–2021)



Rodrigo Romero-Feregrino ^{1,2,3,4,*} , Raul Romero-Cabello ^{1,2,4,5,6}, Mario Alfredo Rodríguez-León ^{1,2,7}, Raúl Romero-Feregrino ^{1,2,4} , Berenice Muñoz-Cordero ^{1,2} and Julieta Isabel Aguilar-Feregrino ^{2,8}

Table 1. Newly diagnosed cases of tuberculosis in Mexico: 2000–2021 period.

Disease/Year	2000 [6]	2006 [7]	2012 [8]	2016 [9]	2018 [10]	2019 [11]	2020 [12]	2021 [13]
Respiratory tuberculosis	15,201	13,985	15,334	16,082	16,700	45,637	31,724	16,008
Meningeal tuberculosis	78	146	187	297	395	396	282	455

- We found that vaccine acquisition, dose application and coverage are highly variable each year. Coverage is 90% or higher, except for the 2017–2020 period.
- Coverage was lower than 90% during the last 4 years, whereas this value decreased to 21% in 2020.
- According to our calculations, between 3,917,616 and 4,961,868 individuals did not receive the BCG vaccine.
- The access to this vaccine is difficult and the number of newly reported cases of tuberculosis have increased during the last years.



How did we get here.....?

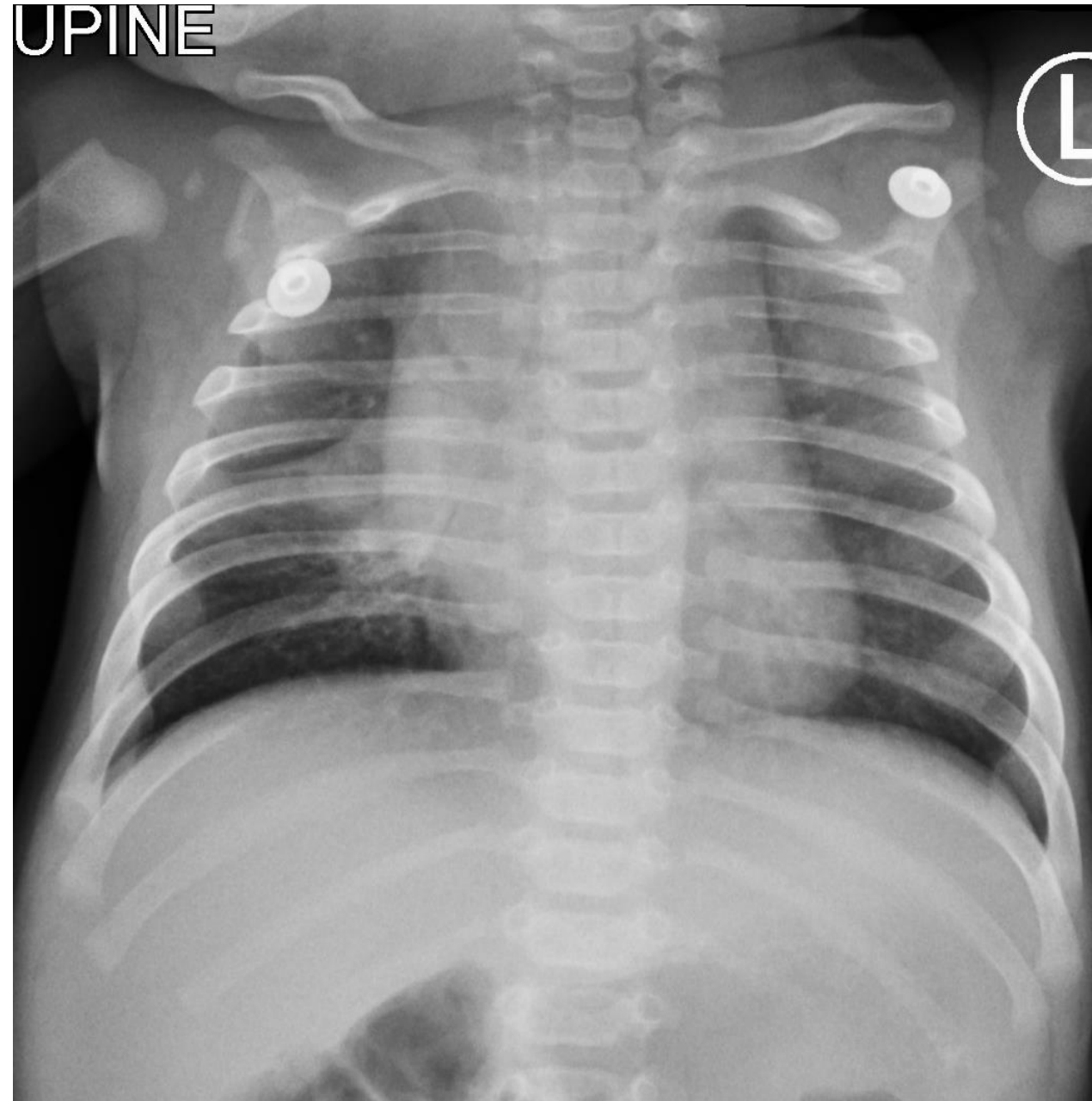


Aug 2023
2 months of age

Admitted with fever, mild
cough

Plt 722

3 days of azithromycin
7 days of cefdinir



Oct 2023
4 months of age

Evaluation for cough,
congestion

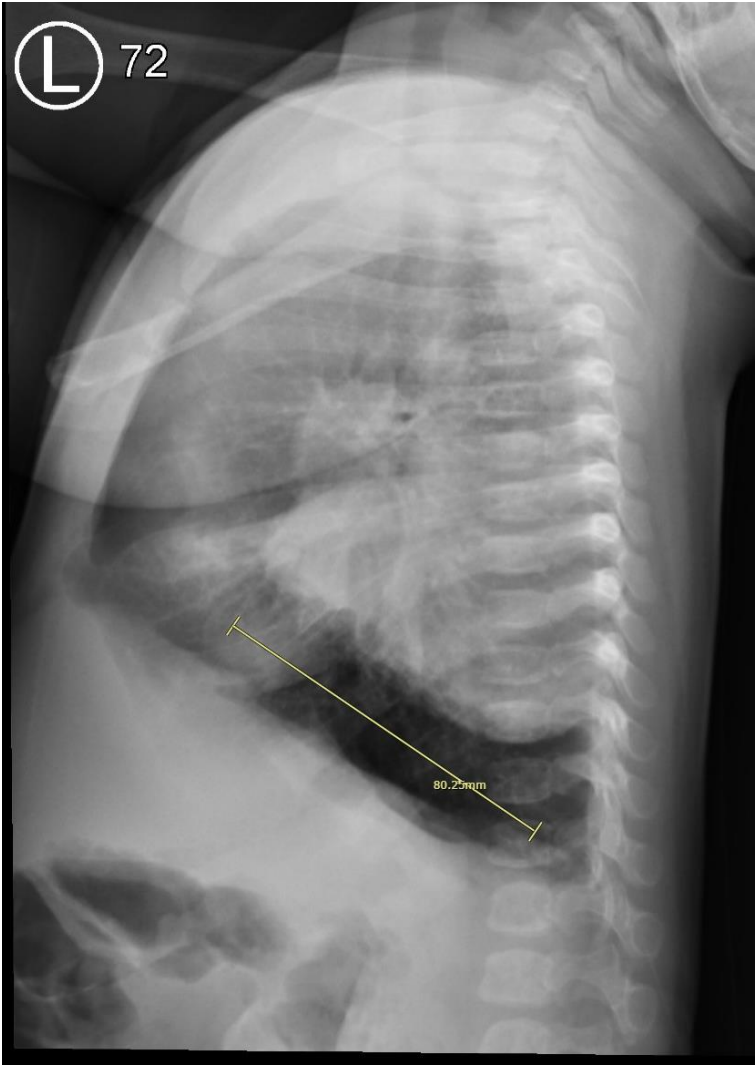
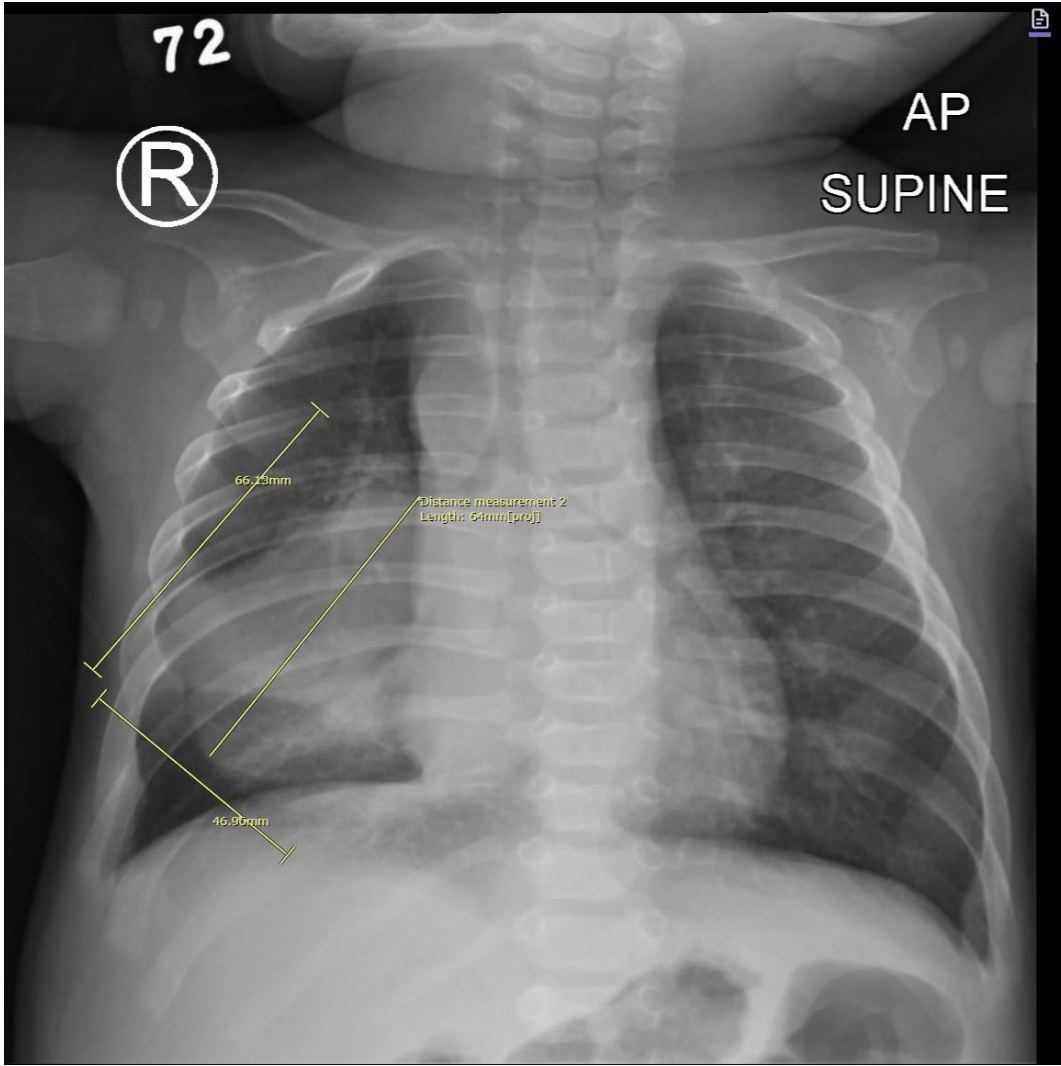
Did not finish course of
antibiotics from before


Poor weight gain since
prior visit: ?milk allergy

Wheezing on exam

Checked for Covid

Prescribed Augmentin





Guidance for national tuberculosis programmes on the management of tuberculosis in children

Second edition



Symptoms

In most cases, children with symptomatic TB develop chronic unremitting symptoms, i.e. symptoms that persist for more than 2 weeks without sustained improvement or resolution following appropriate treatment for other potential diagnoses (e.g. antibiotics for pneumonia; antimalarials for fever; nutritional support for failure to thrive). The commonest symptoms include:

- cough
- fever
- not eating well/anorexia
- weight loss or failure to thrive
- fatigue, reduced playfulness, decreased activity.

The specificity of symptoms for the diagnosis of TB depends on how strict the definitions of the symptoms are. However, no definite cut-offs, e.g. duration of symptoms, have been validated and accuracy will depend on context. Strict symptom criteria have lower sensitivity and specificity in those at greatest risk of severe disease and poor outcome such as infants or very young children (under 3 years), children living with HIV, or severely malnourished children (1). These groups pose the greatest challenge for clinical diagnosis.

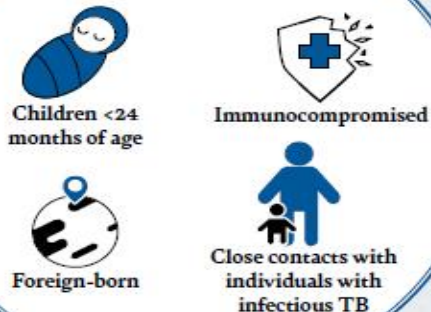
5 month old Sister of a Patient with TB Meningitis

- The 5-month-old sister of a 22-month-old with TB meningitis was being evaluated as part of a source case investigation
- Initially, her CXR was negative and she had no symptoms
- One week later she had cough and an abnormal CXR, she was referred to the ED for evaluation
- Her CSF showed
 - elevated WBC (54),
 - elevated protein (68)
 - low normal glucose (51, serum glucose 79).
- **The treating physician wanted to treat for LTBI.....**



Fighting Tuberculous Meningitis under 5

Risk Factors



CDC

Improving Outcomes

Prompt diagnosis and treatment is essential. Failure to begin treatment swiftly results in poorer outcomes, significant and permanent neurological sequelae, or death.



Window Prophylaxis

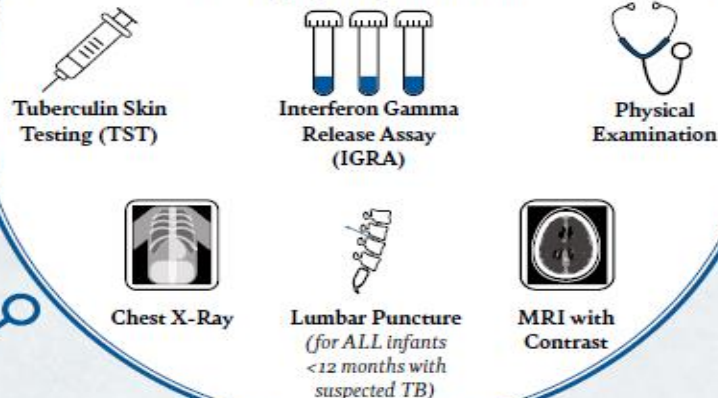
Close contacts to someone with infectious TB who are <5 years of age should receive treatment for latent TB infection once TB disease is excluded by chest radiograph and symptom review. Treatment is needed even when a TST and/or IGRA is negative. A second TST and/or IGRA should be administered 8 - 10 weeks after the last exposure to infectious TB.



CDC

Assessment & Medical Evaluation

Tuberculous meningitis is more difficult to diagnose than other forms of bacterial meningitis, but thinking of TB as a possibility and rapid screening using various methods in order to make a proper diagnosis is crucial.



Outcomes for TB Survivors



On average, 54% of children who survived tuberculous meningitis developed neurological sequelae.

The Lancet, 2014

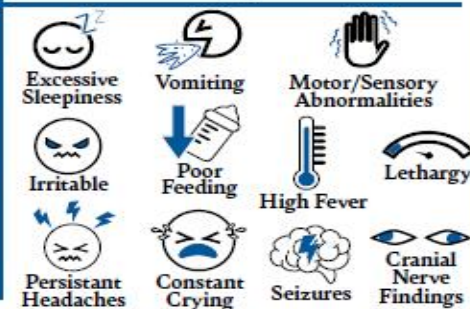
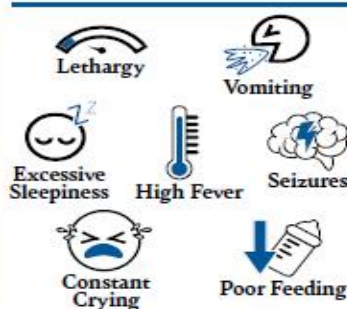
Percent Risk of Disease by Age



Miller, 1963



Watching for Early Signs & Symptoms



Note: Young children may not be able to share or verbalize these symptoms when asked, so collaborating with care givers will be imperative.

HEARTLAND
NATIONAL TB CENTER
THE UNIVERSITY OF TEXAS AT TYLER HEALTH SCIENCE CENTER

For Medical Consultations:
(800) TEX-LUNG or (800) 839-5864
<http://www.heartlandntbc.org/consultation>

Safety and Efficacy of 25 mg and 35 mg versus 10 mg Rifampicin in Pulmonary TB: A Randomised Trial

Bhavani et al., 2023 | *Open Forum Infectious Diseases*

Summary

To find out whether 25 and 35mg rifampicin yield faster culture conversion with toxicity comparable to 10mg when given along with other ATT drugs for 8-weeks.

Study Design



Randomized Controlled Clinical Trial



Multi-centric, open-label



India



New culture-positive, drug-sensitive adult PTB patients

Results

Primary Outcome
Hepatotoxicity

2R₁₀HZE₇/4R₁₀HE₇

3.8% [4/105]

Secondary Outcome
Time to Culture Conversion

44 days;
Reference

2R₂₅HZE₇/4R₁₀HE₇

6.3% [7/112]

34 days; aHR=1.71
95% CI [1.26 - 2.31]

2R₃₅HZE₇/4R₁₀HE₇

11.3% [12/106]

34 days; aHR=1.81
95% CI [1.33 - 2.48]

Conclusion

Hepatotoxicity, clinical jaundice, and treatment interruptions occurred significantly higher with R35 than R10. Since R25 was almost safe as R10 and also highly efficacious than R10, it may be considered for implementation.

Taking Fire From All Directions

- BCG
 - Mexico will not vaccinate babies born outside of Mexico
 - Babies that normally receive BCG protections may not
- Children presenting for TB-related symptoms are not being recognized
- High dose rifampin shows benefit for TB meningitis in adults but data in children is still lacking
- Adequate studies for diagnosis and management of TB meningitis in adults and children are still lacking



Questions?

Lisa.Armitige@dshs.texas.gov

1-800-TEX-LUNG

