

HEARTLAND

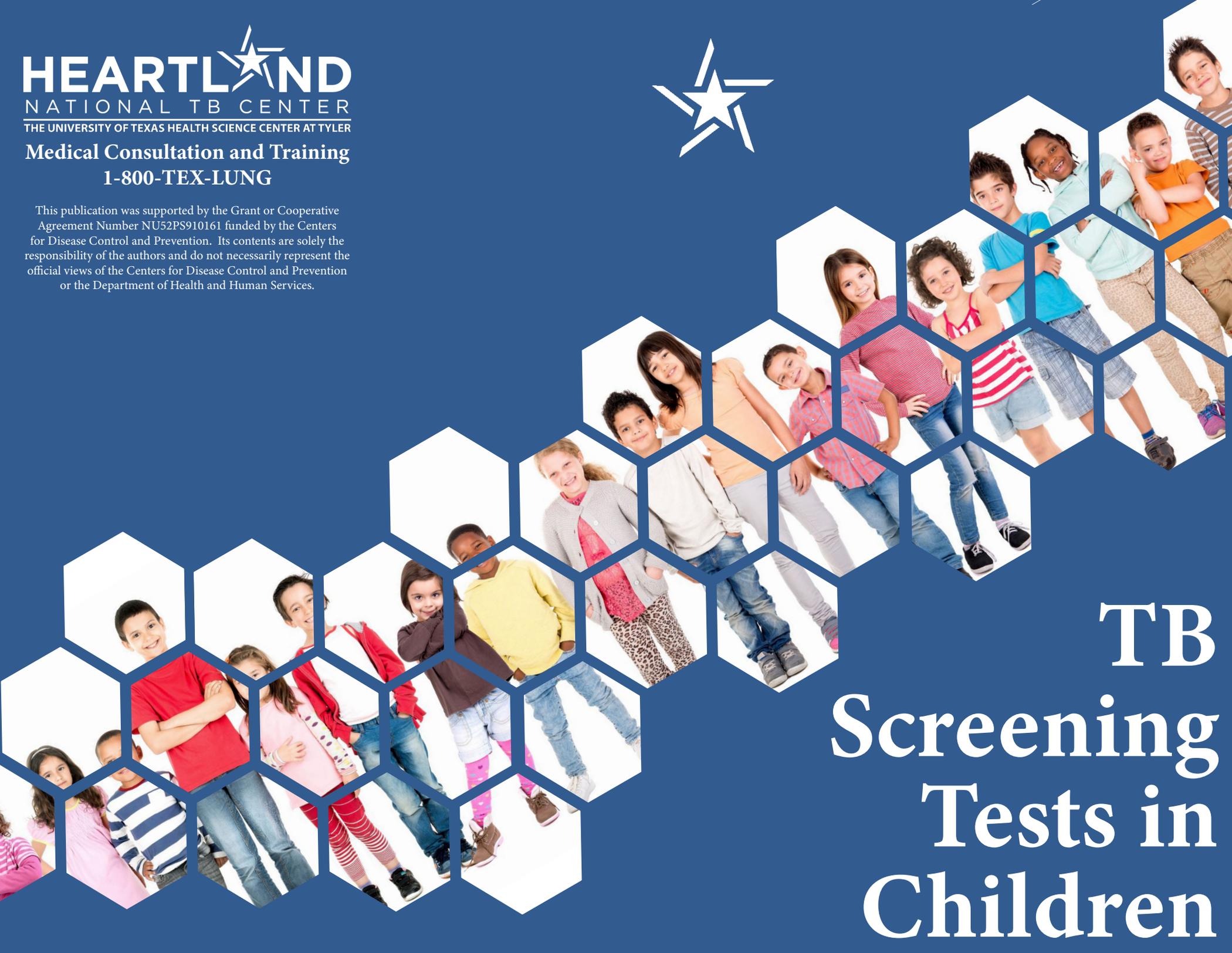
NATIONAL TB CENTER

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT TYLER

Medical Consultation and Training

1-800-TEX-LUNG

This publication was supported by the Grant or Cooperative Agreement Number NU52PS910161 funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.



TB Screening Tests in Children

TB Testing Methods in Children

Tests for TB infection include the tuberculin skin test (TST) and Interferon-Gamma Release Assays (IGRAs). TSTs and IGRAs may be used separately or in combination for children depending on the clinical scenario (Table 1).

1. TB Skin Test. Mantoux tuberculin skin test (TST).

- Requires two visits to a health care provider, one to place the test, the other to read it.
- Measures the delayed-type hypersensitivity reaction to purified protein derivative (PPD) of *Mycobacterium tuberculosis* (*M. tuberculosis*). Because PPD is present in many non-tuberculous mycobacteria (e.g., BCG), it is less specific than other tests.
- Widely available

2. TB Blood Test. Interferon-Gamma Release Assay (IGRA). Two TB blood tests are approved by the US Food and Drug Administration (FDA): the QuantiFERON®-TB Gold Plus and the T-SPOT®.TB.

- QuantiFERON® Gold Plus (QFT-Plus)
 - Only requires one office visit for blood draw, but also requires laboratory capabilities.
 - Measures the quantity of IFN-gamma released by T cells in response to *M. tuberculosis* specific antigens, therefore, it can be more specific (but not necessarily more sensitive) for detecting *M. tuberculosis* than the TST.
- T-SPOT.TB® (T-SPOT®)
 - Only requires one office visit, but also requires laboratory capabilities.
 - Measures the number of T-cells secreting IFN-gamma in response to *M. tuberculosis* specific antigens which can make it more specific (but not necessarily more sensitive) for detecting *M. tuberculosis* than the TST.
 - Uses pediatric specific minimum volume collection depending on age of the child
 - › < 2 years old: 2 mL
 - › 2-9 years old: 4 mL
 - › > 10 years old: 6 mL

None of the currently available tests can distinguish between a diagnosis of latent TB infection (LTBI) and active TB disease. A negative reaction to either test does not exclude the diagnosis of TB in patients with a high risk of TB infection.

All patients with a positive TB screening test should undergo a follow-up assessment (page 6).

Table 5. Interpretation of QuantiFERON® -TB Gold Plus

Nil (IU/ml)	TB1-Nil (IU/ml)	TB2-Nil (IU/ml)	Mitogen-Nil (IU/ml)	QFT-Plus Result	Interpretation
≤8.0	≥ 0.35 and ≥25% of Nil	Any	Any	Positive	<i>M. tuberculosis</i> infection likely
	Any	≥0.35 and ≥25% of Nil			
	<0.35 or ≥0.35 and <25% of Nil		≥0.50	Negative	<i>M. tuberculosis</i> infection <u>NOT</u> likely
		<0.50	Indeterminate		Likelihood of <i>M. tuberculosis</i> infection cannot be determined; repeat test
≥8.0	Any				

Table 6. Interpretation of T-SPOT®.TB Assay

Nil (Spots)	Mitogen-Nil (spots)	Panel A - Nil (spots)	Panel B - Nil (spots)	T-SPOT® Result	Interpretation
≤ 10 spots	≥ 20 spots	≥ 8 spots	≥ 8 spots	Positive	<i>M. tuberculosis</i> infection likely
	< 20 spots				
	≥ 20 spots	5, 6, or 7 spots	5, 6, or 7 spots	Borderline	Equivocal
	< 20 spots				
	≥ 20 spots	≤ 4 spots	≤ 4 spots	Negative	<i>M. tuberculosis</i> infection <u>NOT</u> likely
< 20 spots	≤ 4 spots	≤ 4 spots	Invalid	Repeat Test	
> 10 spots	Any			Invalid	Repeat Test

Follow-up Assessment

All patients with a positive TB screening test should undergo a thorough symptom review, a physical examination, and a high-quality chest x-ray (CXR [PA and lateral]) to evaluate the possibility of active TB. Those providing LTBI screening tests must have processes in place to further evaluate patients with positive results or refer them to a TB program clinic or to a provider with experience managing treatment for LTBI. In a number of U.S. jurisdictions, LTBI is a reportable condition.

Interpretation of TB Screening Tests

Tuberculin Skin Test Reading and Interpretation

The skin test reaction should be read 48 - 72 hours after administration. A patient not returning within 72 hours should be rescheduled for another TST. The TST reaction (induration) should be measured with a small tuberculin ruler and recorded in millimeters. Induration is the measurable reaction: a palpable, raised, hardened area or swelling occurring at or near the injection site (Figure 1). The reader should not measure erythema (redness). If no induration, report 0 mm.

Figure 1. Induration vs. Erythema

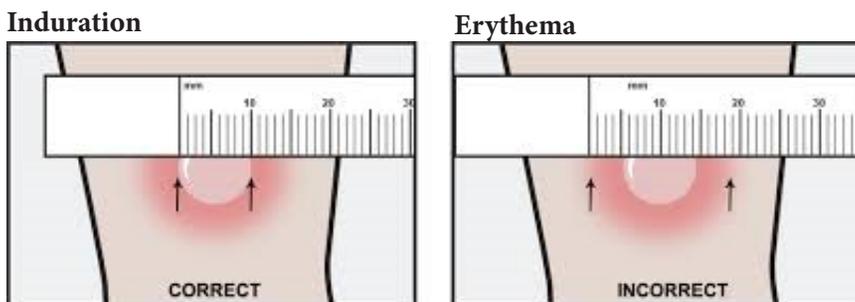


Table 4. TST Interpretation

Induration \geq 5 mm considered positive in:	Induration \geq 10 mm considered positive in:	Induration \geq 15 mm considered positive in:
HIV infected individuals	Immigrants from high-prevalence countries	Any person, including persons with no known risk factors for TB Note: Targeted skin testing programs should only be conducted among high-risk groups.
A recent contact of a person with TB disease	Persons with clinical conditions that place them at high risk	
Persons with fibrotic changes of CXR consistent with prior TB	Residents and employees of high-risk congregate settings	
Patients with organ transplants	Mycobacteriology laboratory personnel	
Individuals immunocompromised for other reasons (e.g. taking TNF-alpha inhibitors, taking equivalent of \geq 15 mg/day of prednisone for \geq 1 month)	Infants, children, and adolescents exposed to adults in high-risk categories	
	Children < 5 years old not in contact with a person with TB disease	
	Injection drug users	

Table 1. Suggested Uses of the TST and IGRA

Suggested Test(s)	Scenario
TST Preferred	Child < 2
IGRA Preferred	Child \geq 2 years
	Child unlikely to return for TST reading
Both TST and IGRA	See Table 3. Testing with Both TST and IGRA

Table 2. Available TB Tests

	Tuberculin Skin Test (TST)	QuantiFERON® Gold Plus	T-SPOT.TB®
What's Needed?	2 visits Trained personnel, accurate test placement and measurement	1 visit 4 mL blood	1 visit 2, 4, 6 mL blood depending on age of child
Antigens Used in Assay	Many	ESAT-6 and CFP-10 (encoded by the region of difference RD1)	
Cross-reactivity with BCG	Yes	No	
Cross-reactivity with non-tuberculous mycobacteria (NTM)	Yes	Yes, but limited to: <i>Mycobacterium kansasii</i> <i>Mycobacterium szulgai</i> <i>Mycobacterium marinum</i> <i>Mycobacterium leprae</i>	
Boosting following TST	Yes	Possibly, if a TST is applied first.	
Distinguish between TB infection and TB disease?	No		

Table 3. Testing with Both TST and IGRA

Initial Test Result:		
Negative	Positive	Indeterminate, Invalid, or Borderline
Performing a second test will increase:		
Sensitivity of test	Confidence of initial test result	Opportunity for a definitive result
Additional reasons for performing a second test:		
Child is at increased risk of TB infection, progression to TB disease, or current active TB is present	Additional evidence of infection will encourage compliance in a healthy child OR additional confirmation of infection is desired	Repeating IGRA or performing the TST may be useful

Screening for TB with TST and IGRA in Children

