

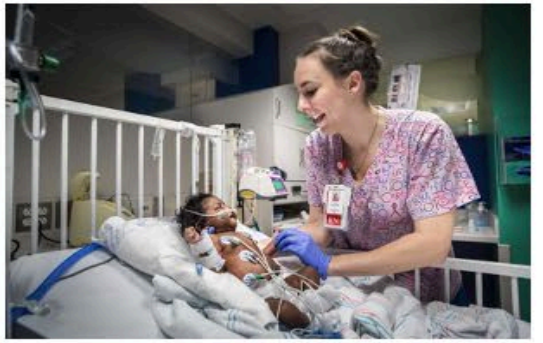

The Clinical Utility of IGRAs to Diagnose TB Infection in Pediatric Patients

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QIAGEN is pleased to welcome:

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- Baylor College of Medicine, Texas Children's Hospital, Houston, Texas

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Overview

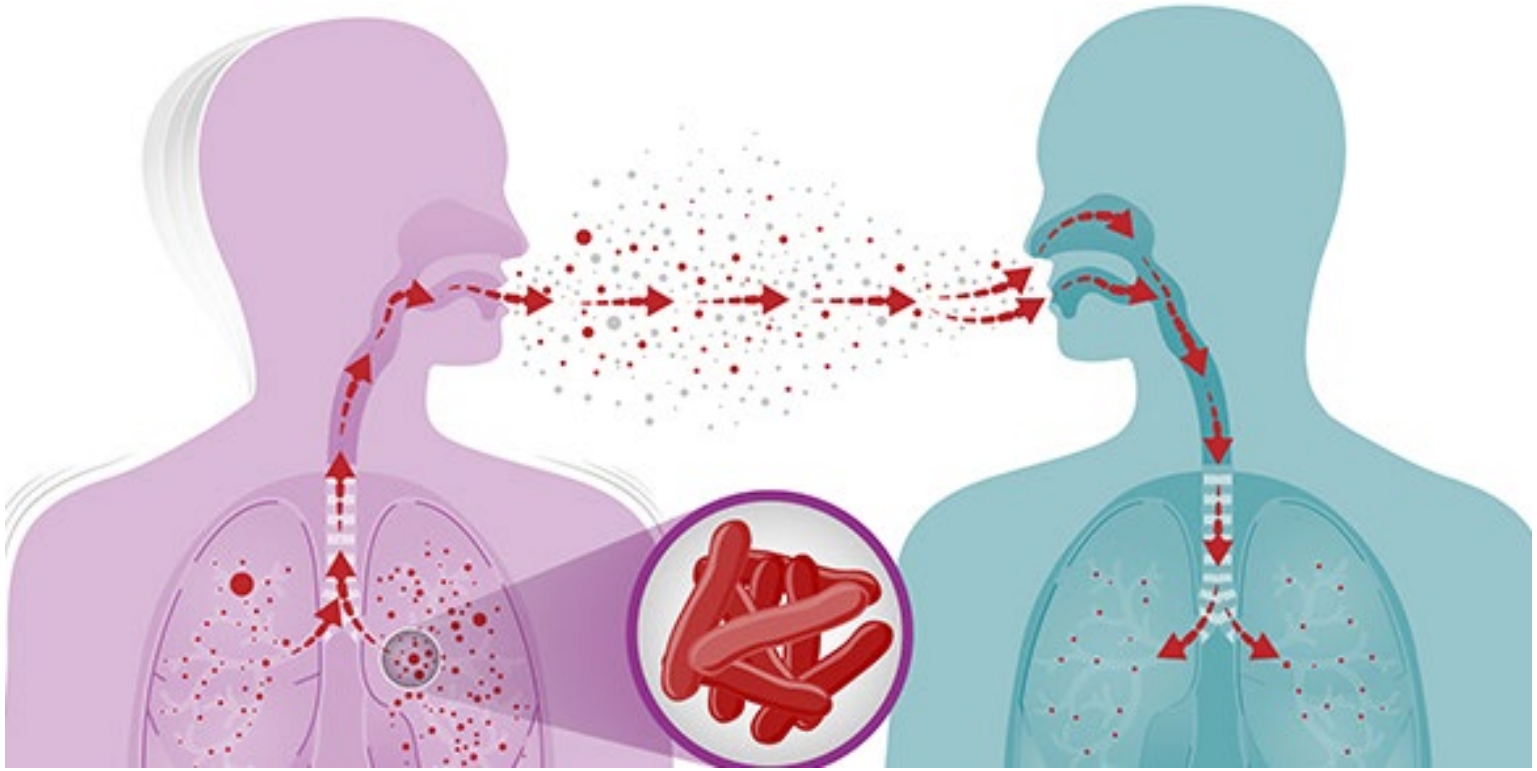
- Background
- Case #1 (Dr. Cameron)
- QFT-Plus results: a systematic approach to interpretation (Dr. Kawamura)
- Case #2 (Dr. Cameron)
- QFT package insert update by QIAGEN (Parth Patel)

Summary

Q&A

Global Tuberculosis Report 2017, WHO

Most M.TB is transmitted <u>to</u> children <u>by</u> adults (or adolescents)



A child newly diagnosed with TB is a sentinel event indicating recent transmission in a community.

Why does it matter?

- Risk of progression influenced by age
- Decades of potential benefit from treatment
- Excellent tolerability of TB medications

Age at infection (y)	No disease (%)	Pulmonary TB (%)	CNS TB (%)
<1	50	**30-40**	**10-20**
1-2	75-80	10-20	2.5
2-5	95	5	0.5
5-10	98	**2**	<0.5
>10	80-90	**10-20**	<0.5

Cruz AT, Starke JR. Peds in Review 2010;31:13

Children with TB infection = reservoir for disease

Important TB Testing Considerations

- A child with suspected TB disease/at high risk of infection → disease
  - ***High sensitivity is imperative***
  - Risk of missing a diagnosis is high
- TB screening in high TB-endemic setting or contact investigation
  - Goal, ***maximize PPV***
- TBI screening in a low-incidence population
  - ***High specificity is imperative***
  - Risk of overtreatment is high

Comparison of Skin Test & IGRA

Characteristic	TST	IGRA
Antigens studied	Many -PPD	ESAT-6, CFP-10, (TB-7.7)
Cross-reactivity with BCG	Yes	**Unlikely**
Cross-reactivity with NTM	Yes	**Less Likely***
Estimated sensitivity, TB in non-US born children ≥ 2 yrs	**50-75%**	***77-95%***
Estimated specificity, TB in non-US born children ≥ 2 yrs	***72-75%***	***90-93%***
Distinguish TB infection vs. disease	No	No
Boosting	Yes	No
Patient visits required	Two	One

Ahmed A, et al. Pediatrics 2020;145(1)
Soler-Garcia A, et al. J Pediatr. 2020;2223:212.
Lighter J, et al. Pediatrics. 2009;123(1):30
Connell TG, et al. Thorax 2006;61(7):616.
Mandalakas AM, et al. Int J Tuberc Lung Dis. 2011;15(8):1018.
Velasco-Arnaiz E, et al. Pediatr Infect Dis J. 2018;37(12):1235.

AAP Red Book Recommendations

Recommendation	2015	2018	2021
Age*	≥ 5 years	**≥ 2 years**	**TST recommended for <2y, IGRA acceptable**
Preferred test for BCG-immunized children	Yes	Unchanged	Unchanged
Use in immunocompromised children	Cautiously	Unchanged	Unchanged

***States that some experts use down to 1 year of age; any negative result (IGRA or TST) should be interpreted cautiously in infants < 3 months of age**

Red Book® Online

Canadian Tuberculosis Standards 8th edition regarding children

- Either TST or IGRA in most situations, except:
  - IGRAs preferred if:
    -BCG in infancy and age 2-10
    -BCG at an older age
    -Expertise to perform TST not available

https://www.tandfonline.com/doi/full/10.1080/24745332.2022.2036503

Clinical Case #1

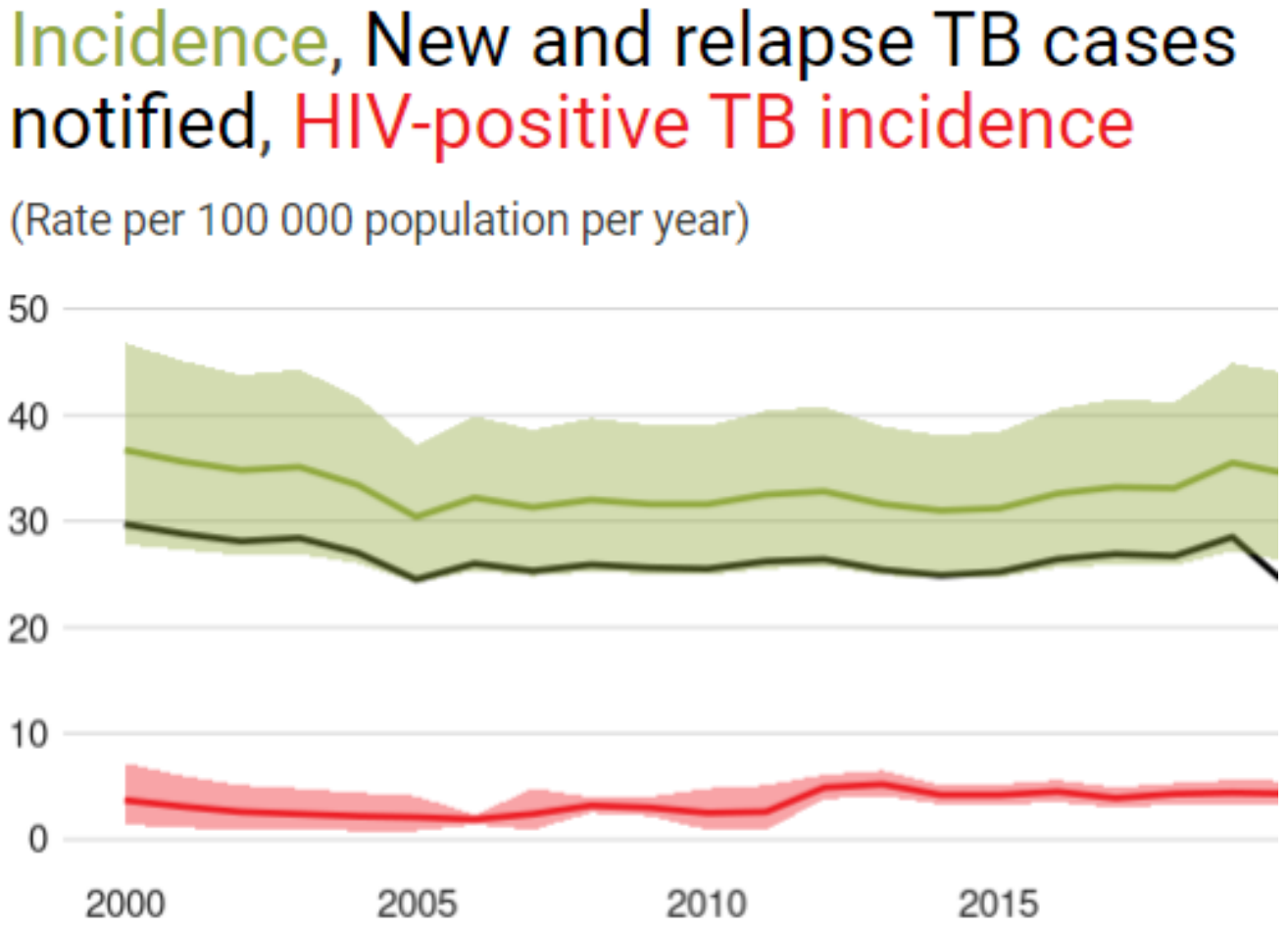
- 9yo, Hispanic F
  - Immigrant from Columbia, BCG immunized
- Arrived in Houston, TX in January 2021
  - With mother and 4mo sibling
  - Father has lived in the US for >12 years
    - Does not recall TB testing, none recent
    - Asymptomatic
  - Mother had an IGRA (negative), CXR (normal)
  - Sibling – negative PPD
- No additional TB risk factors

- Referred to TB clinic for evaluation of a “positive” QFT
  - Obtained during immigration process to the US
  - No quantitative value provided

World Health Organization

Tuberculosis in Columbia

- 41 cases/100,000 (WHO)
  - “moderate”
- 21,000 cases in 2021
  - 1,100 MDR/RR (5%)
  - 2,450 TB associated deaths
    - 69% HIV negative



PMH

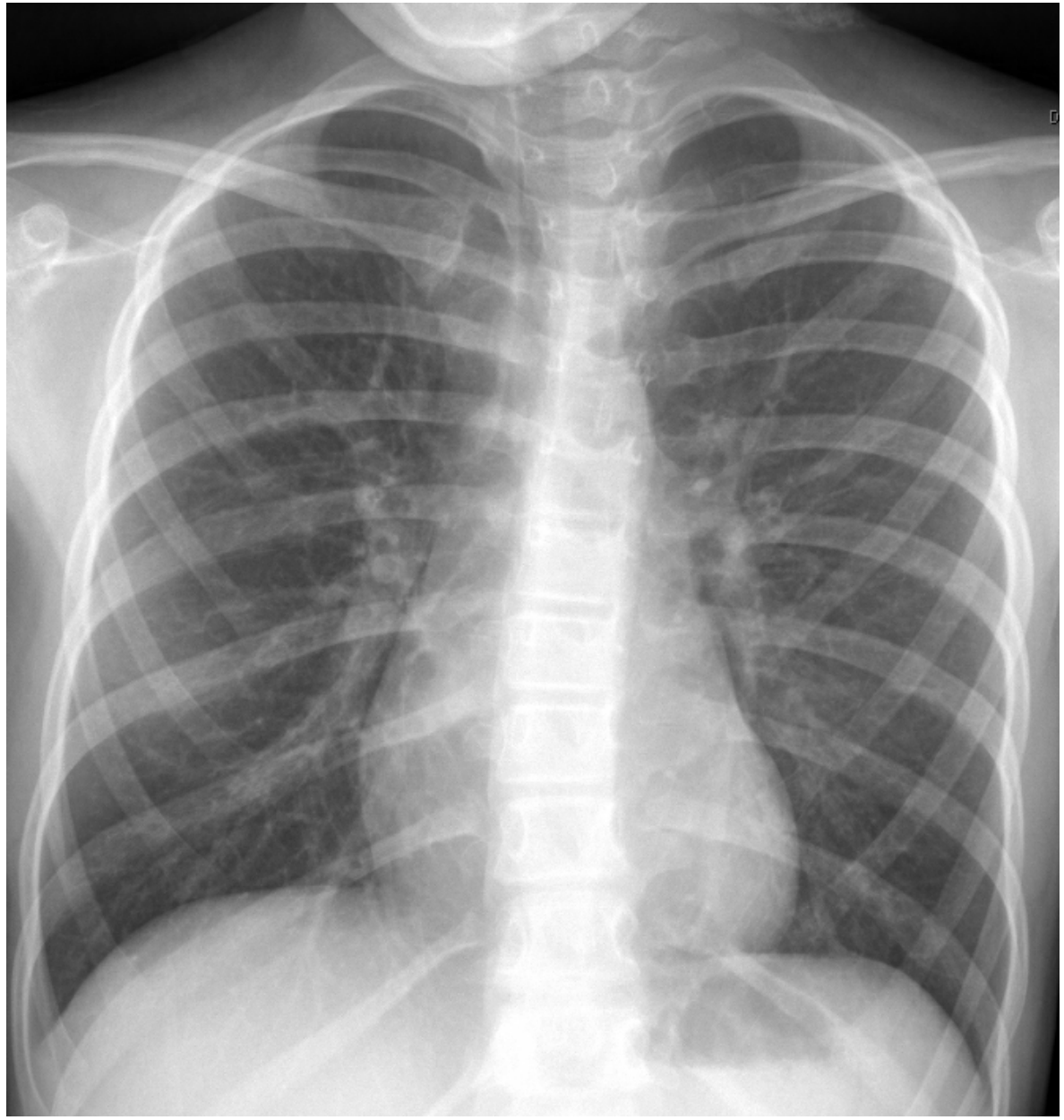
- Previously healthy
- No prior hospitalizations
- No regular medications
- Immunizations UTD (including BCG)
- NKMA

Physical Exam

- Well appearing
- No cervical adenopathy
- BCG scar over L deltoid
- Lungs clear, no axillary adenopathy
- Normal abdominal exam
- No rash

Prior evaluation

- Testing performed in Columbia prior to arrival
- Quantiferon “positive”
  - No quantitative value provided



- ***So what did we do?***

QUANTIFERON IN-TUBE

Order: 292648471

Status: **Final result** Visible to patient: **Yes (seen)** Dx: **Primary TB infection**

0 Result Notes

Component Ref Range & Units	11 mo ago
Quantiferon(R)-TB Gold NEGATIVE	NEGATIVE
Comment: Negative test result. M. tuberculosis complex infection unlikely.	
Quantiferon NIL IU/mL	0.06
Quantiferon Mitogen NIL IU/mL	9.32
Quantiferon TB1 NIL IU/mL	<0.00
Quantiferon TB2 NIL IU/mL	<0.00

Final diagnosis: No TB infection

Reflection

- Why was the QFT repeated?
- What made you confident that the US result was not a false negative?
- Did the QFT-Plus quantitative antigen and controls have any value?

https://www.prlog.org/12774580-americans-need-more-self-reflection-in-2019.html

Step 1: Systematically assessing both qualitative and quantitative results

- Review of control values
- Review of antigen tube results

QuantiFERON® TB Gold Plus

	Nil control	TB 1 Antigen	TB2 Antigen	Mitogen control
				
Cells stimulated	None	CD4+ T-Cells	CD4+ and CD8+ T-Cells	All
Polypeptides		Long peptides (MHC class II)	Long peptides (MHC class II) + Additional short peptides (MHC class I)	
Antigens		•ESAT-6 •CFP-10	•ESAT-6 •CFP-10	

TB1 and TB2 results should be similar if no reactivity to CD8 antigens in the sample

QuantiFERON-TB Gold Plus (QFT-Plus) is a Qualitative test

negative control

Positive control

Nil (IU/ml)	TB1 minus Nil (IU/ml)	TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)	QFT-Plus result	Report/ Interpretation
≤8.0	≥0.35 and ≥25% of Nil	Any	Any	**Positive**	*M. tuberculosis* infection likely
	Any	≥0.35 and ≥25% of Nil			
	<0.35 OR ≥0.35 and <25% of Nil		≥0.5	**Negative**	*M. tuberculosis* infection NOT likely
			<0.5	**Indeterminate**	Likelihood of *M. tuberculosis* infection cannot be determined
>8.0	Any				

1. *QuantiFERON-TB Gold Plus (QFT-Plus) ELISA Package Insert*. Rev. 02. February 2015.1083163

Positive results by TB1, TB2, or both are considered positive.

Step 1: Assessing both qualitative and quantitative results

Review positive and negative control quantitative values to:

- Assess the quality of the host response
- Assess potential technical error

What to expect in a healthy patient (not immunocompromised with NO risk of false negative or indeterminate results)

- Nil value close to zero
- Mitogen value near 10 IU/ml or above

Step 1: Assessing both qualitative and quantitative results

Review quantitative values of antigen (TB1 and TB2) to:

- Assess values in light of control results
- Assess potential technical error (eg. TB1>>>TB2)

What to expect?

- TB1 and TB2 values should be close in value or TB2>TB1 if CD8 antigen reactivity

Indeterminate QFT results – Causes

High Nil (> 8 IU/ml)

- May indicate:
  - Excessive levels of circulating IFN-γ (e.g., another infection)
  - Presence of heterophile antibody
  - Incorrect sample handling or processing
- High Nil indeterminates are rare
  - In clinical studies*, < 0.25% of subjects had IFN-γ > 8 IU/ml for Nil

Mitogen – Nil < 0.5 IU/ml

- Biologic causes: see next slide
- Technical causes:
  - Incorrect sample handling
    - > 16 hours from blood specimen draw to incubation
    - Transportation / incubation at incorrect temperature
  - Inadequate shaking of tubes- most common cause in manual handling
  - Overfilling of tubes

TST and IGRA test interpretation:

Risks for false-negative or indeterminate results

Host factors affecting TST and likely IGRAs

- HIV- low CD4, no ARVs
- Recent TB infection (<8 weeks)
- Infections (viral, fungal, bacterial)
- Other illness affecting lymphoid organs
- Recent live virus vaccination
- Immunosuppressive drugs
- Overwhelming TB
- Malnutrition
- Age (newborn, elderly)

If results are unexpectedly negative or indeterminate…ASK: Does my patient have any of these factors?

Step 2: Review of TB epidemiologic and progression risks

Population TB Exposure Risks warranting TB testing

- Recent contacts of a TB case
- Immigrants from high-prevalence countries (in Canada <50 cases/100,000 pop considered low incidence)
- Injection drug users
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
- Mycobacteriology laboratory personnel
- Children under 5 years of age, or children and adolescents exposed to adults in high-risk categories

Source: https://www.cdc.gov/tb/publications/factsheets/testing/skintestresults.htm

Estimated risk for TB relative to persons with no known risk factor

AIDS	**110~170 times**
HIV infection	50~110
Solid Organ Transplant	20~74
Silicosis	30
Recent TB infection (<2 years)	15
Chronic renal failure	10~25
Carcinoma of head and neck	16
Abnormal chest radiograph with upper lobe fibro nodular disease typical of healed TB infection	6~19
TNF Alpha inhibitor therapy	1.7~9
Glucocorticoid therapy	4.9
Children less than 4 years old	2.2~5
Diabetes mellitus	2~3.6
Underweight (BMI <20)	2~3
Smoker (1 pack/ day)	2~3
Normal healthy individual	1

Source : Lobue and Menzies, Respirology 2010

Step 3: Putting it together: National guidelines on interpretation

National US recommendations on retesting based on risk

- Low to intermediate risk of progression from LTBI
  - No recommendation for repeat testing
  - Consider INFECTED if single test is positive
- Unlikely to be infected
  - If test positive, consider repeat or dual testing to maximize SPECIFICITY
  - A negative results from either test would be considered NEGATIVE
  - Considered infected only if BOTH tests are positive
- High risk of progression
  - If initial test result is negative, consider repeat or dual testing to maximize SENSITIVITY
  - A positive result from either/any test would be considered POSITIVE

Lewinsohn et al, Clin Infect Dis. 2017 Jan 15;64(2):111-115

Canadian Tuberculosis Standards 8th edition

Both TB infection tests may be used sequentially in the following situations:

- If either the TST or IGRA are negative, the other test may be used to increase sensitivity if the risk for infection is high, the risk for progression to tuberculosis disease is elevated, the risk for a poor outcome from tuberculosis disease is high and/or a person has conditions or habits that may reduce the sensitivity of the test.
- If the initial tuberculin skin test is positive, but the likelihood of tuberculosis infection is low, or risk of a false positive result due to BCG is high, then an IGRA may be used to increase specificity

https://www.tandfonline.com/doi/full/10.1080/24745332.2022.2036503

US National guidance on test interpretation and clinical management depend on risk of TB infection or risk of progression and do not refer to quantitative values as low or high for TST, QFT or TSPOT

Canadian National guidance do not refer to quantitative values as low or high for TST, QFT or TSPOT but unlike the US guidelines, both IGRAs have borderline zones:

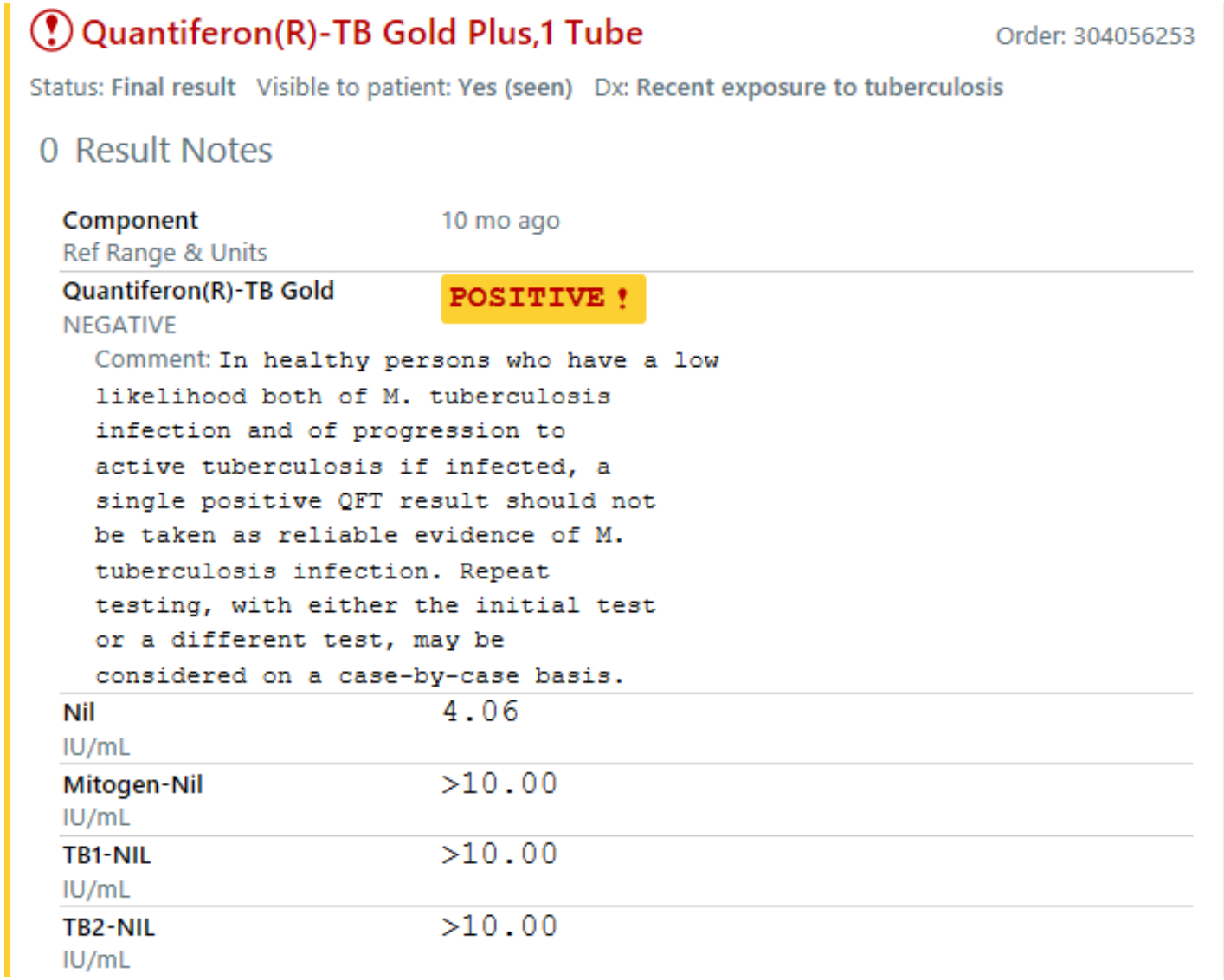
"When the initial IGRA result is borderline (equivalent to 5-7 spots with T-SPOT.TB or 0.2 to 1.0 IU/ml with QFT), the interferon-gamma release assay may be repeated or a tuberculin skin test used to help arrive at a diagnosis"

Clinical Case #2

- 2 mo, U.S. born, African-American, ex-full term M
- Asymptomatic
- Exposed to father -**Smear positive and Xpert MTB PCR positive**
  - Moved to the U.S. from Cameroon in early 2021
  - Household contact

Evaluation

- Well appearing
- Weight 6.4kg, 80%
- Normal exam



Quantiferon(R)-TB Gold Plus,1 Tube Order: 304056253

Status: **Final result** Visible to patient: **Yes (seen)** Dx: **Recent exposure to tuberculosis**

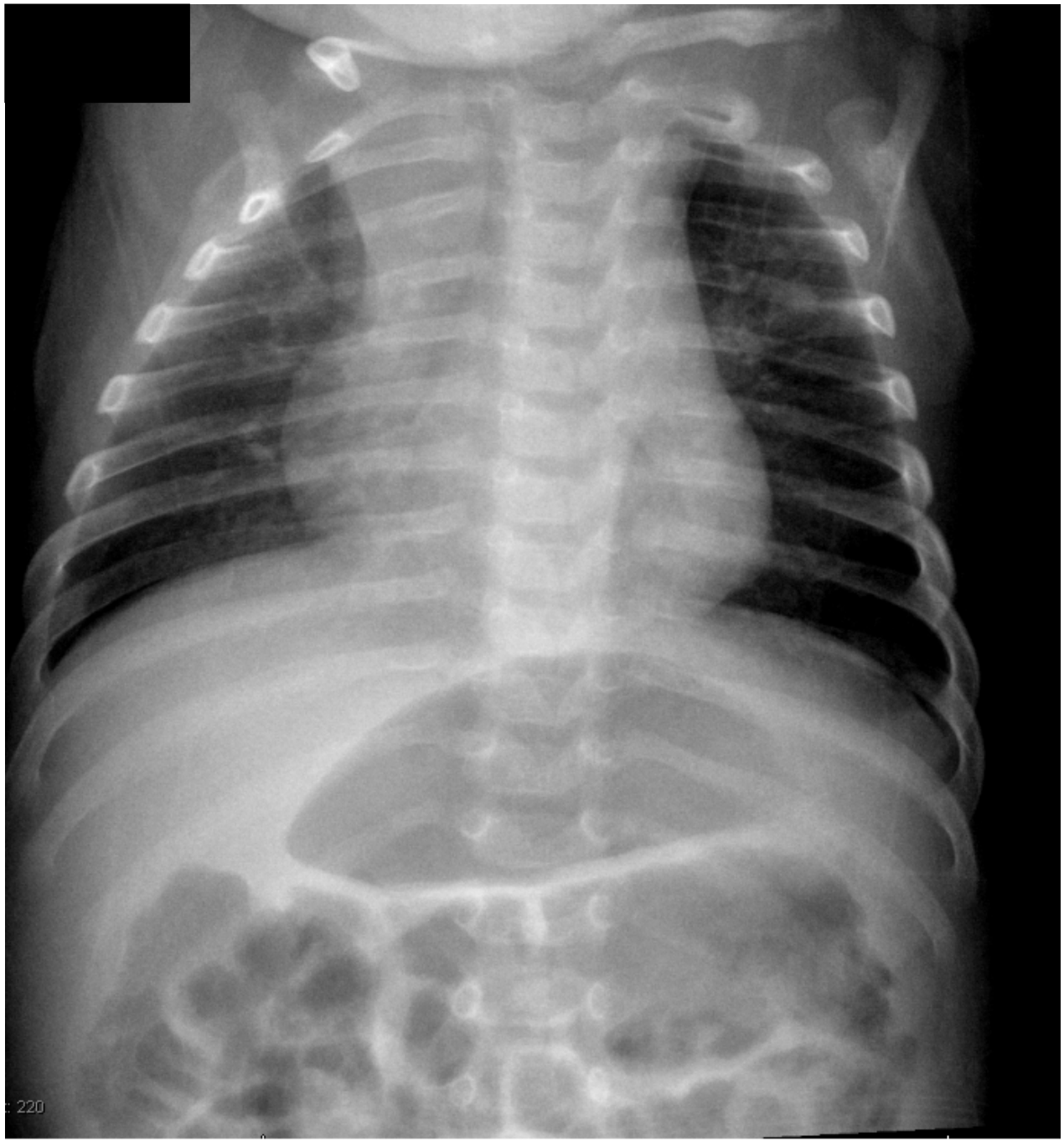
0 Result Notes

Component Ref Range & Units	10 mo ago
Quantiferon(R)-TB Gold NEGATIVE	**POSITIVE !**
Comment: In healthy persons who have a low likelihood both of M. tuberculosis infection and of progression to active tuberculosis if infected, a single positive QFT result should not be taken as reliable evidence of M. tuberculosis infection. Repeat testing, with either the initial test or a different test, may be considered on a case-by-case basis.	
Nil IU/mL	4.06
Mitogen-Nil IU/mL	>10.00
TB1-NIL IU/mL	>10.00
TB2-NIL IU/mL	>10.00

- ***Does a "wicked positive" QFT suggest disease over infection?***

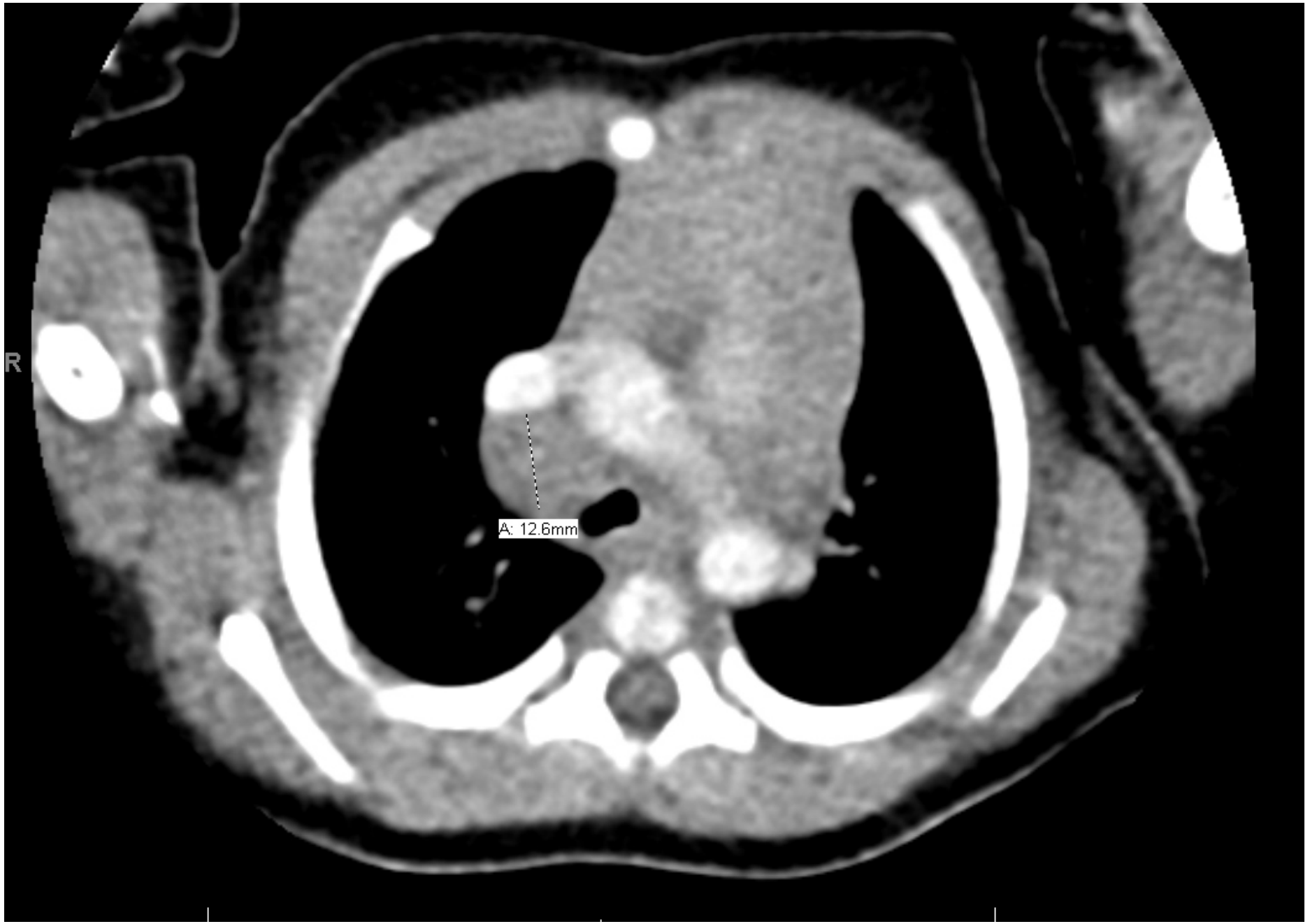
- Hyper-aerated lungs are clear.
- No lymphadenopathy identified.

Is the lung hyper-aeration concerning?



Admitted to TCH

- Work up initiated for disseminated TB
- First morning gastric aspirates x3 collected
  - Smear negative
  - MTB PCR negative
  - Cultures pending



Mediastinal, paratracheal and hilar lymph nodes

9 mm solid pulmonary nodule in LUL.

CNS Evaluation

- LP/CSF evaluation
  - WBC 16 (slightly elevated, L 72%)
  - RBC 2,000
  - Protein 99 (slightly elevated)
  - Glucose normal
- MRI brain w and w/o contrast
  - No evidence of TB meningitis
- Ophthalmology exam
  - Normal

Management

- PO levofloxacin, 10 mg/kg, BID (4/27/22 - present)
- PO isoniazid 150mg once daily (4/29/22 - present)
- PO linezolid 90 mg daily (4/29/22 - present)
- IV imipenem 100 mg q12 (4/29/22 - present)
  - +Augmentin (amoxicillin-clavulanate ES 40mg/kg dose) (4/29/22 - present)

Update: Source Case – Susceptibility

- Silent RIF mutation (molecular)
- DST – pan-susceptible
- RIPE therapy

Definitive Management/Clinical Course

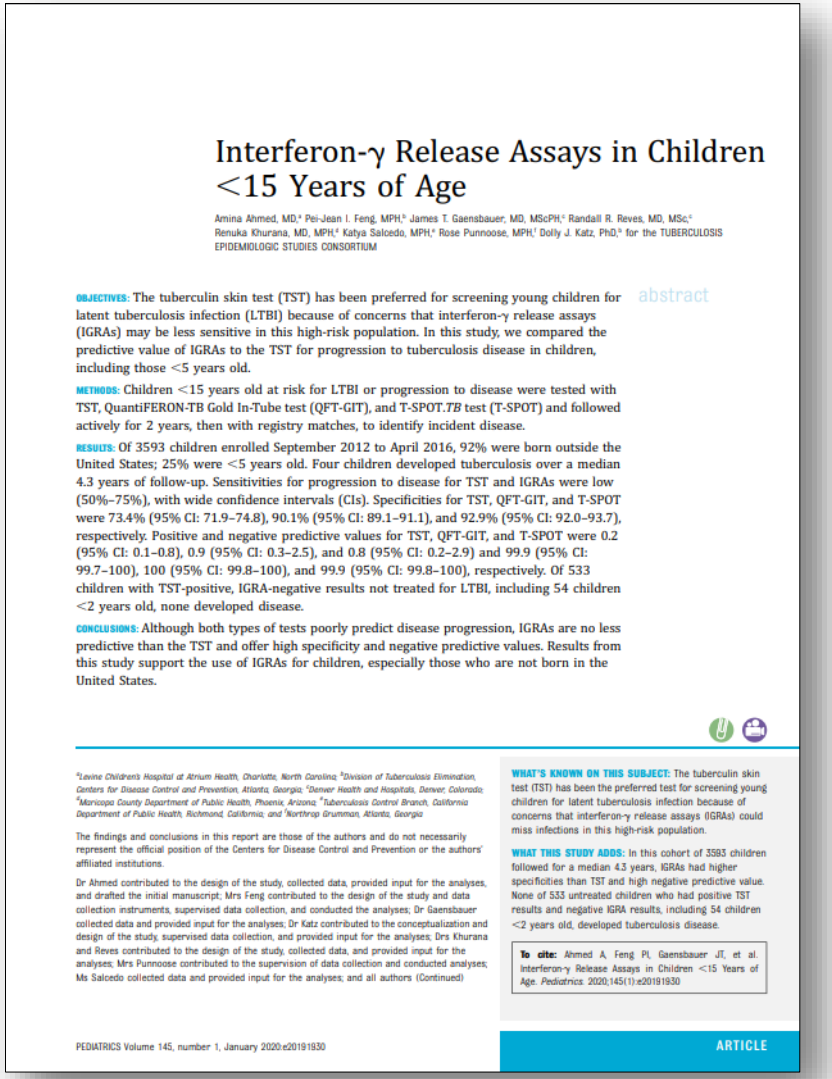
- Gastric aspirate & CSF cultures – negative, final
- Treatment:
  - RIP+levofloxacin x2 months → INH/RIF
  - High dose RIF
- Repeat CXR @ 2 months – normal
- Normal growth & development while on treatment
- Treated for 6 months

Reflection

- Would you have done an additional test if the initial IGRA or TST was negative?
- What concerns are there for using IGRAs un children <2?
- What made you confident that the result was not a false positive?
- Did the QFT-Plus quantitative antigen and controls values provide useful information?
- What role does QFT-plus play in contact investigation?

https://www.prlog.org/12774580-americans-need-more-self-reflection-in-2019.html

Seminal US LTBI Study: Ahmed et al., Pediatrics. 2020 Jan;145(1):e20191930. doi: 10.1542/peds.2019-1930



Interferon-γ Release Assays in Children <15 Years of Age

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abstract

OBJECTIVES: The tuberculin skin test (TST) has been preferred for screening young children for latent tuberculosis infection (LTBI) because of concerns that interferon-γ release assays (IGRAs) may be less sensitive in this high-risk population. In this study, we compared the predictive value of IGRAs to the TST for progression to tuberculosis disease in children, including those <5 years old.

METHODS: Children <15 years old at risk for LTBI or progression to disease were tested with TST, QuantiFERON-TB Gold In-Tube test (QFT-GIT), and T-SPOT.*TB* test (T-SPOT) and followed actively for 2 years, then with registry matches, to identify incident disease.

RESULTS: Of 3593 children enrolled September 2012 to April 2016, 92% were born outside the United States; 25% were <5 years old. Four children developed tuberculosis over a median 4.3 years of follow-up. Sensitivities for progression to disease for TST and IGRAs were low (50%–75%), with wide confidence intervals (CIs). Specificities for TST, QFT-GIT, and T-SPOT were 73.4% (95% CI: 71.9–74.8), 90.1% (95% CI: 89.1–91.1), and 92.9% (95% CI: 92.0–93.7), respectively. Positive and negative predictive values for TST, QFT-GIT, and T-SPOT were 0.2 (95% CI: 0.1–0.8), 0.9 (95% CI: 0.3–2.5), and 0.8 (95% CI: 0.2–2.9) and 99.9 (95% CI: 99.7–100), 100 (95% CI: 99.8–100), and 99.9 (95% CI: 99.8–100), respectively. Of 533 children with TST-positive, IGRA-negative results not treated for LTBI, including 54 children <2 years old, none developed disease.

CONCLUSIONS: Although both types of tests poorly predict disease progression, IGRAs are no less predictive than the TST and offer high specificity and negative predictive values. Results from this study support the use of IGRAs for children, especially those who are not born in the United States.

[a]Levine Children's Hospital at Atrium Health, Charlotte, North Carolina; [b]Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia; [c]Denver Health and Hospitals, Denver, Colorado; [d]Maricopa County Department of Public Health, Phoenix, Arizona; [e]Tuberculosis Control Branch, California Department of Public Health, Richmond, California; and [f]Northrop Grumman, Atlanta, Georgia

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the authors' affiliated institutions.

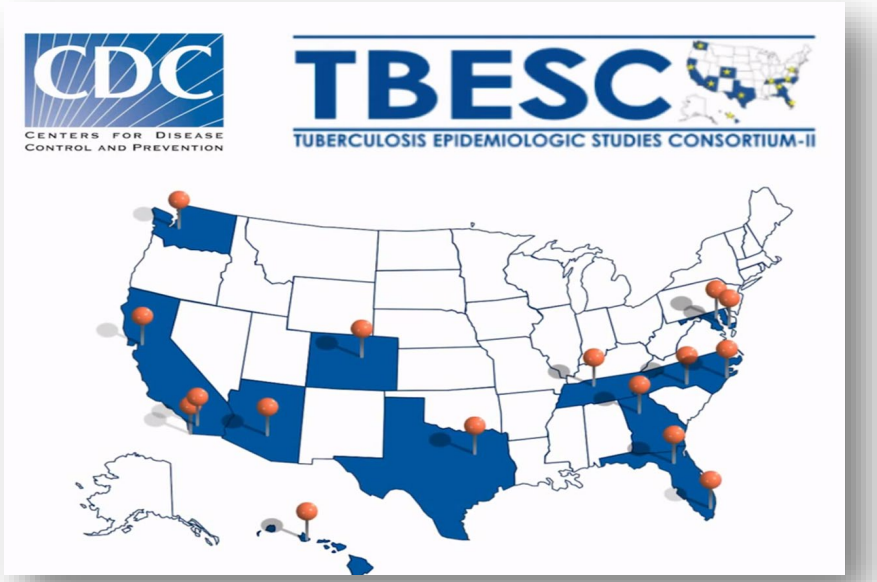
Dr Ahmed contributed to the design of the study, collected data, provided input for the analyses, and drafted the initial manuscript; Mrs Feng contributed to the design of the study and data collection instruments, supervised data collection, and conducted the analyses; Dr Gaensbauer collected data and provided input for the analyses; Dr Katz contributed to the conceptualization and design of the study, supervised data collection, and provided input for the analyses; Drs Khurana and Reves contributed to the design of the study, collected data, and provided input for the analyses; Mrs Punnoose contributed to the supervision of data collection and conducted analyses; Ms Salcedo collected data and provided input for the analyses; and all authors (Continued)

WHAT'S KNOWN ON THIS SUBJECT: The tuberculin skin test (TST) has been the preferred test for screening young children for latent tuberculosis infection because of concerns that interferon-γ release assays (IGRAs) could miss infections in this high-risk population.

WHAT THIS STUDY ADDS: In this cohort of 3593 children followed for a median 4.3 years, IGRAs had higher specificities than TST and high negative predictive value. None of 533 untreated children who had positive TST results and negative IGRA results, including 54 children <2 years old, developed tuberculosis disease.

To cite: Ahmed A, Feng PI, Gaensbauer JT, et al. Interferon-γ Release Assays in Children <15 Years of Age. *Pediatrics*. 2020;145(1):e20191930

Interferon-g Release Assays in Children <15 Years of Age

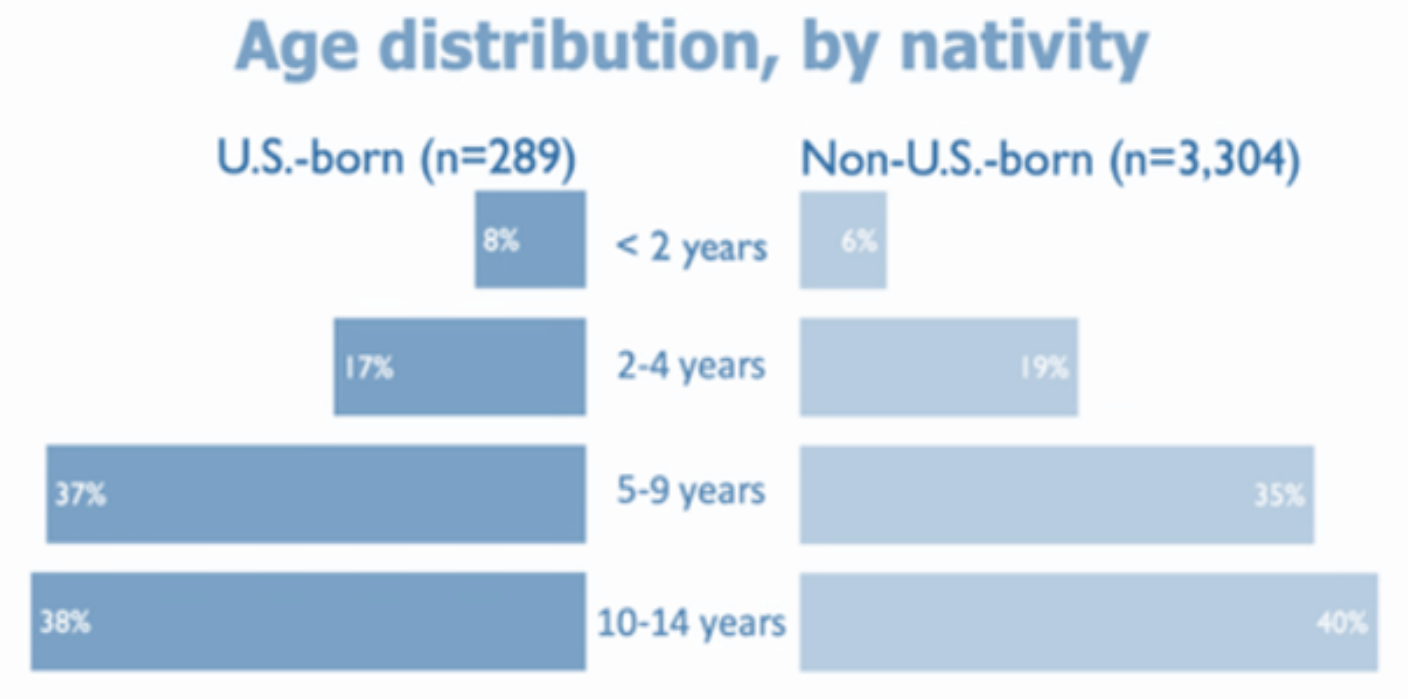


Study done in 16 sites across US

Interferon-g Release Assays in Children <15 Years of Age*

Largest prospective longitudinal pediatric study, compared predictive values of IGRAs vs. TST

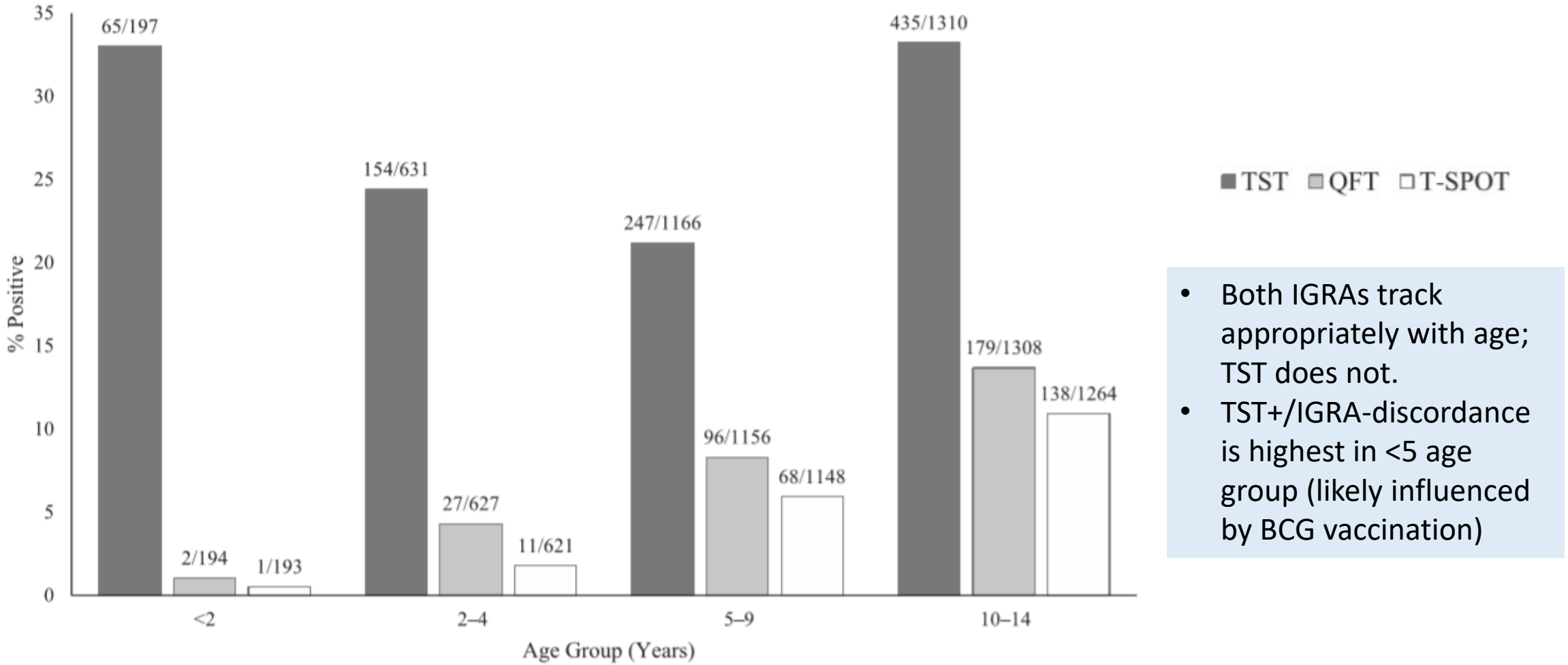
- 3593 Children enrolled
- 92% of the children born outside US
- 25% (n = 900), <5 years, 6% (n= 219), <2 years



*Ahmed et al., Pediatrics. 2020 Jan;145(1):e20191930. doi: 10.1542/peds.2019-1930

Interferon-g Release Assays in Children <15 Years of Age* (2)

- Percentage of positive tests, by age group, for non–US-born children



- Both IGRAs track appropriately with age; TST does not.
- TST+/IGRA-discordance is highest in <5 age group (likely influenced by BCG vaccination)

*Ahmed et al., Pediatrics. 2020 Jan;145(1):e20191930. doi: 10.1542/peds.2019-1930

Interferon-g Release Assays in Children <15 Years of Age* (3)

Performance of TST and IGRAs Based on Incident Cases

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TST	50	73.6	0.2	99.9
QFT	75	90.1	0.8	100.0
T SPOT	50	92.8	0.7	99.9

NOTE: Cohort contain both treated and untreated children

*Ahmed et al., Pediatrics. 2020 Jan;145(1):e20191930. doi: 10.1542/peds.2019-1930

Interferon-g Release Assays in Children <15 Years of Age* (4)

KEY FINDING on SPECIFICITY

- **Specificities of IGRAs were high (90-93% VS 73%) compared to TST**
  - ~70% fewer positive IGRA results than TST results in Foreign-born children

INDETERMINATE RESULTS

- **<1 % had an indeterminate QFT or invalid T-SPOT.TB result**

KEY FINDINGS ON PREDICTING DISEASE and ACCURACY of NEGATIVE RESULTS

- **Sensitivity of QFT for incident cases was highest among the 3 assays**
- **NPV of QFT was 100%**
  - Of the 533 TST+/IGRAs- high-risk children, none developed disease including 54 children <2 years of age.

Authors conclusion: IGRAs can be used in children of all ages

**Ahmed et al., Pediatrics. 2020 Jan;145(1):e20191930. doi: 10.1542/peds.2019-1930*

QIAGEN UPDATE on QFT-Plus Package Insert

Parth Patel DMSc, PA-C

Scientific Officer, Medical Affairs

QIAGEN

Evolution of QFT over the past 20 years

1st generation QuantiFERON®-TB	2nd generation QuantiFERON®-TB Gold (liquid antigen)	3rd generation QuantiFERON®-TB Gold (QFT® in tube)	4th generation QuantiFERON®-TB Gold Plus (QFT®-Plus)
2001: FDA approval	2004: FDA approval	2007: FDA approval	Q4 2014: CE-IVD 2017: FDA approved
• Measured cell-mediated immunity to tuberculin purified protein derivative (PPD) • **Breakthrough:** TST becomes a blood test	• "Liquid antigen" version • Antigens specific for *M.tb with* 99% specificity • **Clinical benchmark:** No cross reactivity with BCG	• Logistical advantage – remote incubation • **Lab benchmark:** Scalable and easily automated • >1200 peer reviewed publications • >30 million tests sold	• Addition of patented CD8 antigens – potential biomarker of intracellular TB burden • New flexible blood draw options
			

March 13, 2023

Cautions removed by FDA and Canada Health

What were the cautions in the PI?

- The performance of the format of the *QFT-Plus test has not been extensively evaluated with specimens from the following groups of individuals*:
- Individuals who have impaired or altered immune functions, such as those who have HIV infection or AIDS, those who have transplantation managed with immunosuppressive treatment or others who receive immunosuppressive drugs (e.g., corticosteroids, methotrexate, azathioprine, cancer chemotherapy), those who have other clinical conditions, such as diabetes, silicosis, chronic renal failure, and hematological disorders (e.g., leukemia and lymphomas), or those with other specific malignancies (e.g., carcinoma of the head or neck and lung)
- Individuals younger than age 17 years
- Pregnant women

Package Insert Cautions Removed

- The cautions were in place based on scientific evidence that was not available at the time of QFT-GIT approval in 2017
- Voluminous data was submitted to FDA and Health Canada (2021 and 2022)
- Systematic review/meta-analysis was performed for each study population to provide evidence for removal of cautions

Rigorous evidence review was required by FDA and Health Canada leading to caution removal

What does this mean?

- Cautions removed for use in the following populations:
  - Pediatrics
  - Pregnant patient
  - Immunocompromised patient
- QFT-Plus is the only IGRA assay with multiple generations and has the most evidence out of all the IGRAs
- Regardless of the PI caution removal, QFT-Plus can and has been used in all patient populations

http://www.legacyletter.org/wp-content/uploads/2013/08/asian-multigenerational-family.jpg

Summary

1. Clinicians and laboratories can use QFT-Plus with confidence in all populations as they did with TST, including children of all ages
2. The greatest advantage of QFT-Plus is its accuracy in BCG vaccinated children
3. In contact investigation, QFT's operational advantages streamlines and simplifies TB testing for clinicians and patients
4. No test is perfect, but there will be less false positive and false negative QFTs compared to TST

- **A clinician's systematic approach** of reviewing the QFT-Plus lab results will improve clinical interpretation of qualitative results
- **Remember why your pediatric patient was tested** and the consequences of having TB or developing TB:
- A patient's **TB risk, symptoms and vulnerability to bad outcomes** are central to result interpretation and clinical management

Questions?

https://www.mummypages.co.uk/images/2115/105/5/0_2/questions.jpg

Head-to-head sensitivity comparison

Interferon-γ Release Assay Performance for Tuberculosis in Childhood*

Cohort: N=360 2010-2015 California TB registry data (≤18 years) with laboratory-confirmed TB.
95 had both TST and IGRA

Sensitivity

Age group	TST	QFT	*P* value
5-18yrs (n=69)	83%	96%	.01 significant
2-4 yrs (n=11)	91%	91%	>.99
<2 yrs (n=15)	87%	80%	>.99

Indeterminate results= 4% Associated with being <1 year old and central nervous system disease

Conclusions on largest North American study comparing TST and QFT as diagnostic aids for active TB

- Similar sensitivity in children <5 yrs old
- Reduced sensitivity of both assays in children <2 yrs
- In children ≥5 years, IGRA has greater sensitivity than TST and should be considered the preferred immunodiagnostic test

* *Kay et al, Pediatrics 2018 May 4. pii: e20173918. doi: 10.1542/peds.2017-3918.*

Question & Answer