



TB Screening Tests and Their Use in TB Nurse Case Management

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Has the following disclosures to make:

- No conflict of interests
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Objectives

1. Review current guidelines when screening for TB.
2. Identify high-risk groups for targeted testing and who should be screened for TB infection.
3. Review tuberculosis screening tools (Mantoux TST, IGRAs) and how to interpret results.

Why is it important to test for TB?

Tuberculosis is the leading cause of death from a single infectious agent.

TB continues to be one of the top 10 causes of death worldwide.

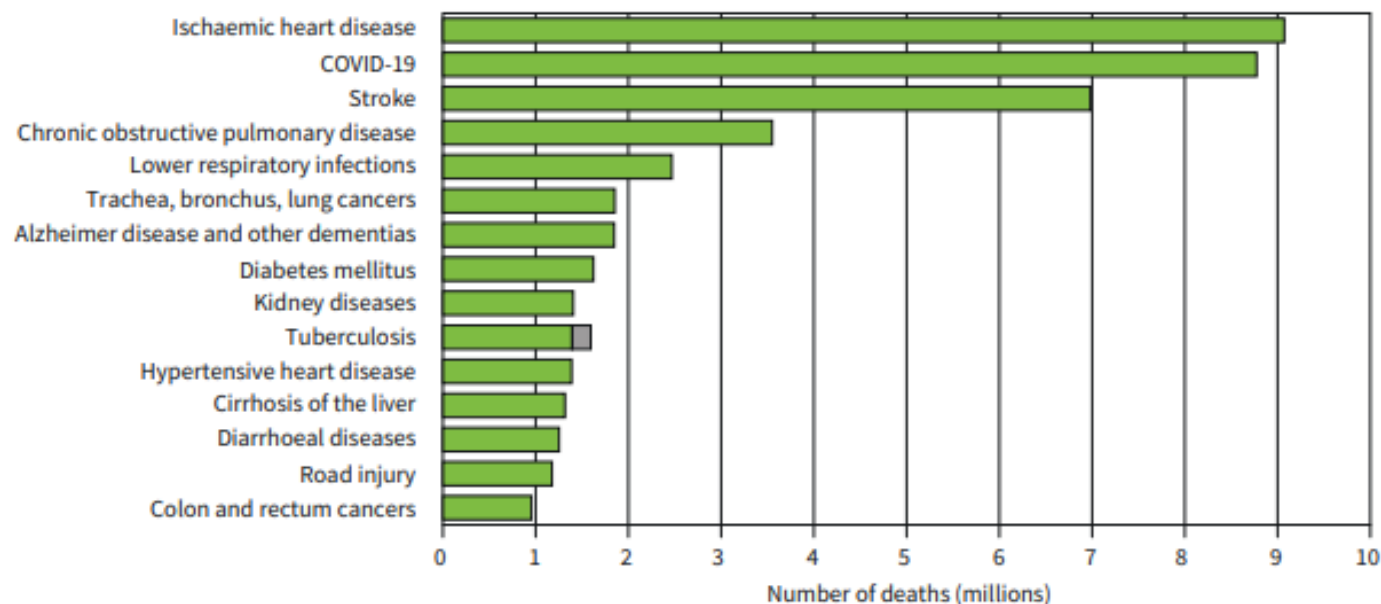
With proper medical treatment, tuberculosis is preventable and curable.

Global Tuberculosis Report 2025

FIG. 11

Top 15 causes of death worldwide in 2021^{a,b}

Deaths from TB among people with HIV are shown in grey.



^a This is the latest year for which estimates for all causes are currently available. See WHO estimates, available at <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/gho-leading-causes-of-death>.

^b Deaths from TB among people with HIV are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases, with TB as a contributory cause.

What is the management plan for TB in the United States?

1. Early and accurate detection, diagnosis, and reporting of people living with infectious TB, leading to initiation and completion of treatment.
2. Identification of contacts of persons with infectious TB and treatment of those at risk with an effective drug regimen.
3. Identification of other persons with LTBI at risk for progression to TB disease and treatment of those persons.
4. Identification of settings in which a high risk exists for transmission of M. tuberculosis and application of effective preventive measures.

All principles involve testing.

A decision to test is a decision to treat.

Current Guidelines



What Guidelines do we have to address TB testing?

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

David M. Lewinsohn,^{1,9} Michael K. Leonard,^{2,9} Philip A. LoBue,^{3,9} David L. Cohn,⁴ Charles L. Daley,⁵ Ed Desmond,⁶ Joseph Keane,⁷ Deborah A. Lewinsohn,¹ Ann M. Loeffler,⁸ Gerald H. Mazurek,⁹ Richard J. O'Brien,⁹ Madhukar Pai,¹⁰ Luca Richeldi,¹¹ Max Salfinger,¹² Thomas M. Shinnick,³ Timothy R. Sterling,¹³ David M. Warshauer,¹⁴ and Gail L. Woods¹⁵

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TUBERCULOSIS TESTING BASED UPON:

Likelihood of Infection with Mycobacterium Tuberculosis

Risk of Progression to active Tuberculosis disease

Persons tested for other reasons:

Administrative, employment testing

Symptoms of active TB disease

Risk of Infection ↑	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	Unlikely to be Infected (TST > 15mm)		
	None	Not demonstrated			
			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	

Targeted Testing

The strategy we use to identify and treat persons with latent tuberculosis infection (LTBI) who are at a high risk for progression to tuberculosis disease.

The goal is early detection (identification) to interrupt progression to TB disease. This is PREVENTION, which is key to stopping the spread of TB.

Targeted Testing

Who is at risk of exposure to or likelihood of M. Tuberculosis infection?

- Contacts of persons with active TB disease
- People living with HIV
- People born in or frequently travel to countries where TB is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, Guatemala, and other countries
- Residents and Employees of high-risk congregate settings: correctional facilities, homeless shelters, hospitals, clinics, nursing homes, substance abuse facilities.
- Patients considering treatment with TNF- α antagonists
- Children exposed to high-risk adults or environments
- Other populations defined locally as having increased risk of LTBI or TB disease.

Figure 3.1. *Groups at high risk for TB infection and disease.* From *Self-Study Module 3: Targeted Testing and the Diagnosis of Latent TB Infection and TB Disease* (p. 6), by Centers for Disease Control and Prevention, 2019.

Targeted Testing

Who is at high risk of progression to TB disease after infection?

- People living with HIV
- Children younger than 5 years of age
- Recent infection with M. Tuberculosis within the past 2 years
- People with a history of untreated or inadequately treated TB infection
- Immunosuppressive therapy, TNF- α antagonists, systemic corticosteroids \geq 15 mg prednisone daily, immunosuppressive therapy after organ transplants
- Persons with silicosis, diabetes, chronic renal failure, leukemia, cancer of the head, neck, or lungs
- Gastrectomy, jejunioileal bypass
- Low body weight
- Cigarette smokers, persons who abuse drugs or alcohol
- Populations defined locally, medically underserved, low-income populations

Figure 3.1. *Groups at high risk for TB infection and disease.* From *Self-Study Module 3: Targeted Testing and the Diagnosis of Latent TB Infection and TB Disease* (p. 6), by Centers for Disease Control and Prevention, 2019.

Screening in Children

Screen children and adolescents when they have **risk factors**:

- exposure to someone with active TB, Travel to or birth in a country where TB is common, immunocompromised status (HIV, transplant, immunosuppressive therapy)

(American Academy of Pediatrics, 2024, as cited in Red Book webpage)

Percent Risk of Disease by Age

Age at Infection	Risk of Active TB
Birth – 1 year*	43%
1 – 5 years*	24%
6 – 10 years*	2%
11 – 15 years*	16%
Healthy Adults	5-10% lifetime risk
HIV Infected Adults ⁺	30-50% lifetime

*Miller, Tuberculosis in Children Little Brown, Boston, 1963

⁺WHO, 2004

Source: Heartland National TB Center (n.d.). Data adapted from Miller, Tuberculosis in Children (1963) and WHO (2004). Retrieved from <https://www.heartlandntbc.org>

Why are contacts of individuals with active TB a priority?

- In the US, we use a dual approach which involves identification and treating
- In close contacts, 30% will have TB infection, 1-3% will develop active TB disease.
- Without treatment, 10% with TB infection will develop active TB (5% from new infections within 2 years, 5% from later after 2 years)
- First 2 years after TB infection is highest risk time frame for progression to TB disease.
- 80% of all active TB cases are from untreated LTBI

Important to know

These guidelines cannot possibly cover all situations and circumstances related to TB. Therefore, they are not intended to enforce or impose a standard. The purpose is to aid in decision-making, to provide a tool for guidance and rationale decision making.

Flexibility should be used when determining which groups are high risk for testing and should be made at the local level(city, county, or state) according to local demographics and TB epidemiology.

Biologics



TB screening prior to Biologics

- Screening prior to starting Biologics such as TNF-alpha inhibitors is **strongly recommended** by all international guidelines
- Variable inconsistent recommendations were found for screening before starting JAK inhibitors and interleukin inhibitors in US FDA- approved prescribing information.

Immunotherapies

- **TNF-alpha inhibitors:**

- Humira (Adalimumab),
- Enbrel (Etanercept)
- Remicade (Infliximab)

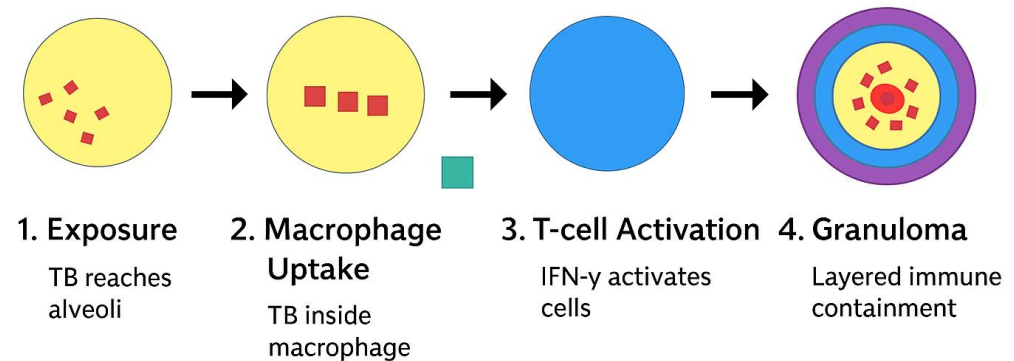
- **JAK inhibitors:**

- Rinvoq (Upadacitinib)
- Xeljanz (tofacitinib)

- **Interleukin inhibitors:**

- Stelara (Ustekinumab),
- Skyrizi (Risankizumab-rzaa)

How TB forms a granuloma



Digital diagram illustrating TB granuloma formation. (2024). How TB forms a granuloma [AI-generated image]. Microsoft Copilot.

What is the reason for testing?

- Contact investigation
- Targeted testing
- Immigration medical exam
- Employment/administrative testing
- Health Care Worker
- TB symptoms
- Abnormal imaging
- Incidental Lab Result
- Other reason

Determine patient's risk factors?

- Born in or traveled to a country where TB is common
- Exposure to someone with infectious TB disease
- Recent TB symptoms- cough lasting longer than 3 weeks, fever, night sweats, hemoptysis, weight loss, fatigue, lymphadenopathy
- Current/former employee or resident of a high-risk congregate setting (correctional facility, long-term residential care facility, shelter for persons experiencing homelessness, nursing facilities)

Diagnostic Tuberculosis Screening Tests

Tuberculosis Skin test (TST)

Interferon Gamma Release Assays (IGRAs):

- QuantiFERON TB Gold Plus (QFT-Plus)
- T-Spot

Group	Testing Strategy	Considerations
<p>Likely to be Infected High Risk of Progression (TST \geq 5mM)</p>	<p>Adults Acceptable: IGRA OR TST Consider dual testing where a positive result from either result would be considered positive</p> <p>Children \leq 5 years of age Preferred: TST Acceptable: IGRA OR TST</p> <p>Consider dual testing where a positive result from either would be considered positive¹</p>	<p>Prevalence of BCG vaccination Expertise of staff and/or laboratory Test availability Patient perceptions Staff perceptions Programmatic concerns</p>
<p>Likely to be Infected Low to Intermediate Risk of Progression (TST \geq 10mM)</p>	<p>Preferred: IGRA where available Acceptable: IGRA or TST</p>	
<p>Unlikely to be Infected (TST > 15mM)</p>	<p>Testing for LTBI is not recommended If necessary: Preferred: IGRA where available. Acceptable: Either IGRA OR TST</p> <p>For serial testing: Acceptable: Either IGRA OR TST</p> <p>Consider repeat or dual testing where a negative result from either would be considered negative²</p>	

Tuberculin Skin Test (TST)



TST Supplies

- Tubersol vial
- 1 ml Tuberculin syringe
- Alcohol pad



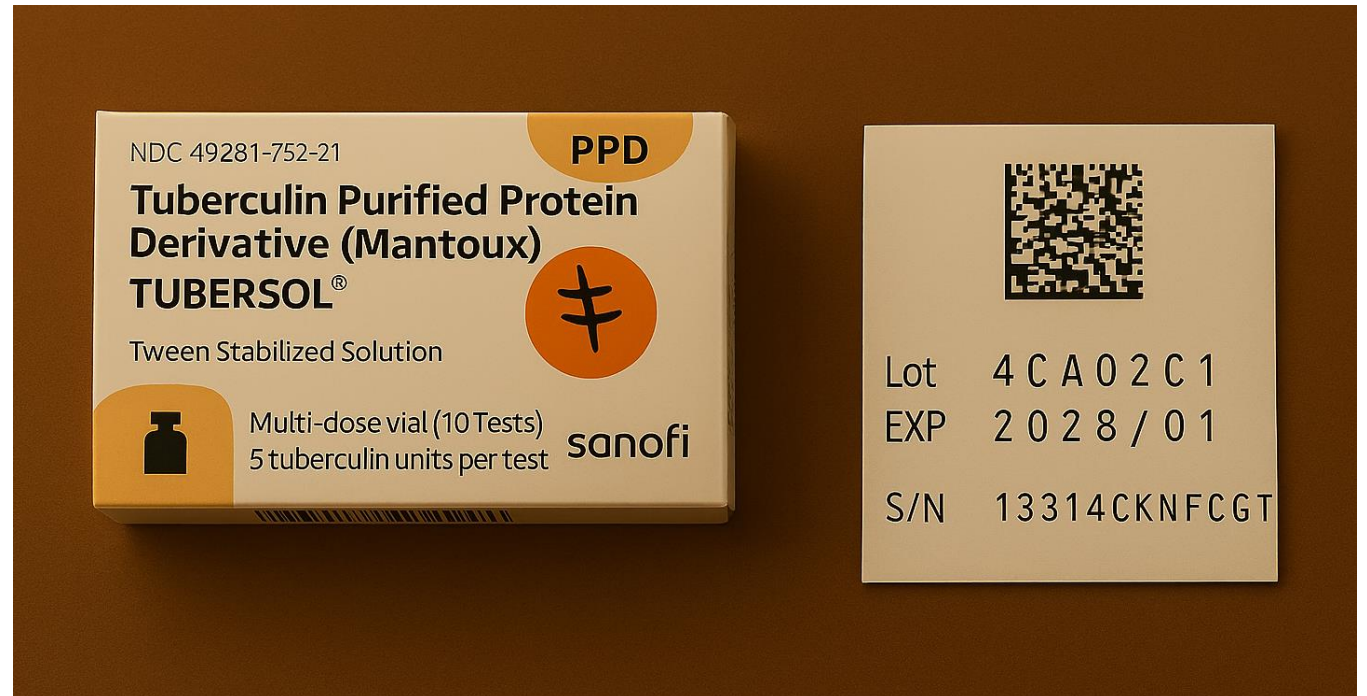
TST Administration

- 0.1 ml of 5 TU of purified protein derivative (ppd) intradermal
- **Induration** read in millimeters (mm) 48-72 hours after injection

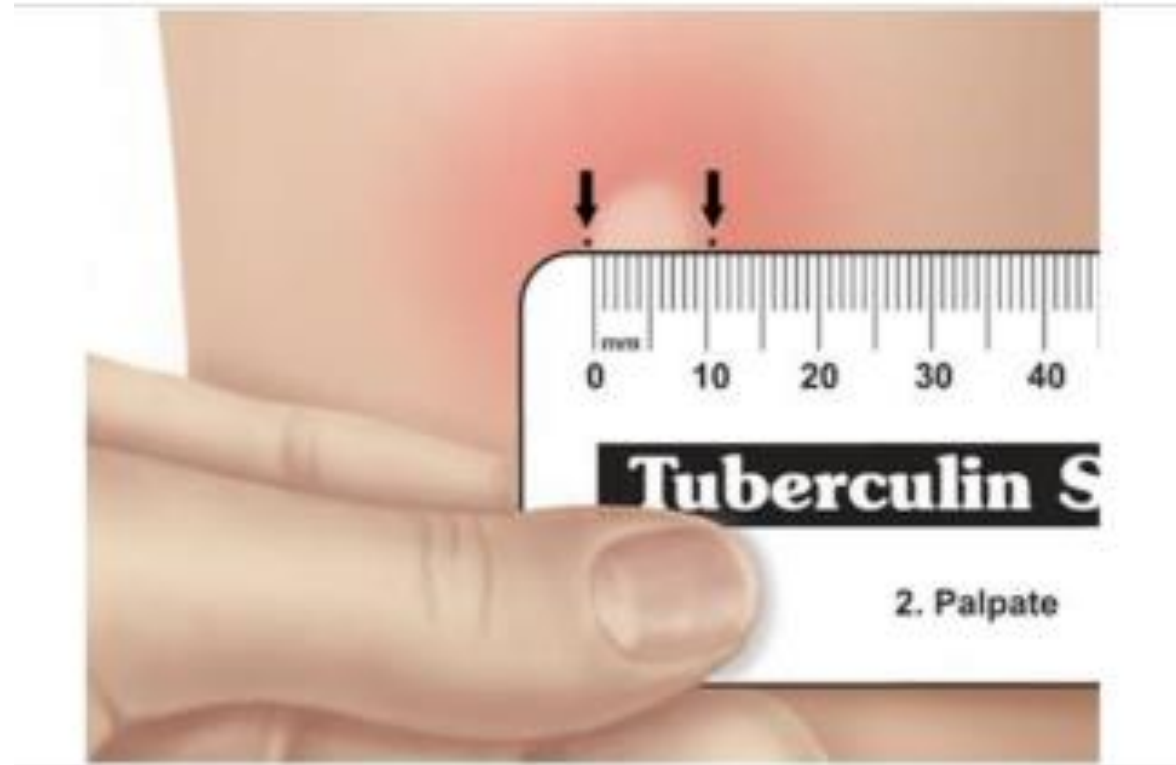


TST Documentation

- Reason for test
- TB symptoms
- date, time administered
- injection site location
- manufacturer
- lot number
- expiration date



Reading the TST



Measure induration, not erythema!

TST Interpretation

Induration 5 mm is positive in:

- HIV-positive persons
- recent contacts of a person being treated for active TB
- persons with fibrotic changes on CXR consistent with prior TB
- persons with organ transplants, immunosuppressed

TST Interpretation

Induration 10 mm is positive in:

- children less than 4 years of age, or children exposed to adults in high-risk categories
- recent immigrants from countries with a high prevalence of TB (arrived <5 years)
- residents and employees of high-risk congregate settings: correctional facilities, nursing homes, long-term care facilities, hospitals, health care facilities, homeless shelters, residential facilities
- mycobacteriology lab personnel
- persons with certain medical conditions that place them at a high risk
- injection drug users

TST Interpretation

Induration 15 mm is positive in:

persons with no known risk factors for TB

Interferon Gamma Release Assays (IGRAs)



Interferon Gamma Release Assays (IGRAs):

Two FDA Approved tests available:

- **QuantiFERON-TB Gold Plus (QFT-Plus)**
Approved in 2017
- **T-Spot**
Approved July 2008

Comparison of the QFT-Plus and the T-Spot

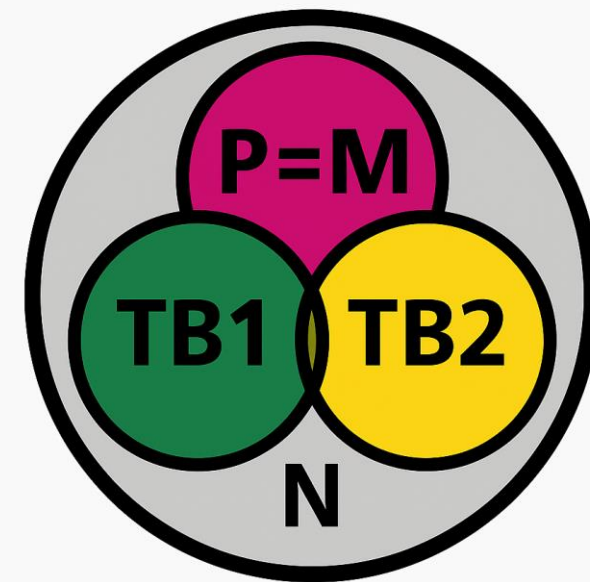
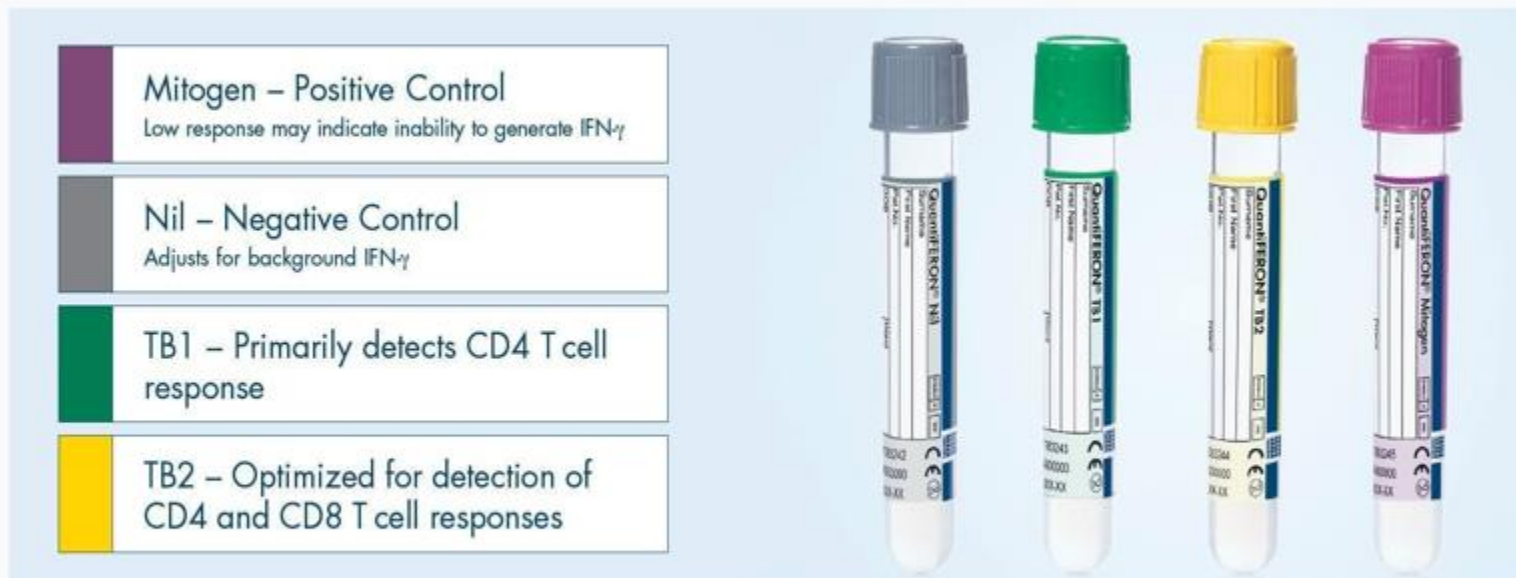
Comparison of the QFT-Plus and the T-Spot

Characteristics	QFT-Plus	T-Spot
Processing time	Within 16 hours (whole blood)	Within 8 to 32 hours (blood cells)
<i>M. tuberculosis</i> antigens	ESAT-6 and CFP-10	ESAT-6 and CFP-10
Measurement	IFN- γ concentration	Number of IFN- γ producing cells (spots)
Possible results	Positive, negative, indeterminate	Positive, negative, invalid, borderline

Comparison of the QFT-Plus and the T-Spot TB blood tests

QuantiFERON-TB Gold Plus (QFT)

QuantiFERON®-TB Gold Plus



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

QFT-Plus Interpretation Table

QFT-Plus result interpretation table

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% on Nil	Any	Any	Positive	<i>M.tuberculosis</i> infection likely
	Any	≥0.35 and ≥25% on Nil			
	<0.35 or ≥0.35 and <25% of Nil	<0.35 or ≥0.35 and <25% of Nil	≥0.50	Negative	<i>M.tuberculosis</i> infection NOT likely
	<0.35 or ≥0.35 and >25% of Nil	<0.35 or ≥0.35 and <25% of Nil	<0.50	Indeterminate	Likelihood of <i>M.tuberculosis</i> infection cannot be determined
>8.0	Any				

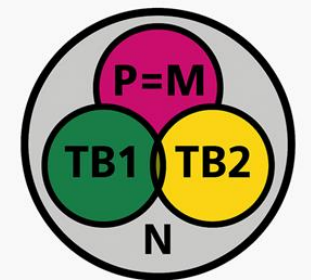


Image source: QIAGEN. (n.d.). QuantiFERON-TB test result interpretation [Table]. <https://www.qiagen.com/us/tb-testing/what-is-quantiferon/how-does-qft-work/quantiferon-tb-test-result-interpretation>

Practice

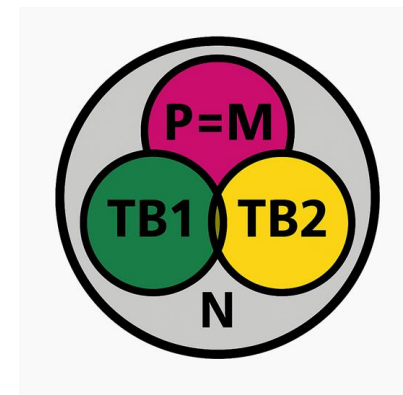
Interpret the following QuantiFERON results:

1.

QuantiFERON TB1 Ag Value ⁰¹	0.44
QuantiFERON TB2 Ag Value ⁰²	0.61
QuantiFERON Nil Value ⁰³	0.13
QuantiFERON Mitogen Value ⁰¹	>10.00

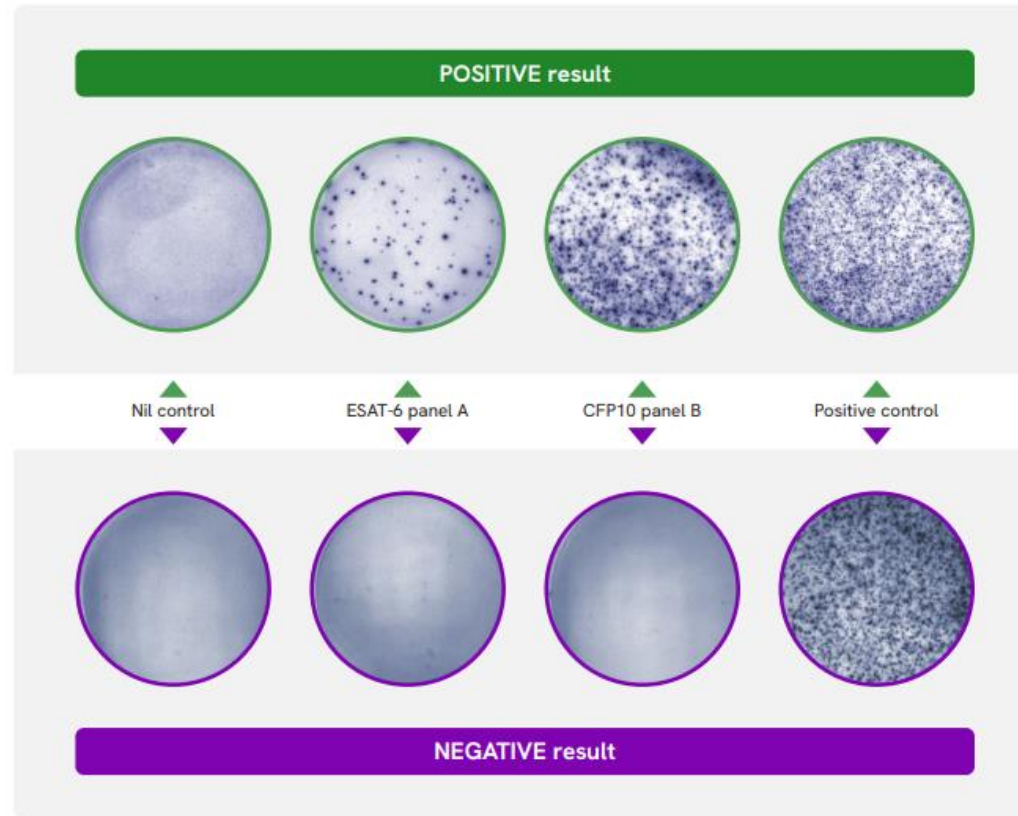
2.

Result, NIL (Ext) IU/ml	0.04
Result, Mitogen Minus Nil (Ext) IU/ml	7.70
Result, TB1 Antigen Minus Nil IU/ml	0.00
Result, TB2 Antigen Minus Nil IU/ml	0.00



Created by Woodberry (2026)

T-Spot



Spot counts in the nil control are deducted from those in the test panels. A positive result is when the spot counts in either Panel A or Panel B are greater than or equal to 6 more than the nil control.⁵

T-Spot interpretation

Interpreting IGRA results

Two IGRAs are approved and commercially available in the U.S: QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and T-SPOT®.TB test (T-Spot).

IGRA Test Result	QuantiFERON	T-Spot	Notes
Positive	TB-Nil is higher than or equal to 0.35 IU/mL	8 spots or more	Infection is likely in individuals with risk factors. Consider retesting in low- or no-risk individuals.
Negative	TB-Nil is lower than 0.35 IU/mL	4 spots or less	Infection is unlikely.
Indeterminate or invalid	High nil value or low mitogen value	High nil value or low mitogen value	Collect another specimen for retesting since these results cannot be interpreted. This occurs if controls do not perform as expected.
Borderline (not clear)	Not applicable	5, 6 or 7 spots	Uncertain likelihood of TB infection. Collect another specimen for retesting.

Practice

Interpret the following T-Spot results:

1.

F	PANEL A SPOT COUNT CORRECTED FOR NEG CONTROL	2
F	PANEL B SPOT COUNT CORRECTED FOR NEG CONTROL	3
F	NEGATIVE CONTROL	Passed
F	POSITIVE CONTROL	Passed

2.

F	PANEL A SPOT COUNT CORRECTED FOR NEG CONTROL	6
F	PANEL B SPOT COUNT CORRECTED FOR NEG CONTROL	5
F	NEGATIVE CONTROL	Passed
F	POSITIVE CONTROL	Passed

3.

F	PANEL A SPOT COUNT CORRECTED FOR NEG CONTROL	>50
F	PANEL B SPOT COUNT CORRECTED FOR NEG CONTROL	>50
F	NEGATIVE CONTROL	Passed
F	POSITIVE CONTROL	Passed

Antigens for Gamma-Release Assays

Tuberculosis complex	Antigens		Environmental strains	Antigens	
	ESAT	CFP		ESAT	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	-	-

Source: Heartland NTBC – Tuberculosis Screening & Testing presentation (n.d.). Retrieved from https://www.heartlandntbc.org/wp-content/uploads/2026/04/4_TB-Screening-and-Testing.pdf

TST vs. IGRAs: Comparison Table

Category	TST	IGRAs (QuantiFERON & T-Spot)
Type	In vivo	In vitro blood tests
Procedure	Intradermal injection; read at 48–72 hrs	Single blood draw; no return visit
Reading	Subjective (induration)	Objective, lab-based
BCG Effect	False positives possible	Not affected
NTM Effect	False positives possible	Limited interference
Cost	Lower	Higher
Other Factors	Reader skill, skin factors, placement	No boosting effect

Knowledge check 1

An 18-month-old boy presents to the clinic for evaluation after his mother is diagnosed with TB disease. He has no symptoms, CXR is normal, and he has a normal physical exam. Which diagnostic test will you order?

- A. TST
- B. IGRA
- C. Either one is fine

New Update for Testing in Children

- Both TST and IGRAs are acceptable
- IGRAs are **now recommended** for **children of all ages.**

preferred if history of BCG vaccination, or when a low likelihood of returning for TST reading.

recent studies support use in very young children without losing test accuracy, less false positives in children with prior BCG vaccination

Knowledge check 2

A 20-year-old female starting her new job at a daycare, tested for employment, presents to the clinic for evaluation after a 15 mm positive TST and normal CXR. She was born in the USA and has no risk factors for TB. What is your next **best course** of action?

- A. Start LTBI treatment
- B. Obtain an IGRA
- C. Do nothing because patient declined treatment
- D. Retest with another TST

Questions?

Thank you

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