The facts about **TUBERCULOSIS (TB) SCREENING**

A resource guide for healthcare professionals

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ABOUT THIS RESOURCE GUIDE

THE PURPOSE OF THIS BROCHURE IS TO INCREASE AWARENESS OF SPECIFIC SCREENING RECOMMENDATIONS FOR TB IN HIGH-RISK PATIENTS. THE FOLLOWING INFORMATION IS DESIGNED TO ANSWER QUESTIONS AND REVIEW THE SCREENING PROCESS.

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WHY, WHO, AND HOW

Q. Why are there recommendations for TB screening for certain high-risk populations?

A. Globally, TB is a common and often deadly infectious disease.[1] The majority of individuals infected with *Mycobacterium tuberculosis (M. tuberculosis)* have latent TB infection (LTBI) rather than active TB disease. As such, identification and treatment of persons with LTBI has been essential in controlling the progression to active TB.[1,2] The Centers for Disease Control and Prevention (CDC) and the American Thoracic Society (ATS) have identified specific populations who are at risk of developing TB and would benefit from treatment of LTBI, if detected.[2] The CDC and ATS recommend tests for LTBI in these high-risk populations and appropriate follow-up and treatment when indicated.

Q. Who is at risk?

A. Individuals with any of the following are considered to be at risk[3,4]:

> Infection with human immunodeficiency virus (HIV)
> Close contact with individuals with active TB
> Abnormal chest radiographic findings consistent with previous TB
> A tuberculin skin test (TST) that converted to positive within the past year
> History of organ transplant
> Receiving immunosuppressive therapy (prednisone equivalent of at least 15 mg/day for at least 1 month), including treatment with tumor necrosis factor (TNF) antagonists
> Having been born in a country where TB is prevalent
> Recently arrived (within 5 years) from a country where TB is highly prevalent
> Substance abuse (injection or noninjection)
> Residence or employment in a congregate setting (eg, jail or prison, nursing home or other long-term facilities for the elderly, hospital or other health care facility, residential facility for patients with acquired immunodeficiency syndrome, and homeless shelter)
> Mycobacteriology laboratory personnel
> Having certain medical conditions (eg, silicosis, diabetes mellitus, chronic renal failure, certain cancers and hematologic disorders, weight loss of 10% or more of ideal body weight, gastrectomy and jejunoileal bypass)
> Children <4 years of age; or infants, children, and adolescents exposed to adults in high-risk categories

Q. Is TB screening recommended with use of all TNF antagonists?

A. Yes. Evidence indicates that development of active TB can be a risk with the use of any agent that blocks TNF-α.[4,5] As such, all patients should be screened for LTBI prior to initiating a TNF antagonist.

Q. How do I go about the screening and treatment process? Are there guidelines?

A. Yes, current guidelines are available. The CDC recommendations for screening, diagnosis, and treatment of LTBI and TB in candidates for TNF antagonist therapy[4] have been included as a reference at the end of this brochure. Treatment for LTBI prior to initiation of any TNF antagonist should be considered in patients identified as being at risk for development of active TB, including those with positive response to tuberculin skin testing, TB blood tests, and/or chest x-ray.[3,4,6]

LATENT VERSUS ACTIVE TUBERCULOSIS

Q. What is LTBI?

A. Latent TB infection occurs when an individual is infected with *M. tuberculosis*, but the mycobacteria is contained by an effective immune response.[6] The mycobacteria remain alive but dormant. The infection is asymptomatic and not communicable. It is possible for patients to develop active TB if they don't receive treatment. The risk of evolving to active TB depends on the ability of the immune system to control the mycobacteria replication and may occur at any time (from weeks to years) after the infection.

Q. How does LTBI differ from active TB?

A. A patient with LTBI has no symptoms, does not feel sick, cannot spread TB to others, usually has a positive TST or TB blood test, and may have either a normal chest x-ray or radiographic signs of LTBI,[3,6] such as calcifications or pleural thickening.[3] Conversely, patients with active TB present with symptoms dependent on where in the body the TB mycobacteria are growing.[6] Because TB mycobacteria usually replicate in the lungs, they may cause symptoms such as severe and persistent cough, pain in the chest, and coughing up of blood or sputum. Other symptoms include weakness or fatigue, weight loss, loss of appetite, chills, fever, and night sweats. Patients with active pulmonary TB may have an abnormal chest x-ray, acid-fast bacilli in sputum, and/or positive sputum culture. Extrapulmonary signs and symptoms may be present and will depend on the organ system affected,[6] such as lymphnodes, pleura, upper airways, genitourinary tract, bones and joints, central nervous system, gastrointestinal tract, pericardium, etc.[7]

Q. Will both LTBI and active TB show up on a TST or TB blood test (eg, interferon-gamma release assay [IGRA])?

A. Evaluation of LTBI consists of a variety of assessments, including medical history and ruling out active TB, as well as diagnostic tests, such as TSTs and/or TB blood tests (eg, IGRA) and/or chest x-rays.[6] Latent TB infection usually produces a positive TST or TB blood test, and treatment should be considered to prevent progression to active disease. Although TSTs and TB blood tests may also be positive in patients with active TB, neither test can distinguish LTBI from active TB.[8] Additionally, these tests are not used to definitively diagnose active TB. Therefore, it is both prudent and practical to further investigate and determine whether the patient has active TB and treat accordingly.

SYMPTOMS OF TUBERCULOSIS

Q. What should I tell my patients who are receiving TNF antagonist therapy about TB?

A. Physicians who prescribe any TNF antagonist therapy should educate their patients about the symptoms of TB.[3] Your patients should be counseled to report any symptoms of active TB, including*:

Pulmonary symptoms of TB[6]
> A cough that lasts 3 weeks or longer
> Pain in the chest
> Coughing up blood or sputum (phlegm from deep inside the lungs)

Other symptoms of TB[6]
> Weakness or fatigue
> Weight loss
> No appetite
> Chills
> Fever
> Sweating at night

Extrapulmonary symptoms of TB[6]
> Depends on the organ system affected

*This list is not meant to be comprehensive.

TREATING TUBERCULOSIS

Q. Who should be treated for TB?

A. Although the treatment regimens differ for active TB and LTBI, both individuals with active disease, as well as those with LTBI who are at high risk of developing TB, should be treated according to appropriate TB guidelines and/or standards of care.[6]

Q. If LTBI is dormant, why is it necessary to treat it?

A. While many individuals infected with *M. tuberculosis* will have LTBI and never develop active TB disease, those with a compromised immune system may not be able to contain the mycobacteria and are at risk of progression to active TB.[6] Therefore, appropriate treatment is recommended for individuals who have LTBI and fall into a high-risk group.[4]

Q. Which high-risk groups should be treated for LTBI?

A. The following groups have the highest risk for developing active TB if they are infected with *M. tuberculosis* and should be treated if their reaction to the TST* is ≥5 mm[3]:

> HIV-infected individuals
> Those who have had contact with a person with active TB
> Those who have had fibrotic changes on a chest x-ray consistent with prior TB
> Organ transplant patients
> Those who are immunosuppressed for another reason, such as individuals receiving immunosuppressive therapy (prednisone equivalent of at least 15 mg/day for at least 1 month), including treatment with TNF antagonists

Q. Are there other groups who should receive treatment for LTBI?

A. The following groups have an increased probability of recent infection or have other clinical conditions that increase the risk for progression to active TB. Treatment should be considered in these individuals if their reaction to the TST* is ≥10 mm[3]:

> Recent immigrants (less than 5 years) from high-prevalence countries
> Injection drug users
> Residents and employees of high-risk congregate settings (eg, correctional facilities, homeless shelters, residential facilities for patients with acquired immunodeficiency syndrome (AIDS), and healthcare facilities)
> Mycobacteriology laboratory personnel
> Individuals with clinical conditions that put them at risk (eg, silicosis, diabetes mellitus, chronic renal failure, leukemia and lymphoma, cancer of the head or neck and lung, weight loss of 10% or more of ideal body weight, gastrectomy, jejunoileal bypass)
> Children younger than 4 years
> Infants, children, and adolescents exposed to adults in high-risk categories

Q. How is LTBI treated?

A. Latent TB infection is typically treated† with a regimen of isoniazid for 6 to 9 months or rifampin for 4 months.[3] A new 12-dose regimen, including a combination of isoniazid and rifapentine, given weekly under directly observed therapy, may also be an option for certain patient populations.[9] Because of the risk of severe hepatoxicity, the use of rifampin and pyrazinamide together is no longer recommended for treatment of LTBI.[10]

*See Getting Down to Basics–Tuberculin Skin Testing on page 9 for more information.

†Refer to the CDC or ATS for more information on treating LTBI.

PUTTING TUMOR NECROSIS FACTOR ANTAGONISTS IN PERSPECTIVE

Q. What is the normal biologic role of TNF-α?

A. TNF-α is a naturally occurring proinflammatory cytokine involved in normal cell-mediated immune response against disease, including mycobacterial infection, such as TB.[11]

Q. How do TNF antagonists work in treating chronic inflammatory diseases?

A. Elevated levels of TNF-α play a key role in stimulating the pathologic inflammation underlying chronic inflammatory diseases such as rheumatoid arthritis (RA), juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and psoriasis.[12,13]

Q. What is the role of TNF-α in the immune response to TB?

A. Tumor necrosis factor plays an important role in protection against murine *M. tuberculosis* infection.[14] In vitro and in vivo studies demonstrate that TNF-α provides protective mechanisms in macrophages against *M. tuberculosis*. The studies further show that the absence of TNF-α has a detrimental effect on the ability of granulomas to contain and restrict the replication of tubercle bacilli.

Q. Why is screening for TB necessary with TNF antagonist therapy?

A. Any immunosuppressive agent, including TNF antagonists, can potentially result in reactivation of LTBI or progression of recently acquired mycobacterial infection to active TB.[2,4,11,15,16] For this reason, the CDC and other experts, including the Infectious Diseases Society of America and ATS, recommend screening for LTBI. They also recommend following through with appropriate management if infection is detected before initiating therapy with any TNF antagonist.

Q. Is screening important in managing the risk of TB?

A. Yes. Tuberculosis screening prior to initiation of TNF antagonist therapy has resulted in a decreased rate of progression of latent TB to active TB.[15,17] For example, in European clinical trials, implementation of TB screening prior to initiation of TNF antagonist therapy for the treatment of RA resulted in a reduction in the incidence rates of TB in the clinical trials.[17,18] Patients receiving TNF antagonist therapies should be monitored for infections, including signs and symptoms of active TB, before, during and after treatment.[4,19,20] Patients who have negative TST results should be monitored, as active TB has developed in these patients as well.[4]

GETTING DOWN TO BASICS – TUBERCULIN SKIN TESTING

Q. What is the standard TB skin test?

A. The Mantoux test, or TST, or Purified Protein Derivative (PPD) test is a method used globally. It contains a tuberculin protein antigen.[20,21] The test is used to aid diagnosis of TB infection in persons at increased risk of developing active disease. Tuberculin skin test results should only be administered, read, and interpreted by a trained healthcare professional.[22] For your reference, you will find complete instructions on preparing and administering the test and interpreting the results in the back of this brochure. You can receive training information from the National CDC Tuberculosis Elimination Web site at **www.cdc.gov/tb**. You can also request a Mantoux TST Training Materials Kit from the CDC National Prevention Information Network at **www.cdcnpin.org**.

Q. I am not trained to perform the TST. Where can I send my patients for testing?

A. Some pulmonologists and infectious disease physicians, as well as specialized nurses, have been trained and routinely do TSTs. Patients can be tested at various local venues, eg, health fairs at hospitals, local Red Cross centers, free clinics, employee health departments, etc. For more information, visit the National CDC Tuberculosis Elimination Web site (**www.cdc.gov/tb**) or your health care system directory.

GETTING DOWN TO BASICS – INTERFERON-GAMMA RELEASE ASSAYS

As an alternative to TSTs, interferon-gamma release assays are now available to aid in the detection of *M. tuberculosis*.

Q. What are IGRAs?

A. Interferon-gamma release assays are whole-blood tests that can aid in diagnosing *M. tuberculosis* infection.[23] They do not help differentiate LTBI from active tuberculosis disease. You will find general instructions on administering the test and interpreting the results in the back of this brochure for your reference.

Q. How do IGRAs work?

A. Interferon-gamma release assays measure a person's immune reactivity to *M. tuberculosis*.[23] White blood cells from most persons that have been infected with *M. tuberculosis* will release interferon-gamma (IFN-γ) when mixed with antigens (substances that can produce an immune response) derived from *M. tuberculosis*.

To conduct the tests, fresh blood samples are mixed with antigens and controls. The antigens, testing methods, and interpretation criteria for IGRAs differ. For more information, visit the National CDC Tuberculosis Elimination Web site (**www.cdc.gov/tb**).

Q. What are the advantages of IGRAs?

A.
> Only one patient visit is required in order to conduct the test[23]
> Results can be available within 24 hours
> Does not boost responses measured by subsequent tests
> Prior Bacille Calmette-Guerin (BCG) vaccination does not cause a false-positive IGRA test result

Q. What are the disadvantages and limitations of IGRAs?

A.
> Blood samples must be processed within 8–30 hours after collection while white blood cells are still viable[23]
> Factors that decrease the accuracy of the test include errors in:
  – Collecting blood samples
  – Transporting blood samples
  – Running and interpreting the test
> Limited data on the use of IGRAs to predict who will progress to TB disease in the future
> Limited data on the use of IGRAs for:
  – Children younger than 5 years of age
  – Persons recently exposed to *M. tuberculosis*
  – Immunocompromised persons, such as those using TNF antagonists
  – Serial testing
> Tests may be expensive

Q. When should IGRAs be used?

A. Interferon-gamma release assays can be used in place of[23] or in addition to[24] (depending on local guidelines) TST in all situations in which CDC recommends TST as an aid in diagnosing *M. tuberculosis* infection with preferences and considerations noted below.[23] This includes contact investigations, testing during pregnancy, and screening of health care workers and others undergoing serial evaluation for *M. tuberculosis* infection.

Despite the indication of a preference, use of the alternative test is acceptable medical and public health practice. Caution in interpretation should be used when testing certain populations because of limited data on the use of IGRAs (see Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection, United States).

> As with TST, interferon-gamma release assays generally should not be used for testing persons who have a low risk of infection and a low risk of disease due to *M. tuberculosis*

> Routine testing with both TST and IGRA is not recommended. Exceptions where both tests might be useful can be found in the Interferon-Gamma Release Assays Fact Sheet

> Populations in which IGRAs are preferred for testing:
  – Persons who have received BCG (either as a vaccine or for cancer therapy)
  – Persons from groups that historically have poor rates of return for TST reading

> Due to limited data on the use of IGRAs in children under the age of 5, the TST is preferred in this population

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QUICK REFERENCES

TUBERCULOSIS SCREENING CHECKLIST

This is a clinical practice tool to assist healthcare professionals with evaluating patients for the risk of developing active TB before, during and after therapy with a TNF antagonist. Consult your local TB guidelines for comprehensive information regarding TB screening and treatment recommendations in your area.

Please mark or fill out correspondingly

_____ _____/_____/_____

Name of Patient Date of Birth

A **Does the patient currently have any symptoms consistent with active TB such as:**

	Yes	No	Comments
Cough ≥3 weeks	☐	☐	
Haemoptysis or sputum production	☐	☐	
Chest pain	☐	☐	
Fever	☐	☐	
Night sweats	☐	☐	
Weakness or fatigue	☐	☐	
Anorexia	☐	☐	
Weight loss ≥10% ideal body weight	☐	☐	

If one or more of the above is answered with "YES", active TB needs to be completely ruled out before initiation of therapy

B **Immunosuppressive therapy (eg, steroids, methotrexate, biologics) may increase the risk of active TB in patients with latent disease. Does the patient have this or other risk factors for activation of latent TB including:**

	Yes	No	Comments
Born or lived in TB endemic area	☐	☐	
Recent contact with active TB case	☐	☐	
Resident or employee of a high risk congregate setting	☐	☐	
Mycobacteriology laboratory personnel	☐	☐	
Child or adolescent exposed to adult in high risk category	☐	☐	
Immunosuppression due to treatment	☐	☐	
Illicit drug use	☐	☐	
Diabetes	☐	☐	
Silicosis	☐	☐	
Organ transplant	☐	☐	
Chronic renal failure	☐	☐	
Gastrectomy or jejunoileal bypass	☐	☐	
Head or neck cancer, leukemia, lymphoma	☐	☐	
Immunosuppression due to another condition	☐	☐	

C **Results of Chest X-ray Screening for TB:**

	Yes	No	Comments
Normal	☐	☐	
Abnormal	☐	☐	
Latent TB	☐	☐	
Others (please specify test and normal/abnormal)	☐	☐	
Date of Chest X-ray			_____/_____/_____

Results of the Tuberculin Skin Test:

Date of TST application	_____/_____/_____
Date of TST reading	_____/_____/_____
Induration at TST site (in mm)	

Results of the Second Tuberculin Skin Test (if appropriate):

Date of TST application	_____/_____/_____
Date of TST reading	_____/_____/_____
Induration at TST site (in mm)	

Results of the Interferon Gamma Release Assay:

Type of assay performed	
Date of assay performed	_____/_____/_____
Assay measurement/Interpretation	_____/_____

D **If the patient presents a positive medical history and/or TST shows an induration of ≥5 mm and/or IGRA results are positive and/or the chest X-ray shows signs of LTBI, respective LTBI treatment should be initiated.**

TST or IGRA	Chest X-ray	LTBI Treatment
<5 mm or Negative	Normal	Not recommended*
≥5 mm or Positive	Abnormal	Medical consultation with Expert recommended
<5 mm or Negative	LTBI signs	Recommended
≥5 mm or Positive	Normal	Recommended
<5 mm or Positive	Normal	Recommended

Prescribed LTBI treatment regimen (drug/dose): _____/_____

Date of LTBI treatment initiation _____/_____/_____

* Medical consultation with Expert recommended in patients with a negative test but having risk factors for TB infection.

E **Does the patient have hepatic disease or any other risk factors for hepatic disease, which may require additional monitoring with LTBI treatment such as:**

	Yes	No	Comments
Underlying liver disease (eg, hepatitis B or C, history of heavy alcohol consumption)	☐	☐	
Pregnant or postpartum (within 3 months of delivery)	☐	☐	
Other risk factors for chronic liver disease	☐	☐	

_____ _____/_____/_____

Name of Doctor Date of evaluation

Abbreviations: IGRA, interferon gamma release assay; LTBI, latent tuberculosis infection; TB, tuberculosis; TNF, tumour necrosis factor; TST, tuberculin skin test.

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CENTERS FOR DISEASE CONTROL AND PREVENTION RECOMMENDATIONS

Centers for Disease Control and Prevention (CDC) recommendations for screening, diagnosis, and treatment of latent tuberculosis infection (LTBI) and tuberculosis (TB) in patients administered or scheduled to receive tumor necrosis factor (TNF) antagonists[1]

- > Screen patients for risk factors for *Mycobacterium tuberculosis (M. tuberculosis)* and test them for infection before initiating immunosuppressive therapies, including TNF antagonists
  - – Risk factors include birth in a country where TB is prevalent or history of any of the following: residence in a congregate setting (eg, jail or prison, homeless shelter, or chronic-care facility), positive tuberculin skin test (TST) result, substance abuse (injection or noninjection), healthcare employment in settings with TB patients, and chest radiographic findings consistent with previous TB
- > Diagnose and treat LTBI and TB in accordance with published guidelines
- > In patients who are immunocompromised (eg, because of therapy or other medical conditions), interpret a TST induration of ≥5 mm as a positive result and evidence of *M. tuberculosis* infection
- > Interpret a TST induration of <5 mm as a negative result but not an exclusion for *M. tuberculosis* infection
  - – Results from control-antigen skin testing (eg, *Candida*) do not alter the interpretation of negative TST result
- > Test to exclude TB before starting treatment for LTBI
- > Start treatment for LTBI before commencing TNF antagonist therapy, preferably with 9 months of daily isoniazid
- > Consider treating for LTBI in patients who have negative TST results but whose epidemiologic and clinical circumstances suggest a probability of LTBI
- > Pursue TB as a potential cause of febrile or respiratory illness in immunocompromised patients, including those receiving TNF antagonists
- > Consider postponing TNF antagonist therapy until the conclusion of treatment for LTBI or TB disease

Reference: Centers for Disease Control and Prevention. Tuberculosis associated with blocking agents against tumor necrosis factor-alpha—California; 2002–2003. *MMWR*. 2004;53:683-686.

CONTACT INFORMATION

The current recommendations for targeted testing for tuberculosis (TB) and treatment regimens for latent TB infection have been endorsed by the Centers for Disease Control and Prevention, the American Thoracic Society, and the Infectious Diseases Society of America.

Contact information for these 3 important national organizations:

TB information—National organizations

Centers for Disease Control and Prevention, Division of Tuberculosis Elimination
> 800-CDC-INFO
> www.cdc.gov/tb

American Thoracic Society
> 212-315-8600
> www.thoracic.org

Infectious Diseases Society of America
> 703-299-0200
> www.idsociety.org

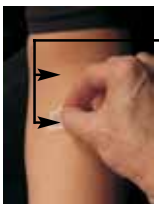
TUBERCULOSIS TEST INSTRUCTIONS

Mantoux Tuberculin Skin Test

1. Administration

For each patient, conduct a risk assessment that takes into consideration recent exposure, clinical conditions that increase risk for tuberculosis (TB) disease if infected, and the program's capacity to deliver treatment for latent TB infection to determine if the skin test should be administered. All testing activities should be accompanied by a plan for the necessary follow-up medical evaluation and treatment.

1. Locate and clean injection site



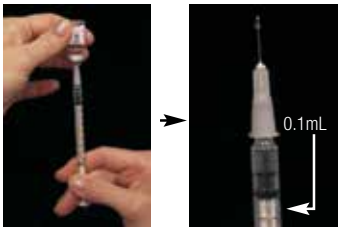
2 to 4 inches (~5-10 centimeters) below elbow joint

> Place forearm palm side up on a firm, well-lit surface

> Select an area free of barriers to placing and reading (eg, scars, sores)

> Clean the area with an alcohol swab

2. Prepare syringe



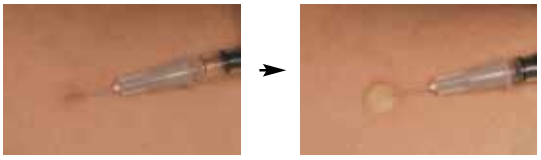
> Check expiration date on vial and ensure vial contains tuberculin (5 TU per 0.1 mL)

> Use a single-dose tuberculin syringe with a ¼-to ½-inch, 27-gauge needle with a short bevel

> Fill the syringe with 0.1 mL of tuberculin

3. Inject tuberculin

> Insert slowly, bevel up, at a 5- to 15-degree angle



> Needle bevel can be seen just below skin surface

> After injection, a tense, pale wheal should appear over the needle

4. Check skin test

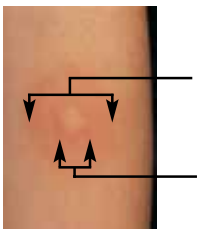
> Wheal should be 6 to 10 mm in diameter. If not, repeat test at a site at least 2 inches (~5 centimeters) away from original site

5. Record information

> Record all the information required for documentation by your institution (eg, date and time of test administration, injection-site location, lot number of tuberculin)

2. Reading

The skin test should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will probably need to be rescheduled for another skin test.



1. Inspect site

> Visually inspect site under good light

Erythema (reddening of the skin) — do not measure

Induration (hard, dense, raised formation)

2. Palpate induration

> Use fingertips to find margins of induration

3. Mark induration

> Use fingertip as a guide for marking widest edges of induration across forearm

4. Measure induration (not erythema)

> Place "0" ruler line inside left dot edge

> Read ruler line inside right dot edge (use lower measurement if between two gradations on mm scale)

5. Record information

> If no induration, record as 0 mm

> Do not record as "positive" or "negative"

> Only record measurement in millimeters (mm)

Adapted from the CDC NCHSTP Office of Communications' Mantoux Tuberculin Skin Test Wall Chart 2004.

TUBERCULOSIS TEST INSTRUCTIONS

Mantoux Tuberculin Skin Test

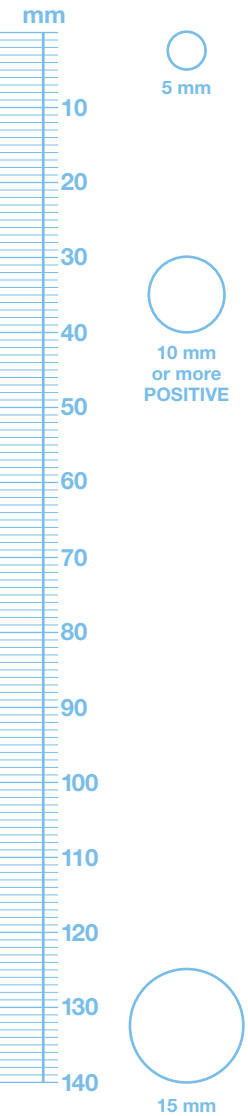
3. Interpretation

Skin test interpretation depends on 2 factors:

> Measurement in millimeters (mm) of the induration

> Person's risk of being infected with TB and progression to disease if infected

The 3 cut points to the left should be used to determine whether the skin test reaction is positive. A person with a positive reaction should be referred for a medical evaluation for latent TB infection and appropriate follow-up and treatment if necessary.
A measurement of 0 mm or a measurement below the defined cut point for each category is considered *negative*.



INDURATION OF ≥5 MM IS CONSIDERED POSITIVE IN

> Human immunodeficiency virus (HIV)–infected persons

> Recent contacts of TB case patients

> Persons with fibrotic changes on chest radiograph consistent with prior TB

> Persons with organ transplants and other immunosuppressed patients (eg, receiving the equivalent of ≥15 mg/d of prednisone for 1 month or more), patients receiving TNF blockers

INDURATION OF ≥10 MM IS CONSIDERED POSITIVE IN

> Recent immigrants (ie, within the last 5 years) from countries with a high prevalence of TB

> Injection drug users

> Residents and employees* of the following high-risk congregate settings:
- Prisons and jails
- Nursing homes and other long-term facilities for the elderly
- Hospitals and other healthcare facilities
- Residential facilities for patients with acquired immunodeficiency syndrome (AIDS)
- Homeless shelters

> Mycobacteriology laboratory personnel

> Persons with the following clinical conditions that place them at high risk:
- Silicosis
- Diabetes mellitus
- Chronic renal failure
- Some hematologic disorders (eg, leukemias and lymphomas)
- Other specific malignancies (eg, carcinoma of the head, neck, or lung)
- Weight loss of ≥10% of ideal body weight
- Gastrectomy
- Jejunoileal bypass

> Children less than 5 years of age

> Infants, children, and adolescents exposed to adults at high risk for developing active TB

INDURATION OF ≥15 MM IS CONSIDERED POSITIVE IN

> Persons with no known risk factors for TB

*For employees who are otherwise at low risk for TB and who are tested as part of an infection control screening program at the start of employment, a reaction of ≥15 mm is considered positive. Some healthcare workers participating in an infection control screening program may have had an induration >0 mm that was considered negative at baseline. If these healthcare workers have an increase in induration size upon subsequent testing, they should be referred for further evaluation.

Note: Reliable administration and reading of the tuberculin skin test involves standardization of procedures, training, supervision, and practice. Always follow your institution's policies and procedures regarding infection control, evaluation, and referral. Also remember to provide culturally appropriate patient education before and after administration, reading, and interpretation of the skin test.

For more information on tuberculosis, visit **www.cdc.gov/tb** and **www.findtbresources.org**.

Adapted from the CDC NCHSTP Office of Communications' Mantoux Tuberculin Skin Test Wall Chart 2004.

TUBERCULOSIS TEST INSTRUCTIONS

Interferon-Gamma Release Assays

1. Administration

Confirm arrangements for testing in a qualified laboratory, and arrange for delivery of the blood sample to the laboratory in the time the laboratory specifies to ensure testing of samples with viable blood cells.

> Draw a blood sample from the patient according to the test manufacturer's instructions
> Schedule a follow-up appointment for the patient to receive test results
> Based on test results, provide follow-up evaluation and treatment as needed

2. Interpretation

> Interpretation based on the amount of interferon-gamma (INF-γ) that is released or on the number of cells that release INF-γ
> Both the standard qualitative test interpretation (positive, negative, or indeterminate) and the quantitative assay measurements (Nil, TB, and Mitogen concentrations or spot counts) should be reported
> As with the tuberculin skin tests, interferon gamma release assays should be used as an aid in diagnosing infection with *M. tuberculosis*
  – Positive test result: *M. tuberculosis* infection is likely
  – Negative test result: *M. tuberculosis* infection is unlikely
  – Indeterminate test result: uncertain likelihood of *M. tuberculosis* infection
  – Borderline test result (T-Spot only): uncertain likelihood of *M. tuberculosis* infection
> Diagnosis of LTBI requires that TB diagnosis be excluded by medical evaluation, including:
  – Checking for signs and symptoms suggestive of TB disease
  – Chest radiograph
  – Examination of sputum or other clinical samples for the presence of *M. tuberculosis*, when indicated
  – Considerations of epidemiological and historical information

For more information on tuberculosis, visit **www.cdc.gov/tb** and **www.findtbresources.org**.

Reference: Centers for Disease Control and Prevention. Interferon-gamma release assays (IGRAs) –blood tests for TB infection [fact sheet]. Available at: http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm. Accessed March 5, 2012.

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