A Case for Source Case Investigation: Responding to Pediatric TB in Los Angeles and Beyond

Curry International Tuberculosis Center

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END TB

County of Los Angeles Public Health

Disclosures

- I have no financial relationships to disclose.
- I have no conflicts of interest to disclose.

Learning Objectives

- Identify incident TB disease in children <5-years-old as a **public health sentinel event.**
- Apply principles of TB control and management to **source case investigation** to improve patient and program outcomes.

A quick scenario

- Previously healthy siblings: 4yo boy and 14yo girl
- Recently arrived with mother from Nicaragua in December 2022
- Both are QFT+ in March 2023 during screening by primary care provider
- CXR’s are negative, started on preventive treatment

Polling Q: what do you do now in your LHJ?

A) We conduct source case investigations for every young child <5yo who is diagnosed with culture-confirmed TB-3 (TB disease).

B) We conduct source case investigations for every young child <2yo with TB-2 (TB infection).

C) Both A & B.

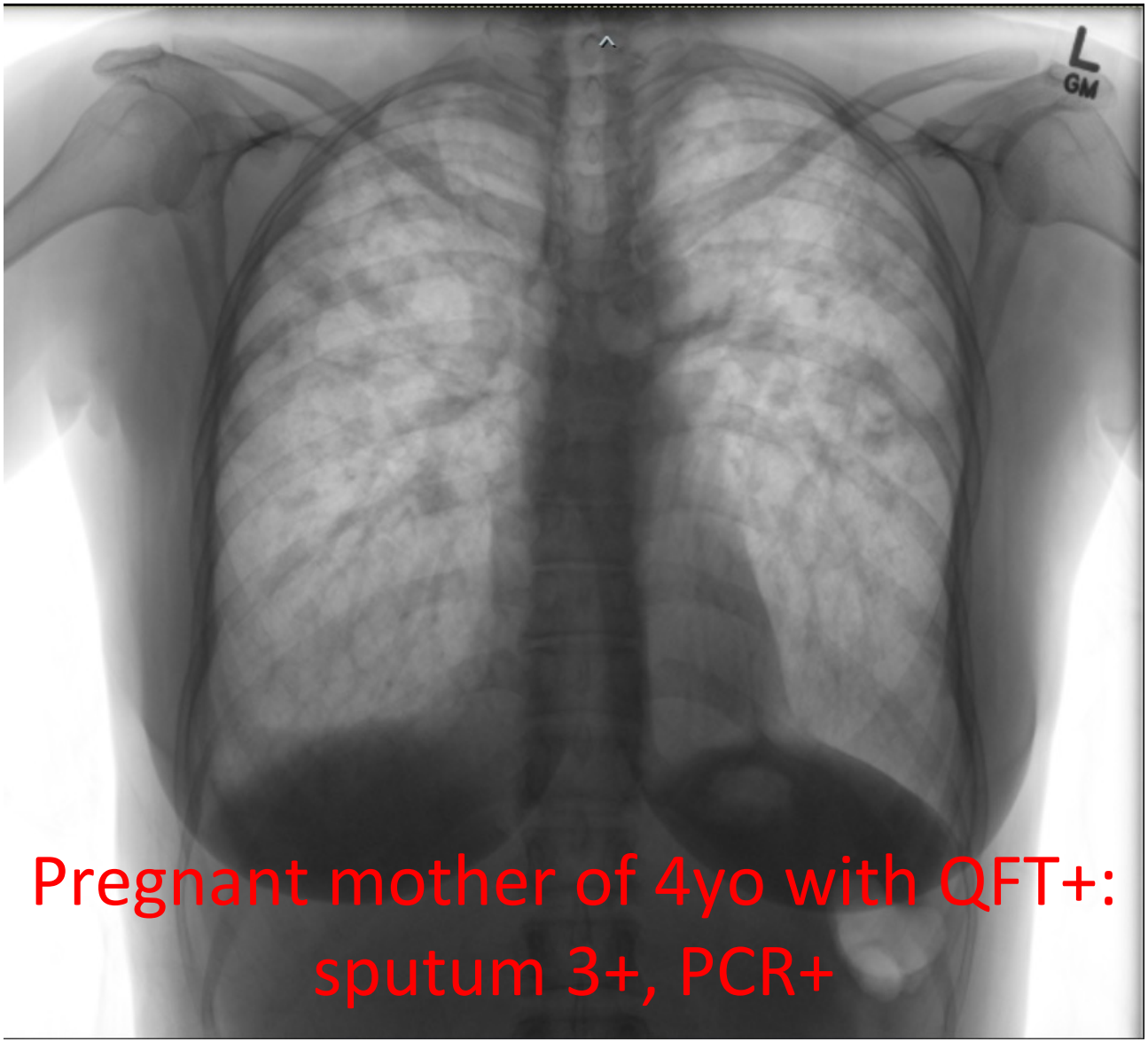
D) We conduct source case investigations for a subset of young children in the categories above.

E) We do not routinely conduct source case investigations.

A quick scenario (continued): siblings with +QFT

- 4yo and 14yo do not complete preventive treatment prescribed by primary care provider in March 2023, attributed to lapse in Medi-Cal coverage
- No public health follow up or intervention

- Mother presents with cough and nausea to local urgent care in July 2023
  - Diagnosed with community acquired pneumonia and pregnancy (estimated gestation ~12 weeks)



Pregnant mother of 4yo with QFT+: sputum 3+, PCR+

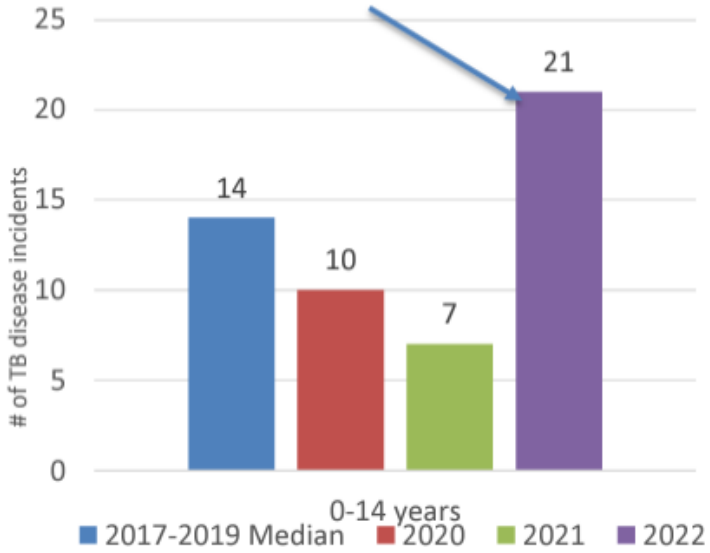
AAP *Red Book* Online (Redlined updates, Nov 2022)

"A diagnosis of [TB infection] or TB disease in a young child is a **public health sentinel event** often representing recent transmission."

https://publications.aap.org/redbook

Pediatric TB in Los Angeles County (2022)

2022 pediatric TB incidents were **50% HIGHER** than the 2017-2019 median.



Pediatric TB disease incident characteristics

Year	% Microbiologically Confirmed	% Latinx/Hispanic race/ethnicity
2017-2019 Median	47%	83%
2020	70%	50%
2021	29%	71%
2022	43%	81%

Note: Pediatric age group defined by TB surveillance conventions, not for clinical purposes.
Microbiologically confirmations include: positive culture, positive NAAT, positive smear/tissue.
Data exclude Pasadena and Long Beach TB disease incidents and are provisional to change. Based on TRIMS data and initial case count reported, updated March 23, 2023.

Slide credit: Edward Lan

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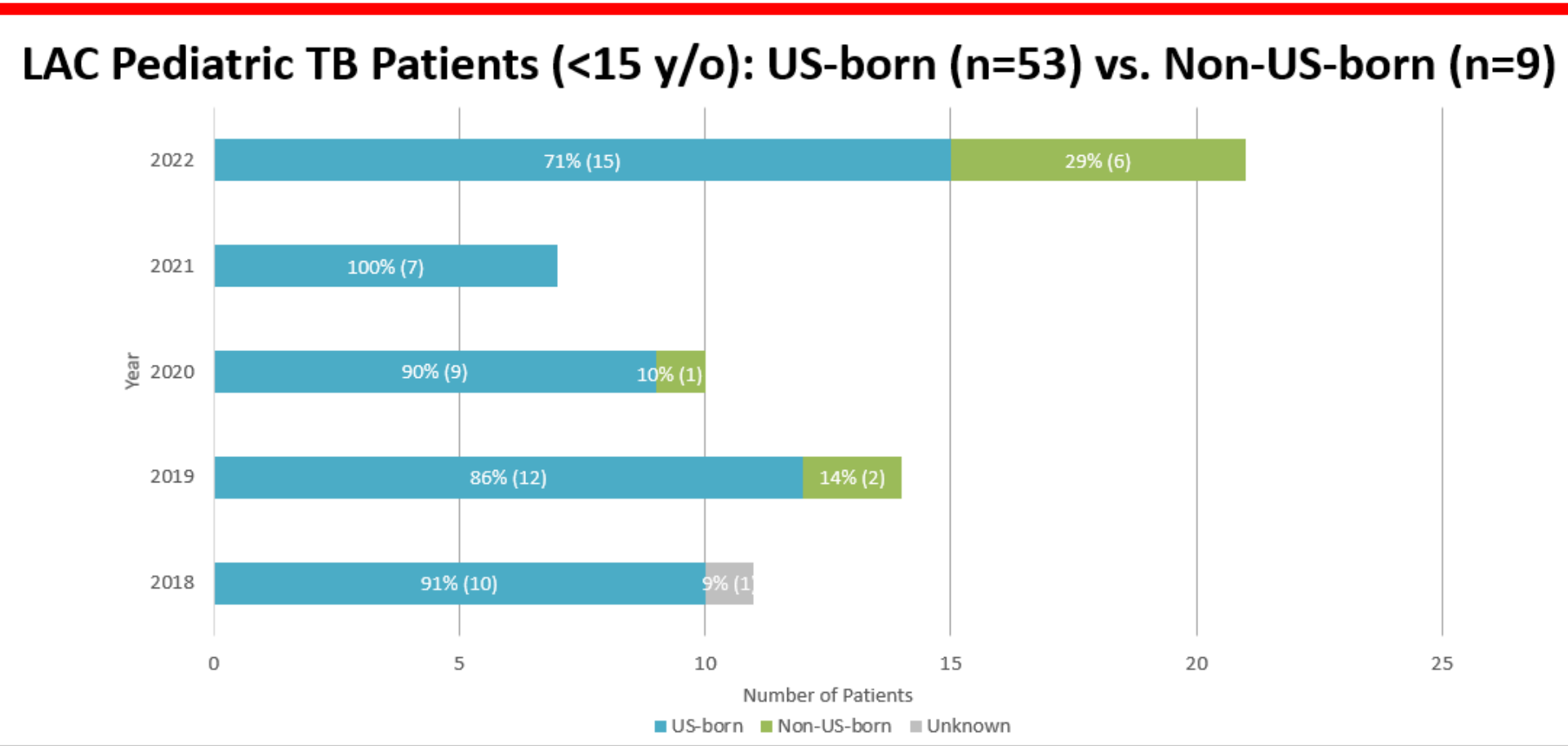
Pediatric TB in LAC (2018-22): Nativity



Slide credit: Melissa Zhang & CDR Sophia Hsu

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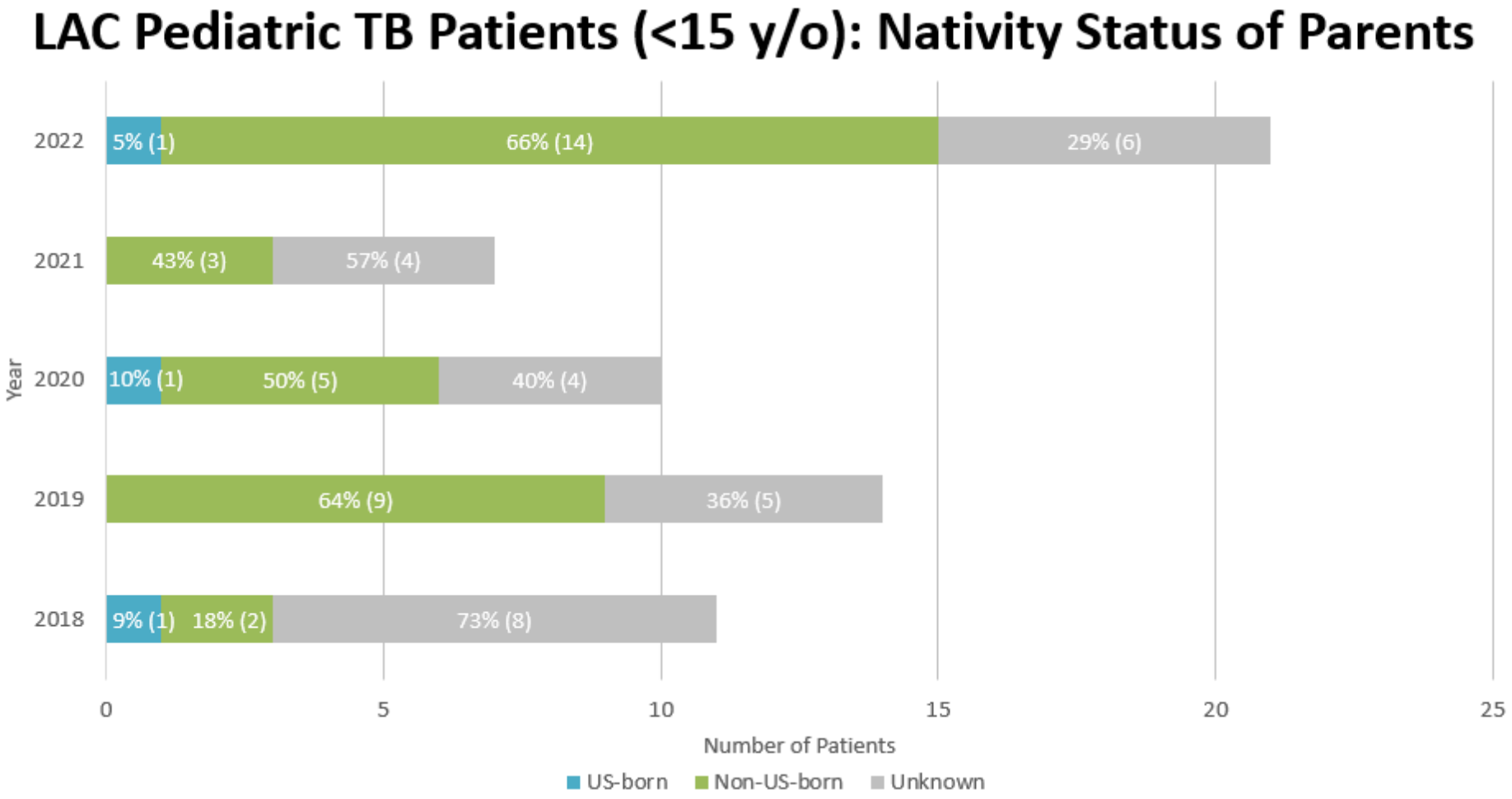
Pediatric TB in LAC (2018-22): Binational families



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Pediatric TB in California (2020-2)

- Since the advent of the pandemic (2020-2), n = 150 children between 0-14yo in California have been diagnosed with TB disease.
  - ~40% increase in TB incidents among 0-14yo between 2021 to 2022, which has happened just one other time in the past decade (2016 to 2017).
- On average, a child is diagnosed with TB disease almost **every week** in California!

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/TBCB-Provisional-Data-Tables-2022.xlsx

CDC (2005)

Source-Case Investigations

A source-case investigation seeks the source of recent *M. tuberculosis* infection, perhaps newly diagnosed TB disease (*43*). TB disease in children aged <5 years typically indicates that the infection must be recent. For this reason, it is a sentinel public health event. Young children usually do not transmit TB to others, and their contacts are unlikely to be infected because of exposure to them (*150*). A source-case investigation moves in the opposite direction of contact investigation, but the principles used in contact investigation apply. Source-case investigations concerning adults with TB disease are not

Source-case investigations typically have low yield for the effort required. They are not recommended unless a TB control program is achieving its objectives (in particular, treatment of infected contacts) when investigating infectious cases.

CDC (2005)

Source-Case Investigation for a Child with TB Disease

The yield of source-case investigations for children who have TB disease varies, typically <50% on average (*152–156*). Source-case investigations can be considered for children aged <5 years. A younger age cut-off might be advisable because the focus would be on more recent transmission. An investigation may be started before the diagnosis of TB is confirmed because waiting for confirmation can decrease the chances of finding associates.

https://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

CDC (2005)

Source-Case Investigation for a Child with Latent *M. tuberculosis* Infection

A search for the source of infection for a child who has LTBI is unlikely to be productive (*157–159*). These kinds of investigations are recommended only regarding infected children aged <2 years and only if data are monitored to determine the value of the investigation.

https://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

CDC (2005)

Procedures for Source-Case Investigation

Seeking a source case follows the same overall procedures as a standard contact investigation. Parents or guardians usually are the best informants. Such persons are termed associates. Attention focuses on ill associates who have symptoms of TB disease. A source-case investigation should begin with the closest associates (e.g., household members).

Limited data are needed for assessing the productivity of source-case investigations. These data include the number of index patients investigated for their sources, the number of associates screened for TB disease, and the number of times that a source is found.

https://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

How Are Source Case Investigations Conducted?

A source case investigation moves in the opposite direction of a contact investigation, but the same principles and investigative skills apply. A source case investigation usually begins by reviewing existing information (e.g., medical records) to confirm that the person has been recently infected with *M. tuberculosis*. Once it has been determined that the person has been recently infected, the next step is to determine potential source cases. This is done by interviewing the person who has been recently infected or by conducting proxy interviews if the source case investigation involves a young child.

Conducting Source Case Investigations Involving Children

If the source case investigation is for a child, their parent, guardian, or someone else who knows the child's lifestyle should be interviewed. The principles of a source case interview are similar to the standard TB contact investigation interview; however, the emphasis is on finding the source of TB instead of finding contacts to the case.

https://www.cdc.gov/tb/education/ssmodules/pdfs/Modules8-508.pdf

How Are Source Case Investigations Conducted?

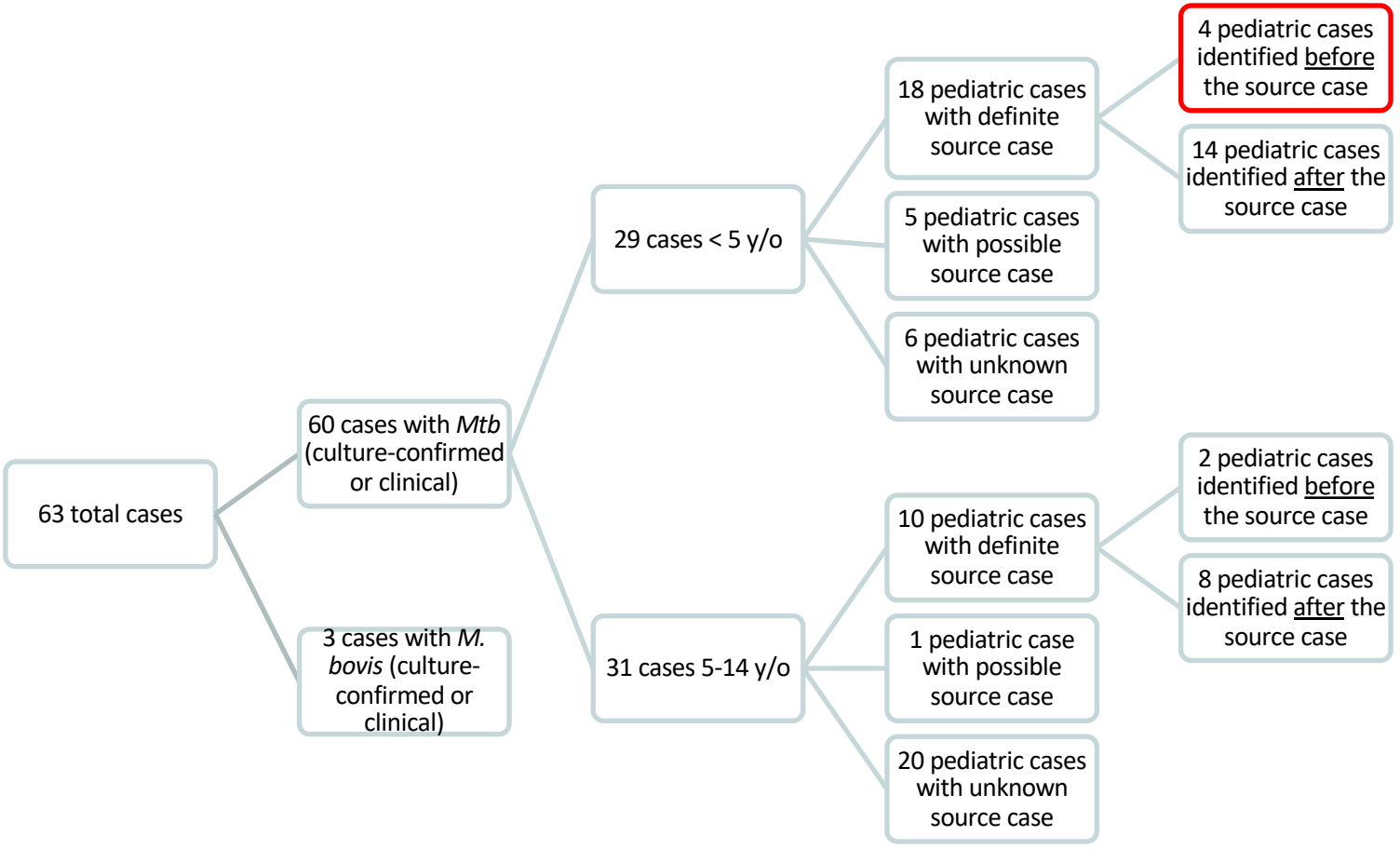
Once potential sources have been identified, they should be located and assessed. Assessments during source case investigations typically focus on symptom reviews, potentially followed by chest x-rays and respiratory specimen collection for AFB smear and culture. Compared to a contact investigation, less emphasis is usually placed on testing for infection unless investigators are concerned about potential ongoing transmission.

https://www.cdc.gov/tb/education/ssmodules/pdfs/Modules8-508.pdf

What differentiates Source Case Investigation from Contact Investigation?

- Direction of investigation: upstream vs. downstream ("reverse CI")
- All associates ≥10-years-old should have baseline chest radiograph
  - Low threshold to collect sputa if signs/symptoms or abnormal CXR
- Findings in associates can improve diagnostic certainty in young children with TB-5
- Goal is to identify and treat infectious source case(s) to reduce morbidity/mortality AND interrupt ongoing TB transmission

Source Case Summary LAC Pediatric TB Patients (<15 y/o): 2018-2022



Slide credit: Melissa Zhang & CDR Sophia Hsu

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Adult TB Contact Investigation vs. Pediatric Source Case Investigation Yield

1. Fox, G.J., Barry, S.E., Britton, W.J., Marks, G.B. (2013). Contact investigation for tuberculosis: a systematic review and meta-analysis. *European Respiratory Journal, 14*(1), 140-155. DOI: 10.1183/09031936.00070812

Slide credit: Melissa Zhang & CDR Sophia Hsu

A not-so-modest proposal…

- Perhaps this is **not** a **zero-sum game**; perhaps we have suffered from the problems of **"limited good and limited vision."***
- Perhaps **source case investigations** are **not distractions** from more important TB control and elimination activities.
- Perhaps **standardization** and **improvement** in **source case investigations** could have **spillover effects** impacting TB elimination interventions in the broader population…?

**Soc Sci Med* 2005;61(4):847-59.

Another quick case:

- 5-week-old previously healthy boy: conceived via assisted reproduction in Mexico, born in USA at 39 weeks gestation via C-section for failure to progress
- Now admitted with fever and slightly decreased PO intake x 2 days
- During sepsis evaluation, infant is found to have lymphocyte-predominant CSF pleocytosis, hypoglycorrhachia, hepatosplenomegaly, and multifocal pneumonia and nodular opacities
- Brain MRI showed R parietal lobe hemorrhage and cortical vein thrombosis

Another quick case (continued): 5-week-old boy

- Gastric aspirate: 1+ smear-positive
- Endotracheal tube/mini-BAL aspirates: 2+ smear-positive; PCR positive: MTBc detected, RIF-R not detected

- Grandfather reported to have chronic cough but not immediately available for evaluation
- Mother is asymptomatic

Sputum smear-negative, PCR+, Culture(+):

MTBc (bovis)

Urine AFB culture: +MTBc

Mother of 5-week-old with disseminated TB-3

Placental pathology @ CDC-IDPB:

Diagnosis:

Placenta (05/04/2023): Chorionitis and subchorionitis (maternal inflammatory response stage 2, grade 1).

- No evidence of microorganisms on Fite, Ziehl-Neelsen acid fast (ZN-AFB), Grocott's methenamine silver, and tissue Gram stains.
- No immunohistochemical or molecular evidence of mycobacteria, including *Mycobacterium tuberculosis* complex species (see comments).

Was this "congenital" (in utero) versus post-natal?

And does it really matter…?

Source Case Investigation Guidance (LAC, 2023)

- Source case investigation should be conducted for all children <5yo with TB-3.
  - Highest priority is given to culture-confirmed incidents.
  - Recommend exam, CXR, IGRA, and sputa x 3 for household contacts >=10yo.
  - Also consider when source case identification or susceptibilities will impact clinical or public health management.
- Source case investigation should be conducted for all children <2yo with TB-2.
  - Recommend exam, CXR, and IGRA for household contacts >=10yo.
  - Close collaboration with community providers is critical for augmenting local health jurisdiction capacity.
  - Consider expansion to TB-2 in <5yo…?

References | Source Case Investigation

- *MMWR Recomm Rep* 2005;54(RR-15):1-47.
- *Soc Sci Med* 2005;61(4):847-59.
- American Academy of Pediatrics. *Red Book* Online. Nov 2022 (redlined update).
- Centers for Disease Control and Prevention. Module 8: Contact Investigation for Tuberculosis, in: *Self-Study Modules on Tuberculosis.* 2014.

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