Interferon-γ Release Assays (IGRAs)

Lisa Armitige, MD, PhD

August 1, 2024

Understanding the IGRA: What You Need to Know Webcast
August 1, 2024
Broadcast live from Heartland National TB Center

Interferon-γ Release Assays (IGRAs)

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Heartland Webcast
August 1, 2024

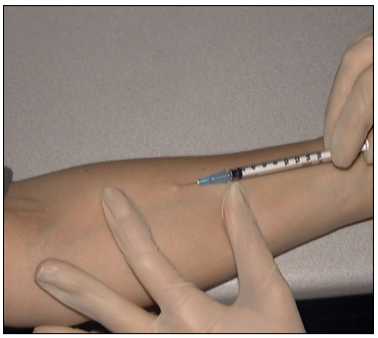
Overview

- Development of interferon-gamma release assays (IGRAs)
- FDA-approved IGRAs
- Current recommended use: CDC/ATS/IDSA recommendations

Development of IGRAs

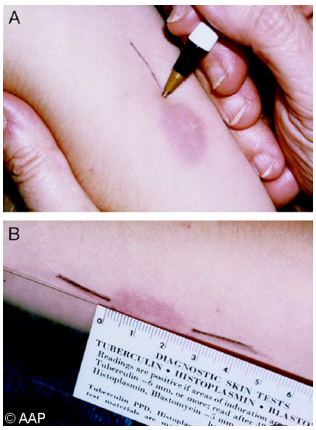
The Tuberculin Skin Test (TST)

- Where we started……
  over 100 years ago
- 0.1 ml of 5 TU PPD tuberculin injected intradermally
- Induration in millimeters read 48-72 hours after injection



Reading the TB Skin Test

Measure induration, not erythema!!!



TB Skin Test (TST)

- Pros:
  - Inexpensive
  - Simple to perform
    (if you know what you are doing)
- Cons:
  - Must return in 48-72 hrs
  - Interpretation is somewhat subjective
  - Repeated applications can cause boosting
  - False Negatives:
    - Elderly
    - Immunosuppressed
  - False Positives:
    - Low risk populations
    - Non-tuberculous mycobacteria
    - BCG vaccination

Classifying the Tuberculin Reaction

- Requires that you know something about the patient
- 5 mm is classified as positive in High-Risk Individuals
  - HIV/Immune suppressed
  - Recent contact with a person with infectious TB
  - Persons with evidence of old disease (e.g. calcified granulomas on CXR)
- 10 mm is positive in Persons in High-Risk Settings
  - Immigrants from or residents of countries with high rates of TB (>20/100,000)
  - Residents/Employees of congregate settings
- 15 mm is positive…..period

Original QuantiFERON-TB (QFT) versus TST

QFT	TST
1 patient visit	2 patient visits
Measurement of IFN-γ by machine (more objective)	Induration measured by human (more subjective)
Antigen: PPD	Antigen: PPD

Antigens for Newer Generation IGRAs

- Negative control or nil
  - (e.g., saline, heparin)
- Positive control or mitogen
  - non-specific immune response stimulator (e.g., phytohemagglutinin)
- *M. tuberculosis*-specific antigens
  - Unlike PPD used in TST, do not cross-react with BCG or NTM (some exceptions)
  - ESAT-6, CFP-10, TB 7.7 (actually simulated using overlapping peptides)

Antigens for Gamma-Release Assays

Tuberculosis complex	Antigens ESAT	Antigens CFP	Environmental strains	Antigens ESAT	Antigens CFP
M tuberculosis	+	+	M abcessus	-	-
M africanum	+	+	M avium	-	-
M bovis	+	+	M branderi	-	-
BCG substrain			M celatum	-	-
gothenburg	-	-	M chelonae	-	-
moreau	-	-	M fortuitum	-	-
tice	-	-	M gordonii	-	-
tokyo	-	-	M intracellulare	-	-
danish	-	-	M kansasii	+	+
glaxo	-	-	M malmoense	-	-
montreal	-	-	M marinum	+	+
pasteur	-	-	M oenavense	-	-
			M scrofulaceum	-	-
			M smegmatis	-	-
			M szulgai	+	+
			M terrae	-	-
			M xenopi	-	-

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FDA-Approved IGRAs

QuantiFERON®-TB Gold Plus

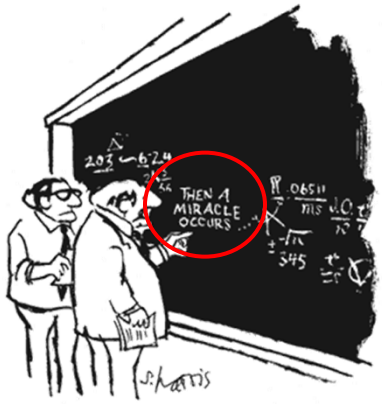
- **Mitogen – Positive Control**
  Low response may indicate inability to generate IFN-γ
- **Nil – Negative Control**
  Adjusts for background IFN-γ
- **TB1 – Primarily detects CD4 T cell response**
- **TB2 – Optimized for detection of CD4 and CD8 T cell responses**

- Essentially 2 tests in one blood draw
- TB1 and TB2 should be close in value

Interpretation Criteria for the QFT-GIT Test

Nil (IU/mL)	TB Antigen minus Nil (IU/mL)	QFT-GIT (IU/mL)	Mitogen	Interpretation
≤ 8.0	≤ 0.35 or < 25% of Nil value	Negative	≥ 5.0	*M. tuberculosis* infection unlikely
≤ 8.0	≥ 0.35 and ≥ 25% of Nil value	Positive	ANY	*M. tuberculosis* infection likely
≥ 8.0	ANY	Indeterminate	ANY	Indeterminate
≤ 8.0	≤ 0.35 and or < 25% of Nil value	Indeterminate	< 5.0	Indeterminate

QFT calculation…..



"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

QuantiFERON-TB Gold

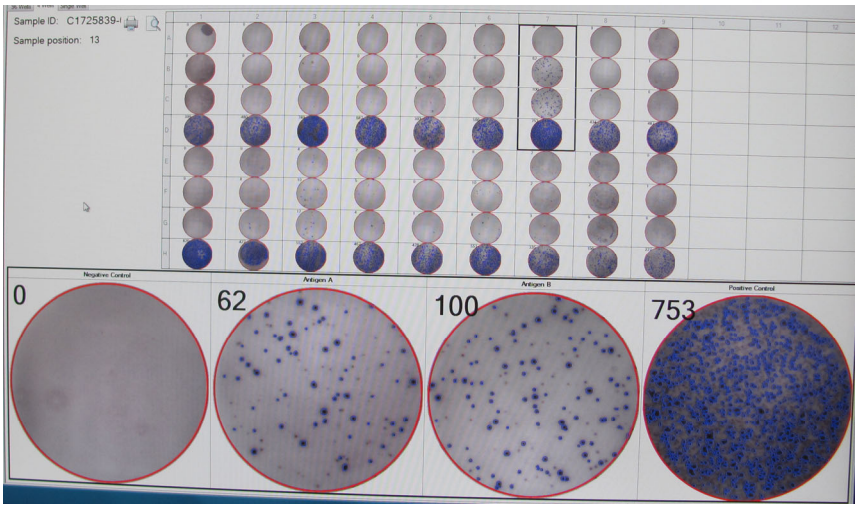
TABLE 2. TEST SENSITIVITY AND SPECIFICITY FOR CFP-10 AND ESAT-6 AT VARIOUS CUTOFFS IN WHOLE-BLOOD IFN-γ ASSAY

Cutoff, IFN-γ	CFP-10		ESAT-6		CFP-10 and/or ESAT-6	
(*IU/ml*)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)
0.05	92.5	81.4	94.8	94.9	89.4	97.5
0.10	94.4	77.1	96.2	90.7	92.0	95.8
0.15	95.8	72.9	97.6	88.1	93.9	93.2
0.20	96.7	71.2	99.1	86.4	96.2	91.5
0.25	97.2	67.8	99.1	84.7	96.7	91.5
0.30	97.7	66.9	99.1	83.1	97.2	89.8
0.35	**98.6**	**65.3**	**99.5**	**81.4**	**98.1**	**89.0**
0.40	98.6	61.9	99.5	79.7	98.1	88.1
0.45	98.6	60.2	100.0	78.8	98.6	86.4
0.50	99.1	60.2	100.0	75.4	99.1	83.9

Sensitivity was determined on the basis of data from 118 patients with culture-positive tuberculosis, and specificity was determined on the basis of data from 213 low-risk subjects. The chosen cutoff (0.35) is in boldface.

Mori et al 2004 Am J Respir Crit Care Med ,170: 59–64

T-Spot.*TB*



Interpretation Criteria for the T-Spot.TB

Result	Nil*	TB Response# #	Mitogen++	Interpretation+
Positive	≤ 10 spots	≥ 8 spots	Any	*M.tuberculosis* infection likely
Borderline	≤ 10 spots	5, 6, or 7 spots	Any	Uncertain likelihood of *M. tuberculosis* infection
Negative	≤ 10spots	≤ 4 spots		M Tb infection unlikely
Indeterminate	> 10 ≤ 10	Any < 5 spots	Any < 20 spots	Uncertain likelihood of *M. tuberculosis* infection

Indeterminate and Borderline Results

- Indeterminate
  - Negative control result is too high
    - High background production of IFN-γ
  - Positive control result is too low
    - Immunocompromised patients may not respond to mitogen
  - Something went wrong with performing the test
- Borderline (T-Spot only)
  - Falls within borderline zone close to negative/positive cut point

Repeat the test

Reproducibility and Variability

- At least 4 sources of variability
  - Type of measurement (ELISA or ELISPOT)
  - Reproducibility of complex biological reaction
  - Natural variability of immune responses
  - Variability introduced during test performance or manufacturing
- QFT 11% variance overall
  - 8% between first/second testing of same specimen
- T-spot variance
  - 4% (with robust response)
  - 22% (near the cut point)

Potential sources of variability and their impact on results in IGRAs

Potential source of variability[b]	QFT-GIT	T-SPOT
Manufacturing		
Between-lot variability	↑ ↓	?
Preanalytical		
Time of blood draw (a.m. vs p.m.)	↑ p.m.	?
Skin disinfection	↑ ↓	?
Traumatic blood draw	?	?
Blood vol (0.8 to 1.2 ml)	↓ 1.2 ml	NA
Shaking of blood tubes	↑ ↓	?
T-cell and APC count	?	?[d]
Transportation temp	?	↓
Incubation delay	↓ <30°C	?
Incubation time	No effect	?
Plasma separation delay	?[e]	NA
Plasma/PBMC storage	No effect	No effect

Banaei, Gaur, Pai. *J. Clin. Microbiol. April 2016 54 (4): 845-850*

Boosting and Special Considerations

- Boosting by prior TST has been observed in as little as 3 days post-TST and may wane over several months
- If both tests are to be used, do the IGRA first
- Because the IGRAs are a functional assessment of viable lymphocytes, special attention should be paid to technical aspects of the test (how blood is drawn/stored, etc.)

ATS/CDC/IDSA Guidelines

Clinical Infectious Diseases

IDSA GUIDELINE

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children

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[1]Oregon Health & Science University, Portland, Oregon, [2]Emory University School of Medicine and [3]Centers for Disease Control and Prevention, Atlanta, Georgia, [4]Denver Public Health Department, Denver, Colorado, [5]National Jewish Health and the University of Colorado Denver, and [6]California Department of Public Health, Richmond; [7]St James's Hospital, Dublin, Ireland; [8]Francis J. Curry International TB Center, San Francisco, California; [9]Foundation for Innovative New Diagnostics, Geneva, Switzerland; [10]McGill University and McGill International TB Centre, Montreal, Canada; [11]University of Southampton, United Kingdom; [12]National Jewish Health, Denver, Colorado, [13]Vanderbilt University School of Medicine, Vanderbilt Institute for Global Health, Nashville, Tennessee, [14]Wisconsin State Laboratory of Hygiene, Madison, and [15]University of Arkansas for Medical Sciences, Little Rock

Lewinsohn et al. CID. 2016

Groups with Increased Likelihood of Infection with Mtb	Benefit of Therapy	LTBI Testing Strategy	
Household contact or recent exposure of an active case	Yes	Likely to be Infected Low to Intermediate Risk of Progression (TST ≥ 10mM)	Likely to be Infected High Risk of Progression (TST ≥ 5mM)
Mycobacteriology laboratory personnel	Not demonstrated		
Immigrants from high burden countries (>20 / 100,000)	Not demonstrated		
Residents and employees of high risk congregate settings	Yes		
None	Not demonstrated	Unlikely to be Infected (TST > 15mM)	

Risk of Infection

Risk of Developing Tuberculosis if Infected

Low	Intermediate (RR 1.3 -3)	High (RR 3-10)
No risk factors	Clinical predisposition Diabetes Chronic renal failure Intravenous drug use	Children age less than 5 HIV infection Immunosuppressive therapy Abnormal CXR consistent with prior TB Silicosis

Benefit of Therapy

Not demonstrated	Yes

In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Group	Testing Strategy	Considerations
Likely to be Infected **High** Risk of Progression (TST ≥ 5mM)	**Adults** **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either result would be considered **positive** **Children ≤ 5 years of age** **Preferred**: TST **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either would be considered **positive**[1]	Prevalence of BCG vaccination Expertise of staff and/or laboratory Test availability Patient perceptions Staff perceptions Programmatic concerns
Likely to be Infected **Low** to **Intermediate** Risk of Progression (TST ≥ 10mM)	**Preferred**: IGRA where available **Acceptable**: IGRA or TST	
Unlikely to be Infected (TST > 15mM)	**Testing for LTBI is not recommended** **If necessary:** **Preferred:** IGRA where available. **Acceptable**: Either IGRA OR TST **For serial testing**: **Acceptable**: Either IGRA OR TST Consider repeat or dual testing where a negative result from either would be considered **negative**[2]	

1. Performing a second diagnostic test when the initial test is negative is a strategy to increase sensitivity. This may reduce specificity, but the panel decided that this is an acceptable tradeoff in situations in which the consequences of missing LTBI (i.e., not treating individuals who may benefit from therapy) exceed the consequences of inappropriate therapy (i.e., hepatotoxicity).
2. Performing a confirmatory test following an initial positive result is based upon both the evidence that false-positive results are common among individuals who are unlikely to be infected with Mtb and the committee's presumption that performing a second test on those whose initial test was positive will help identify initial false-positive results.

Recommendations

Should an IGRA or a TST be performed in individuals 5 years or older who are likely to be infected with *Mtb*, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted?

- Recommendation 1a:

  We recommend performing an IGRA rather than a TST in individuals 5 years or older who meet the following criteria:

  (1) are likely to be infected with *Mtb*,
  (2) have a low or intermediate risk of disease progression,
  (3) it has been decided that testing for LTBI is warranted, and
  (4) either have a history of BCG vaccination or are unlikely to return to have their TST read
  (*strong recommendation, moderate-quality evidence*).

Justification

- Accuracy studies indicate that IGRAs are more specific and equally or more sensitive than TST in individuals who have received BCG
- Testing with an IGRA does not depend on a return visit for a result.

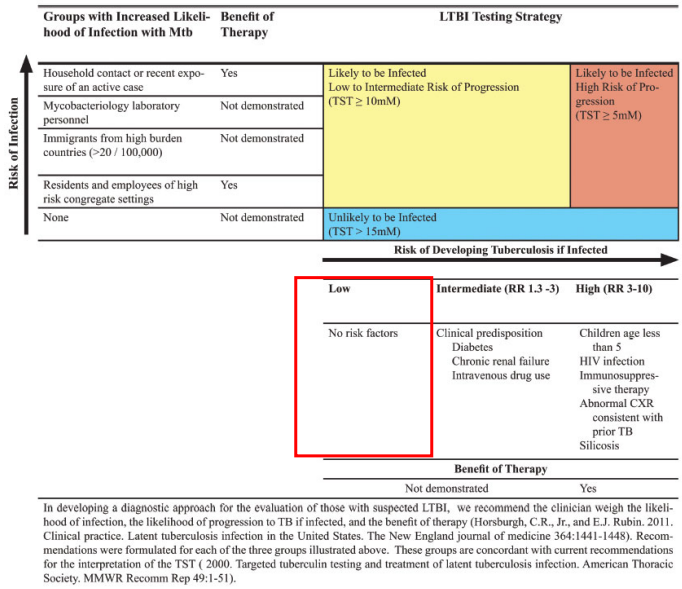
Recommendations

Should an IGRA or a TST be performed in individuals 5 years or older who are likely to be infected with *Mtb*, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted?

- Recommendation 1b:

  We recommend performing an IGRA rather than a TST in individuals 5 years or older who meet the following criteria:

  (1) are likely to be infected with *Mtb*,
  (2) have a low or intermediate risk of disease progression,
  (3) it has been decided that testing for LTBI is warranted, and
  ~~(4) either have a history of BCG vaccination or are unlikely to return to have their TST read~~
  (*conditional recommendation, moderate-quality evidence*).



In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Recommendations

Should an IGRA or a TST be performed in individuals 5 years or older who are unlikely to be infected with *Mtb*, but in whom it has been decided that testing for LTBI is warranted?

Suddenly Positive

- 35-year-old US-born man takes a new job at a hospital in the accounting department. He has been tested annually at his old hospital job and has been TST negative for the past 10 years.
- He has a positive IGRA (nil 0, TB1-nil 0.42, TB2-nil 0.27) on testing at the new job.
- He has no recent travel nor known contact to anyone with TB disease.
- What should you do with him?

QuantiFERON-TB Gold

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Sensitivity was determined on the basis of data from 118 patients with culture-positive tuberculosis, and specificity was determined on the basis of data from 213 low-risk subjects. The chosen cutoff (0.35) is in boldface.

Mori et al 2004 Am J Respir Crit Care Med ,170: 59–64

Recommendations

Should an IGRA or a TST be performed in individuals 5 years or older who are unlikely to be infected with *Mtb*, but in whom it has been decided that testing for LTBI is warranted?

- Recommendation 3a:

  We suggest performing an IGRA instead of a TST

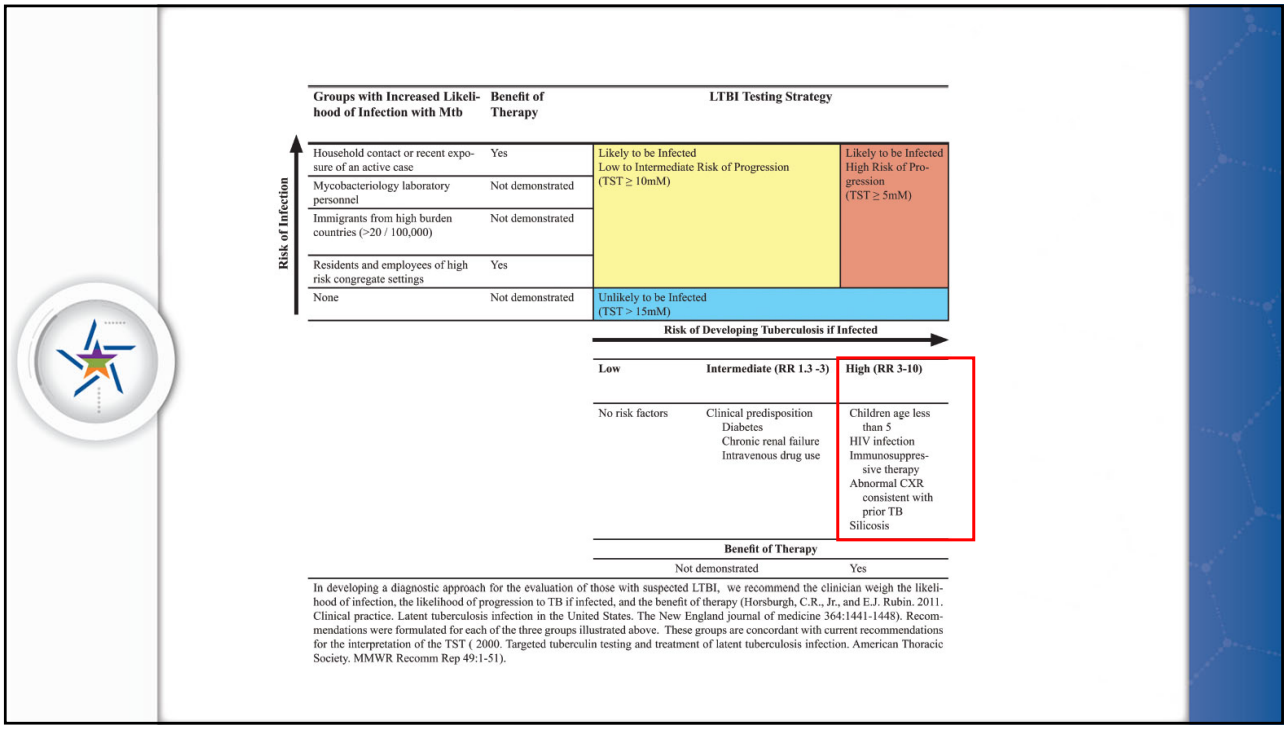
  (*conditional recommendation, low-quality evidence*).

- Recommendation 3b:

  We suggest a second diagnostic test if the initial test is positive

  (*conditional recommendation, very low-quality evidence*).

  Remarks: The confirmatory test may be either an IGRA or a TST. When such testing is performed, the person is considered infected only if both tests are positive.



World Traveler with RA

- 56 y/o WF about to be started on Humira for rheumatoid arthritis
  - She has traveled extensively, in the Peace Corp in her 20's and on humanitarian visits to Haiti, Sudan and Guatemala in the past 15 years
  - She has a TST performed at the local public health clinic and it is 10 mm
- Do you:
  - Treat for TB infection (LTBI)?
  - Retest with an IGRA?

Recommendations

Should an IGRA or a TST be performed in individuals 5 years or older who are likely to be infected with *Mtb*, who have a high risk of progression to disease, and in whom it has been decided that testing for LTBI is warranted?

- Recommendation 2:

  There are insufficient data to recommend a preference for either a TST or an IGRA as the first-line diagnostic test in individuals 5 years or older who are likely to be infected with *Mtb*, who have a high risk of progression to disease, and in whom it has been determined that diagnostic testing for LTBI is warranted.

World Traveler with RA

- 56 y/o WF about to be started on Humira for rheumatoid arthritis
  - She has traveled extensively, in the Peace Corp in her 20's and on humanitarian visits to Haiti, Sudan and Guatemala in the past 15 years
  - Her TST returns positive
- Do you:
  - Treat for TB infection (LTBI)?
  - Retest with an IGRA?

Answer: Treat!!!
Do not confuse things by retesting

Recommendations

Should an IGRA or a TST be performed in healthy children <5 years of age in whom it has been decided that testing for LTBI is warranted?

- Recommendation:

  We suggest performing a TST rather than an IGRA in healthy children <5 years of age for whom it has been decided that diagnostic testing for LTBI is warranted (*conditional recommendation, very low-quality evidence*).

This is old information!

IGRAs 2024 AAP REDBOOK

- IGRAs can be used in immunocompetent children of any age in all situations when a TST would be used
- IGRAs are the preferred test for children who have received a BCG vaccination
- Neither IGRAs nor the TST are perfect; always need clinical judgment, especially in very sick children and children < 6 months

Pediatric Considerations for TB Screening

- Young immune systems, like young bodies, are growing
- By the time you have 5 candles on your birthday cake, your immune system behaves like an adult's
- There is grey area in children < 6 months of age (any test….every test), treat any positive and some negatives
- We overtreat and we are not sorry

Additional Considerations for Serial Testing with IGRAs

- IGRA advantages include obtaining results in a single visit and no need for two-step testing (IGRAs don't boost subsequent test results)
- Disadvantages include a potential greater risk of false test conversion
  - IGRA conversion is defined as a change from negative to positive without any consideration of magnitude
  - Using lenient criterion to define conversion might produce more conversions than are observed with the more stringent criteria applied to TSTs
  - Recent published studies appear to validate this concern

Screening HCW for TB

TABLE. Comparison of 2005* and 2019† recommendations for tuberculosis (TB) screening and testing of U.S. health care personnel (HCP)

Category	2005 Recommendation	2019 Recommendation
Baseline (preplacement) screening and testing	TB screening of all HCP, including a symptom evaluation and test (IGRA or TST) for those without documented prior TB disease or LTBI.	TB screening of all HCP, including a symptom evaluation and test (IGRA or TST) for those without documented prior TB disease or LTBI (**unchanged**); individual TB risk assessment (**new**).
Postexposure screening and testing	Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB disease or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure.	Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB disease or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure (**unchanged**).
Serial screening and testing for HCP without LTBI	According to health care facility and setting risk assessment. Not recommended for HCP working in low-risk health care settings. Recommended for HCP working in medium-risk health care settings and settings with potential ongoing transmission.	Not routinely recommended (**new**); can consider for selected HCP groups (**unchanged**); recommend annual TB education for all HCP (**unchanged**), including information about TB exposure risks for all HCP (**new emphasis**).
Evaluation and treatment of positive test results	Referral to determine whether LTBI treatment is indicated.	Treatment is encouraged for all HCP with untreated LTBI, unless medically contraindicated (**new**).

Abbreviations: IGRA = interferon-gamma release assay; LTBI = latent tuberculosis infection; TST = tuberculin skin test.
* Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. MMWR Recomm Rep 2005;54(No. RR-17). https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm.
† All other aspects of the Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005 remain in effect, including facility risk assessments to help guide infection control policies and procedures.

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TB Testing in Pregnant Persons

- Test in every instance you would test if they were not pregnant
  - HIV
  - Contact to an active case
  - Immigrant from or resident in a high-risk country
- The immune system may not react as expected
- Yes, you can/should get a CXR

Yes! You can X-ray a pregnant patient!

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG COMMITTEE OPINION

Number 723 • October 2017 (Replaces Committee Opinion Number 656, February 2016)

Committee on Obstetric Practice

This document is endorsed by the American College of Radiology and the American Institute of Ultrasound in Medicine. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Obstetric Practice. Member contributors included Joshua Copel, MD, Yasser El-Sayed, MD, R. Phillips Heine, MD, and Kurt R. Wharton, MD. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Table 2. Effects of Gestational Age and Radiation Dose on Radiation-Induced Teratogenesis

Gestational Period	Effects	Estimated Threshold Dose*
Before implantation (0–2 weeks after fertilization)	Death of embryo or no consequence (all or none)	50–100 mGy
Organogenesis (2–8 weeks after fertilization)	Congenital anomalies (skeleton, eyes, genitals)	200 mGy
	Growth restriction	200–250 mGy
Fetal period	**Effects**	**Estimated Threshold Dose***
8–15 weeks	Severe intellectual disability (high risk)†	60–310 mGy
	Intellectual deficit	25 IQ-point loss per 1,000 mGy
	Microcephaly	200 mGy
16–25 weeks	Severe intellectual disability (low risk)	250–280 mGy*

*Data based on results of animal studies, epidemiologic studies of survivors of the atomic bombings in Japan, and studies of groups exposed to radiation for medical reasons (eg, radiation therapy for carcinoma of the uterus).

†Because this is a period of rapid neuronal development and migration.

Modified from Patel SJ, Reede DL, Katz DS, Subramaniam R, Amorosa JK. Imaging the pregnant patient for nonobstetric conditions: algorithms and radiation dose considerations. Radiographics 2007;27:1705–22.

Table 3. Fetal Radiation Doses Associated With Common Radiologic Examinations

Type of Examination	Fetal Dose* (mGy)
Very low-dose examinations (<0.1 mGy)	
Cervical spine radiography (anteroposterior and lateral views)	<0.001
Head or neck CT	0.001–0.01
Radiography of any extremity	<0.001
Mammography (two views)	0.001–0.01
Chest radiography (two views)	0.0005–0.01
Low- to moderate-dose examinations (0.1–10 mGy)	
Radiography	
Abdominal radiography	0.1–3.0
Lumbar spine radiography	1.0–10
Intravenous pyelography	5–10
Double-contrast barium enema	1.0–20
CT	
Chest CT or CT pulmonary angiography	0.01–0.66
Limited CT pelvimetry (single axial section through the femoral heads)	<1
Nuclear medicine	
Low-dose perfusion scintigraphy	0.1–0.5
Technetium-99m bone scintigraphy	4–5
Pulmonary digital subtraction angiography	0.5
Higher-dose examinations (10–50 mGy)	
Abdominal CT	1.3–35
Pelvic CT	10–50
^{18}F PET/CT whole-body scintigraphy	10–50

Which is the better test?

- For use in testing, the QFT-Gold Plus and T-spot can be considered equivalent.
- The goal is to get an answer!

More important questions

- Who are you testing?
- What does your lab say?
- Where are you testing/how often do you test?

Who are you testing?

- BCG vaccinated populations
- Those unlikely to return for a reading
- Children
  - 4 tubes of blood from little people that don't like needles……
- Persons living with HIV/persons with low WBCs (such as with chemotherapy)
  - May not have that many cells to start with, concentrating them may help

What does your lab say?

- Where will the tubes go once the blood is drawn?
- How can we make our clinic hours and lab hours work together?
- Is my lab giving me what I need or do I need to consider other options?

Where are you testing and how often?

- Hospitals and low volume clinics may have more issues with QFT
- Get to know your rep and have them come out for training if need be

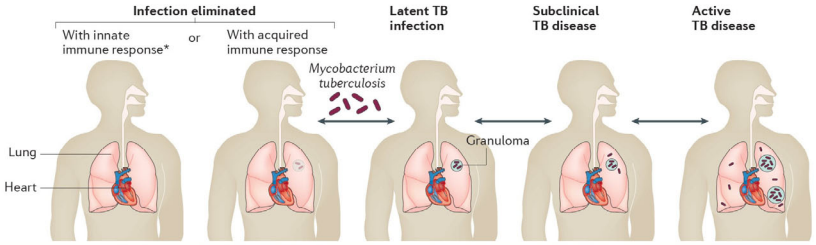
What about boosting?

- IGRAs can be boosted by performing a TST then following with an IGRA
- What this means is not entirely clear
- You can't boost something that's not there!

Remember

- A decision to test is a decision to ~~treat~~ think!
- No definitive test for LTBI exists
- No test (TST or IGRA) overrides clinical, epidemiologic or historical data

Tuberculosis Spectrum of Disease



TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therapy	Multidrug therapy	Multidrug therapy

TB Testing Take Homes

- TST expertise is fading fast
  - When can I still use it?
    - If you trust the person placing/reading it knows what they are doing
    - Testing US born individuals
    - No history of BCG
    - To add sensitivity
    - Repeatedly indeterminate or borderline IGRAs
- IGRAs are fast becoming the preferred screening tests for TB
  - Single visit
  - Objective result (positive or negative…..ish)
- TB screening tests are tools that add to the answer
  - They are not the answer themselves
  - They do not distinguish between TB infection (LTBI) and TB disease

Conclusions

- Screening for TB should be considered in non-US born individuals who have not been previously screened or who spend significant time in higher risk countries.
- HCW screening is focused less on annual screening of low risk individuals and more on treatment of workers who test positive.
- Current TB screening tests are tools, not an answer

I just want a test that gives me the answer.

- TB doc in Texas

Questions?

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