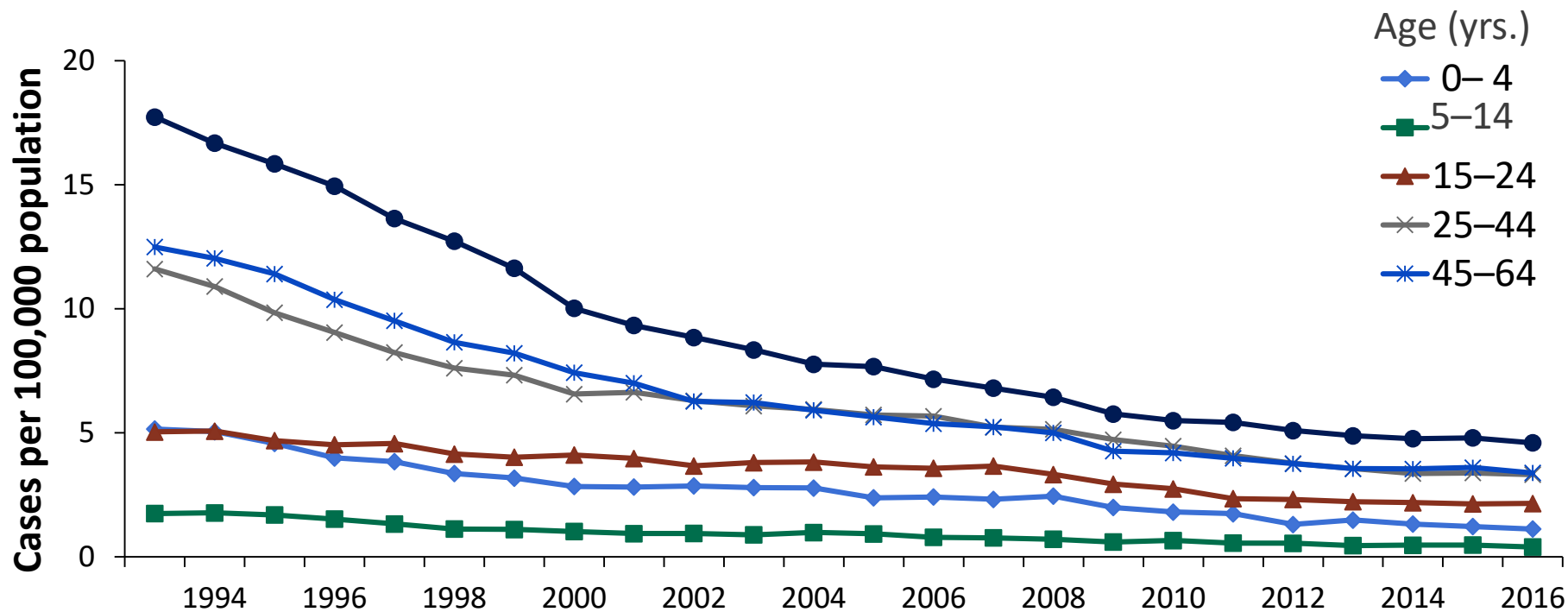


A horizontal decorative bar at the top of the slide, consisting of a green segment on the left and a blue segment on the right.

Pediatric TB in Michigan

TB Case Rates* by Age Group, United States, 1993–2016



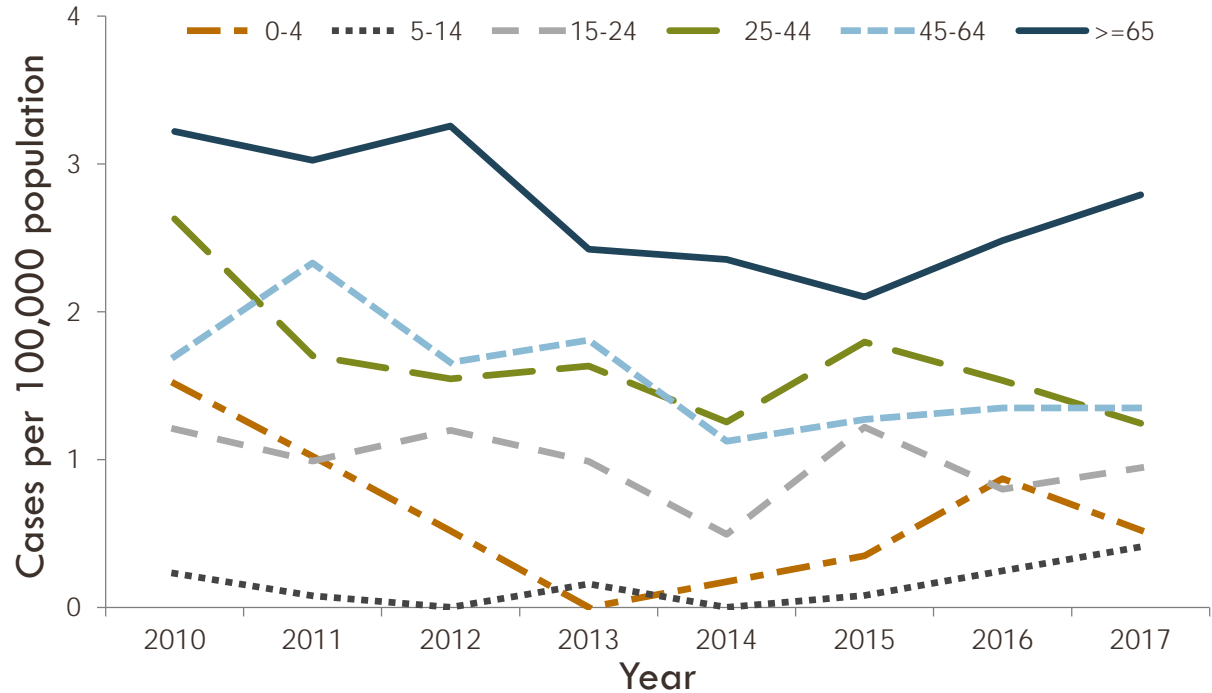
*Cases per 100,000 population; as of June 21, 2017.

TB Rates by Age Group

Michigan, 2010-2017

Age Group	%	Rate
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0-4	2%	0.5
5-14	4%	0.4
15-24	10%	1.0
25-44	23%	1.3
45-64	28%	1.4
65	34%	2.9



TB Among Children Age 0 to 14

Michigan, 2013-2017

11 cases <5 y.o.

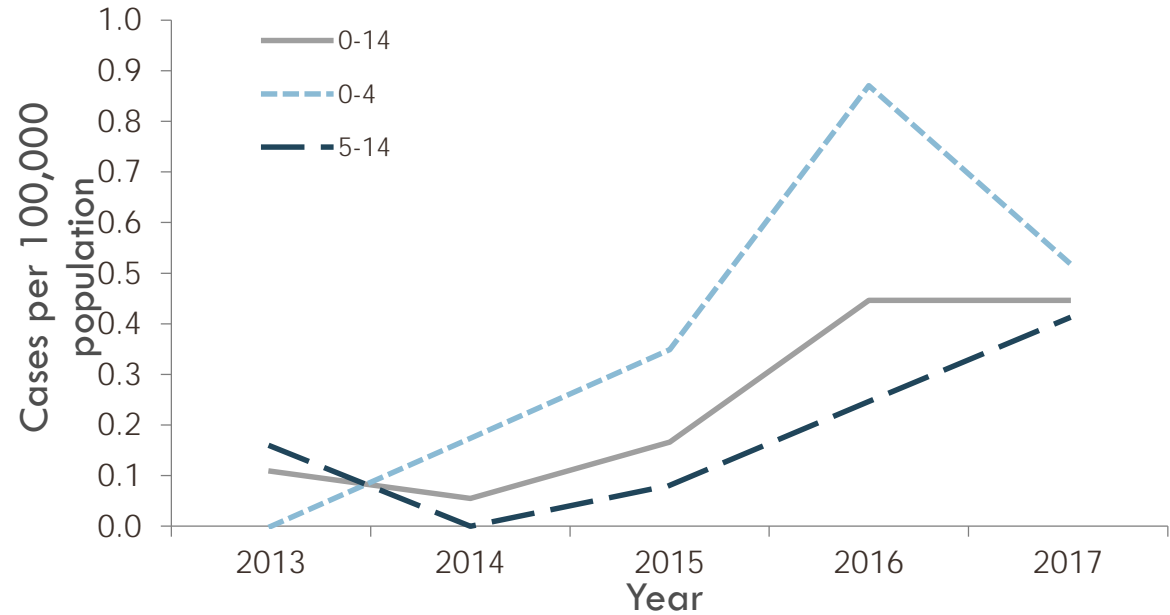
5 cases 5-14 y.o.

59% U.S.-born

32% culture confirmed

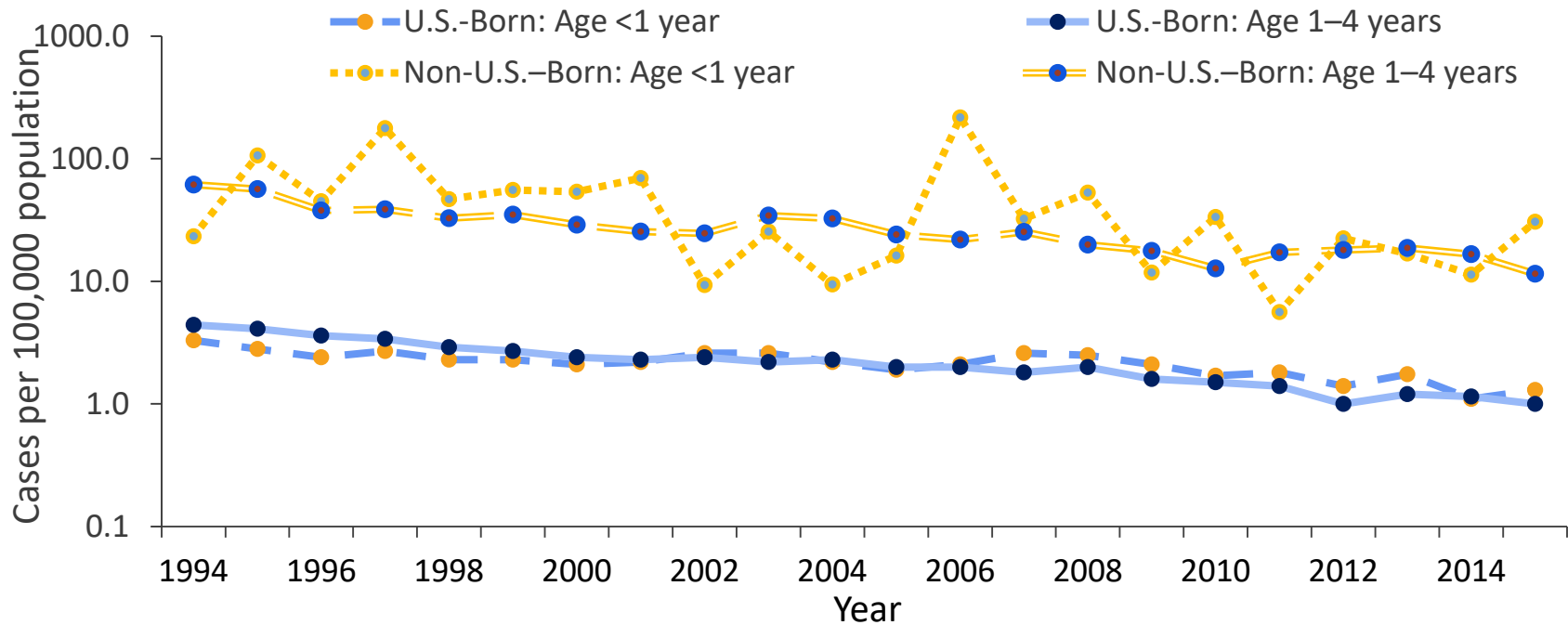
73% pulmonary

32% lymphatic



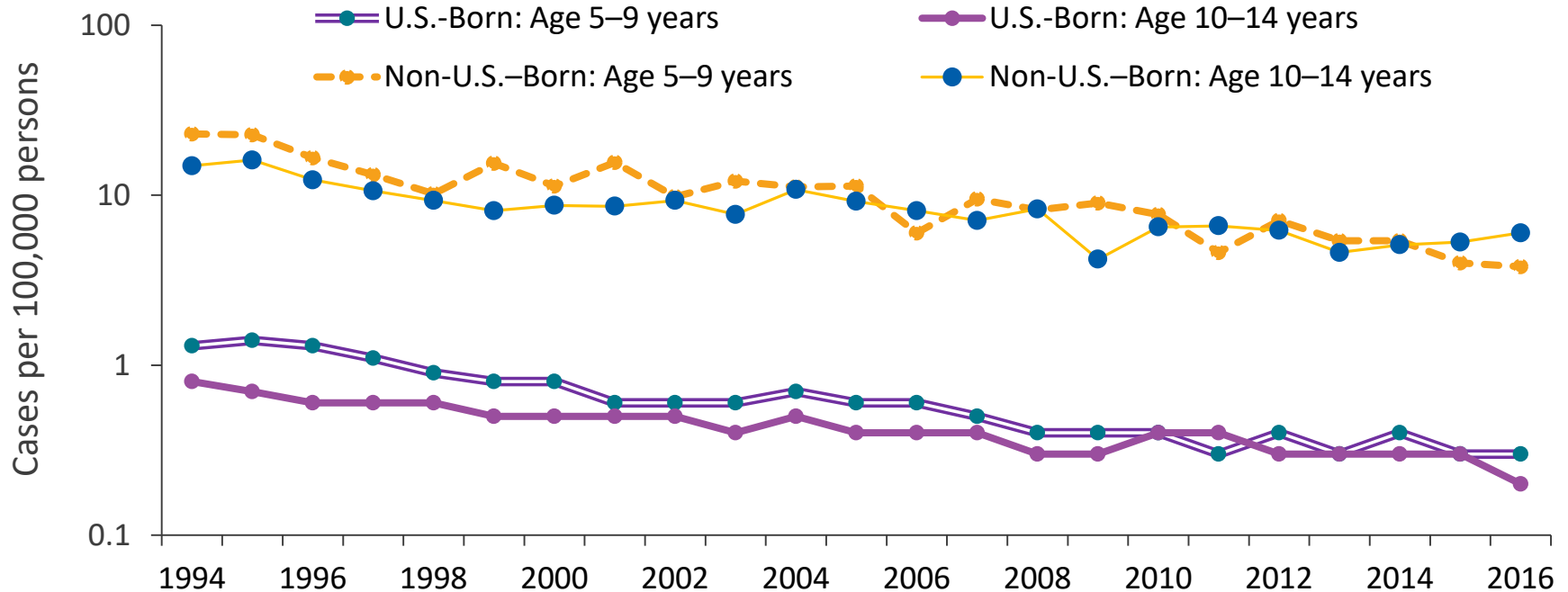
Overall increase in case count and rate since 2013

TB Case Rates* Among U.S.-Born and Non-U.S.-Born Children Age 0 to 4, 1994–2016



* Rates presented on a logarithmic scale. Data is not available before 1994.

TB Case Rates* Among U.S.-Born and Non-U.S.-Born Children Age 5 to 14, 1994–2016



* Rates presented on a logarithmic scale. Data is not available before 1994.



PEDIATRIC TUBERCULOSIS

ARSALA BAKHTYAR, MD

BEAUMONT HEALTH SYSTEM

WAYNE COUNTY MICHIGAN

DISCLOSURE

- None of the speakers or planners involved in this activity has any relevant conflict of interests.
- The use of trade names and commercial sources during this presentation is for identification only, and does not imply endorsement.
- No commercial support has been received for this program.

LEARNING OBJECTIVES

- Understand the burden, pathogenesis and transmission of Pediatric TB
- Describe challenges in finding, diagnosing and treating Pediatric TB cases.
- Discuss the new Pediatric TB case in Wayne county.

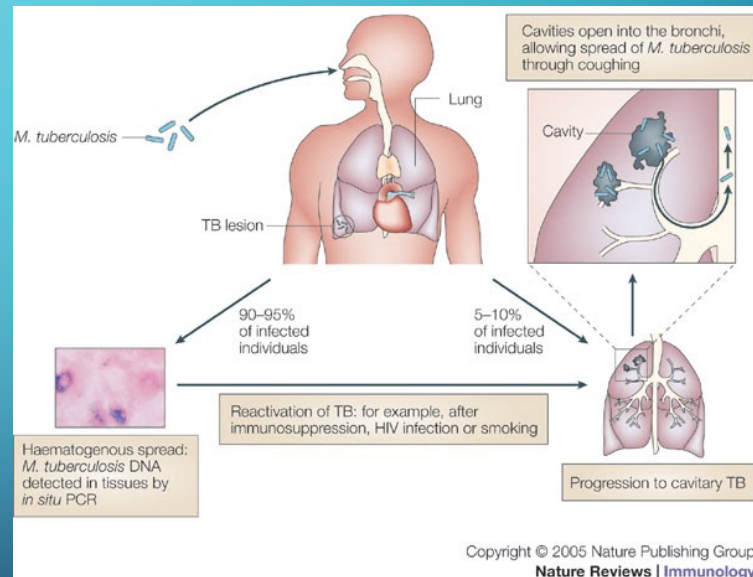
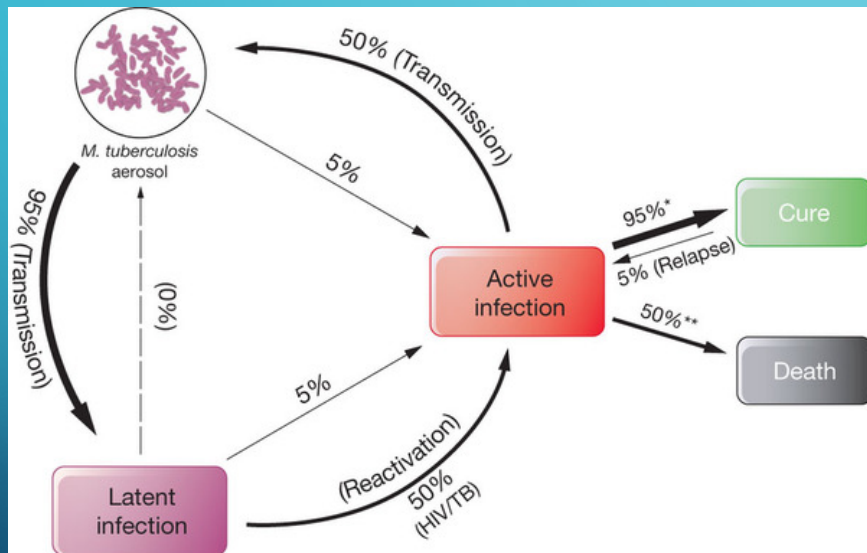
PEDIATRIC TUBERCULOSIS

- TB occurring in children age <15 years
- Number of Pediatric TB cases have escalated worldwide in the past 25 years.
- Control of TB in children is often neglected as children are considered ineffective transmitters of TB.
- TB during childhood contributes to future reservoirs of disease.
- Factors that can decrease the burden of Pediatric TB: risk factor based screening, implementation of prophylaxis and high degree of suspicion by clinician.

PATHOGENESIS

- Airborne
- Lymph node enlargement is common.
- Inhalation → Gohn complex → contain, spread or reactivate.
- Incubation periods are different for different clinical manifestations.
 - Miliary or disseminated TB: 2-6 months after infection
 - Renal TB: 5 years
 - Skeletal TB: 1-2 years after infection
 - Pulmonary and Lymphatic TB: 4-12 months

TRANSMISSION



SIGNS AND SYMPTOMS OF PULMONARY TB

Table 3. **Signs and Symptoms of Pulmonary Tuberculosis**

Clinical Feature or Disease Type	Infants	Children	Adolescents
Symptom			
Fever	Common	Uncommon	Common
Night sweats	Rare	Rare	Uncommon
Cough	Common	Common	Common
Productive cough	Rare	Rare	Common
Hemoptysis	Never	Rare	Rare
Dyspnea	Common	Rare	Rare
Sign			
Rales	Common	Uncommon	Rare
Wheezing	Common	Uncommon	Uncommon
Decreased breath sounds	Common	Rare	Uncommon
Location of Disease			
Pulmonary	Common	Common	Common
Pulmonary + Extrapulmonary	Common	Uncommon	Uncommon

PHYSICAL EXAM

- Very focused
- Temperature and growth parameters
- Alertness and meningeal signs
- Peripheral lymph nodes
- Abdomen
- Palpate back and extremities

DIAGNOSTIC CHALLENGES

- Major challenge is establishing accurate diagnosis in children.
- Less than 15% children are smear positive
- Only 30-40% are culture positive, obtainment of culture specimen is difficult.
- We rely in non endemic countries like USA usually on a triad:
 - 1) close contact with an infectious index patient,
 - 2) a positive tuberculin skin test (TST) result, and
 - 3) presence of suggestive abnormalities on a chest radiograph.

HOW ARE MOST PEDIATRIC CASES FOUND

- 25%-80%- During contact investigation
- 3%-25%- during routine screening
- 17%-44% -symptoms lead to screening

CULTURE YIELD IN CHILDREN

Type of specimen	Yield of <i>M. tuberculosis</i> in culture, %	Remarks
Gastric lavage	40–92	Difficult, invasive procedure; increased yield in infants and patients with extensive disease; 3 consecutive specimens required after overnight fasting; can be done by trained nurses
Bronchoalveolar lavage	4–43	Extremely invasive; requires tertiary care facilities; useful if performed with diagnostic bronchoscopy
Nasopharyngeal aspiration	24–30	Less invasive; appropriate for low-income countries with limited facilities
Laryngeal swab	27–63	Useful in older children who are unable to expectorate
Induced sputum	20–30	Yield comparable to gastric lavage and nasopharyngeal aspiration; requires training; can be done by nurses; useful in hospital setting; infection-control procedures needed
String test	Not determined	Patients as young as 4 years of age tolerated the procedure well; peak discomfort at the time of swallowing and mild during string retrieval; additional studies required

NOTE. Adapted from [16, 18].

IGRA

- TST has been available for decades.
- BCG and misconceptions
- IGRA measures ability to produce interferon-gamma after their Lymphocytes are stimulated with antigens found in MTB.
- Advantages of IF-gamma are:
 - One office visit
 - No risk of boosting phenomenon
 - More specificity for LTBI as it is not positive with NTMbi or BCG.
 - Now approved in younger children

IMAGING STUDIES IN CHILDREN

- Should be routinely obtained in children with positive TST or IGRA
- Children usually have normal radiographs
- Significant finding on CXR of children:
 - Isolated calcified lesion (LTBI)
 - Hilar or mediastinal lymphadenopathy
 - Infiltrates, pleural effusion, cavities, military disease.
- CT scan not routinely indicated, low resolution CT are available.

TREATMENT CHALLENGES

- Treatments and regimens are same as adults.
- Standard for uncomplicated cases-6 months
- For military, meningeal, bone and joint TB-9-12 months
- No studies in children, data is extrapolated from adult studies.
- Require higher doses than in adults due to excretion. Correct doses in pediatrics is essential
- Another challenge → Pediatric formulations and administration
- DOT always
- Side-effects

CHALLENGES OF PEDIATRIC TUBERCULOSIS

- TB is amongst the top 10 causes of death amongst children world wide.
- Low priority to children with TB, most tests are not validated in children.
- Trials of new drugs or first line second line pediatric formulations are lagging.
- Children with HIV and comorbid TB need more studies and the efficacy of BCG in that populations needs more research.
- Multi-centric trials are urgently required to help develop improved diagnostic strategies and formulate shorter, more effective, safe, and evidence-based regimens for treatment and prevention of drug susceptible and drug-resistant TB.

The background is a teal-to-blue gradient. In the corners, there are white line-art patterns resembling circuit boards or neural networks, with lines connecting to small circles.

- CASE PRESENTATION

PRESENTATION TO TB CLINIC

- **3 year old female presented with a positive IGRA and an abnormal X-ray.**
- Birth History/birth records:
 - Born to a 33-year-old G10 P4 at 31 2/7 weeks' gestation. Pregnancy complicated by preeclampsia in mother. Maternal history positive for smoking cigarettes. All other prenatal screening was negative on mother .
 - 5 week hospitalization in NICU after birth.
 - Cranial ultrasound from 7/22/2014: "Small left grade 1 germinal matrix hemorrhage. Possible small right grade 1 germinal matrix hemorrhage."
Normal Neuro exam described upon hospital discharge.
 - Passed newborn hearing screen.
Hepatitis B vaccine given 7/18/2014
ROP exam negative on discharge
Cardiology follow-up scheduled upon discharge
- Current: Speech delay and Social emotional delay.

AT THE PCP

- Child was placed in a foster family in April 2017, however; was removed from there for unknown reasons.
- She is now living with her current Foster family since June 2017.
- In October 2017, she was first taken to the PCP at University of Michigan for a well child check. At that time an IGRA was ordered as a part of screening test for a child in foster care. IGRA was not done by Foster family at that time.
- Early December, patient was seen at Urgent care for cough and otitis media and was treated with Antibiotics.
- Followed up with PCP on 12/8 and was doing well at that time. IGRA was ordered on that day.

CHEST XRAY

- 12/13 IGRA came back as **Positive**. PCP ordered a CXR on 12/13/17.
- 1. Mildly prominent parahilar, peribronchial lung markings could represent viral pneumonia and/or reactive airways disease. No focal airspace opacity is seen to suggest bacterial pneumonia. The pleural spaces are clear.
-
- 2. There is moderate prominence convexity of the right mid mediastinal border, asymmetric from the left. While this could represent prominence of the thymus, mediastinal lymph node enlargement is also possible. The hila do not appear enlarged. CT could be performed for further evaluation.
-
- 3. Normal heart size and pulmonary vascularity.

SOCIAL HISTORY

- Child was missing since October 2016. A CPS investigation started on a child's mother to remove children from her home. All children were removed but case patient was missing. Child was last seen with her father in October 2016.
- Eventually the child was recovered in April 2017 in poor condition. She was with her father, living in a basement of the father's cousin.
- Placed with a Foster family in April 2017, removed in June and was placed with the current Foster family In June of 2017.

TB CLINIC

- Child was seen by us 12/15/17 for positive IGRA and abnormal CXR.
- Foster mother reported resolution of the cough. She also stated that patient felt very tired and slept a lot. She also felt that child despite of eating appropriately, did not gain much weight. Weight in the office at the time was 50th %ile for her age.
- CT scan was ordered at the TB clinic and patient was asked to follow up in 1 week.

PHYSICAL EXAM:

- VS: Pulse:100,Temp:97.8 F, Weight: 14.7kg 50%ile
- PE: GEN: appeared well, alert, not very friendly, non verbal
- HENT: NC/AT, Normal nose, PERLA. Normal Oropharynx.
- Neck: Cervical adenopathy present.
- CVS: S1,S2 normal
- LUNGS: CTAB, no wheezing
- Abdomen: Soft, non tender, very small inguinal lymph nodes bilaterally palpable.
- GU: Erythematous vulva
- NEURO: appears delayed for age.
- SKIN: normal.

1 WEEK LATER..

- CT scan: Indication Positive IGRA/Abnormal CXR
- IMPRESSION:
 - 1. Soft tissue density encasing the bilateral hilar structures, left greater than right, likely representing hilar lymphadenopathy.
 - 2. Bilateral airspace opacities, predominantly involving the bilateral lower lobes. Given the constellation of imaging features as well as provided history, findings are concerning for infectious process such as primary tuberculosis.

ADMISSION TO UNIVERSITY OF MICHIGAN

- Child was now a suspected case of TB
- Tried inducing sputum production through nebulization, unsuccessful.
- Admitted to U of M and collected three days of morning Gastric aspirates with urine AFB culture.
- All negative to date.
- Due to high suspicion of TB , DOT with 4 drugs was started 12/25/17.

TB DRUGS

- Color vision was checked in office
 - INH, Rifampin, Pyrazinamide and Ethambutol 5 days per week for 40 doses.
 - Follow up visit : Doing well.
-
- Contact Investigation
 - Foster mother Negative
 - Foster Sibling PPD negative, on window prophylaxis 2 years old.
 - Previous Foster family had a baby who developed “pneumonia” tested for TB?
 - Isolation

SCREENING IN FOSTER CARE

- Comprehensive:
- mental, developmental, behavioral.
- The guidelines for testing children and adolescents in foster care for these conditions vary from state to state. However, at entry into foster care, laboratory testing for hepatitis B and C, syphilis, and HIV is recommended. They should be immunized against hepatitis B if they are not immune . Tuberculosis screening may be warranted for children with increased risk, including exposure to an infected individual or an individual at high risk whose status is unknown.

CONCLUSION

- High incidence of childhood TB.
- Vague clinical presentation
- Difficult to get sputum
- Poor bacillary count.
- Imaging is usually normal

CONCLUSION

- Refinement of existing tools and testing of new tools are required to improve diagnosis and treatment of TB in children.
- Global priority and funding is required to reduce the morbidity and mortality.
- In addition to reducing the burden of adult TB, attention to childhood nutrition, and improvement in the socioeconomic condition of communities is likely to have a significant impact on TB transmission in children.

The background is a blue gradient with white circuit-like lines in the corners. The lines consist of straight segments and small circles, resembling a printed circuit board layout.

• QUESTIONS???