II. Mantoux Tuberculin Skin Testing and Interferon Gamma Release Assays (IGRAS)

The Mantoux tuberculin skin test (TST) and interferon gamma release assays (IGRAs) are tests for the presence of infection with *Mycobacterium tuberculosis*. These tests should be performed in people who are at risk of infection with *M. tuberculosis* and/or at high risk for progression to active TB if infected. These tests have several limitations:

- They do not distinguish between latent tuberculosis infection (LTBI) and active TB disease
- Both false-negative (negative results in people truly infected with *M. tuberculosis*) and false-positive (positive results in people not infected with *M. tuberculosis*) results may occur
- They have issues with test-retest reliability, so if the same person is tested on more than one occasion, a different result may be obtained despite no change in TB infection. These issues arise from multiple sources, including reader variability (TST), biologic variability, specimen handling (IGRAs), and laboratory variability (IGRAs)
- Testing of low-risk populations is likely to yield many false-positive results, resulting in unnecessary treatment

At the time of this writing, two IGRAs are commercially available in North Carolina: the QuantiFERON Plus® and T-SPOT.TB®. For most purposes these tests are roughly equivalent, and either can be used when an IGRA is indicated.

While either a TST or an IGRA may be used to screen for latent TB, in certain situations one test may be preferred. The decision to perform a TST or an IGRA will depend on several factors, including cost, logistics, and local test availability. The table below provides general guidance as to which type of test would be preferred in different clinical situations.

Situation	Preferred test
Person 2 years or older born outside the U.S.	IGRA
Person known to have received BCG (vaccine or bladder cancer treatment)	IGRA
Person unlikely to return for TST reading	IGRA
Child under 2 years old	TST*
Person at low risk for TB infection (e.g. administrative screening)	IGRA
Testing in settings where the TST is infrequently performed	IGRA

* Emerging evidence suggests that IGRAs may reduce false-positive tests among BCG-vaccinated children, so an IGRA is a reasonable alternative for such children

Mantoux skin testing

The Mantoux tuberculin skin test is the only skin test recommended for latent TB screening by NC TB Control.

- The TST should be repeated when interpretations are ambiguous or inconclusive.
- Healthcare personnel responsible for placing and reading TSTs should receive training about TB transmission, pathogenesis, testing and treatment of active tuberculosis and latent TB infection. Practical training on proper placement and reading of TSTs should also be provided, including hands-on experience. Facilities that place or read TSTs should have written policies describing the required training and documentation that training has been provided. As an example, the CDC Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005 (https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e) document suggests that healthcare personnel should be observed placing and reading at least 10 positive TST's and 10 negative TST's. A copy of the Quality Control (QC) procedural observation checklists (Appendix F) from this document can be found at the end of this chapter

A. Administration

1. Use 0.1 cc of 5TU Purified Protein Derivative (PPD)

2. Use tuberculin syringe with a 3/8-inch, 26-27-gauge needle

3. Clean volar(flexor) surface of left forearm approximately 2-4 inches below the elbow; allow to dry completely

4. Give intradermal injection with needle bevel upward; a tense, white wheal of 6-10mm in diameter should be produced when the TST is accurately administered.

5. Repeat injection at another site at least 2 inches away if part of the antigen is lost or the injection is given too deeply. Specify location of the retest in the record.

6. Follow your agency blood borne pathogens guidelines for standard precautions

7. Tuberculin solution can be adversely affected by exposure to light or temperature extremes. For storage and handling, **see Chapter VII., C. 1.**

8. Administer TST prior to or simultaneously with live virus vaccines, e.g., measles, mumps, rubella, smallpox and chicken pox. If the TST is not given simultaneously, wait 4-6 weeks after these vaccines before giving the TST.

9. Immediate hypersensitivity reactions to tuberculin (redness, swelling, pruritus, heat) can occur shortly after

injection and usually disappear within 24 hours. This has no clinical significance and is not considered a positive test.

10. There is no contraindication to repeating a TST that was previously positive; a TST should be administered if there is no documentation of a prior mm reading.

11. TST is both safe and reliable throughout the course of pregnancy

12. TST is safe for infants of any age. A negative reading is considered valid for infants at least 6 months of age or older (adjust age for premature infants). A positive reading is valid at any age.

13. TST is not contraindicated for individuals who have been vaccinated with BCG, but as noted above IGRAs are preferred for most such individuals

B. Reading

1. Read TST 48-72 hours after placement, preferably at 72 hours

   a. Instruct individuals to return to the health department if induration occurs after the TST is read
   b. positive TST reactions occurring after 72 hours are considered valid
   c. negative TST reactions should be repeated when individuals fail to return within 72 hours

2. Locate induration (not redness) by palpating in a crosswise motion

3. Measure transversely (crosswise or “east to west”) to the long axis of the forearm and record this as a single measurement

4. Record reaction in mm (example: 0mm, 16mm) and document date of reading and signature of person reading the test

5. Cold packs or over the counter topical steroid preparations (e.g. 1% hydrocortisone) may be used for the relief of pruritus and local discomfort

6. Evidence of scarring at an old TST site denotes a prior positive reaction and a repeat TST may not be indicated

C. Interpretation

1. A reaction of ≥ 5mm induration is considered positive for:

   a. close contacts to an individual with known or suspected infectious tuberculosis within the past 2 years
   b. those suspected of having active TB disease based on clinical and/or chest X-ray evidence
   c. individuals with HIV infection
   d. individuals with fibrotic changes on chest X-ray consistent with prior TB
   e. individuals with organ transplants and other immunosuppressed patients, including those receiving ≥ 15 mg per day of Prednisone for one month or longer or people taking or considering taking tumor necrosis factor (TNF) inhibitors such as etanercept (Enbrel®), infliximab (Remicade®), adalimumab (Humira®) or anakinra (Kineret™), or other similar biologic immunosuppressive agents

2. A reaction of ≥ 10mm induration is considered positive for:
   a. children younger than 4 years of age
   b. foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
      Low-prevalence countries for TB disease are USA, Canada, Japan, Australia, Western Europe and New Zealand
   c. HIV-negative individuals who inject illicit drugs or use crack cocaine
   d. individuals with medical conditions that have been reported to increase the risk of tuberculosis disease once infected:
      - diabetes mellitus
      - chronic malabsorption syndrome
      - chronic renal failure
      - leukemia, lymphomas, Hodgkin's disease
      - cancer of the head or neck
      - weight loss of ≥ 10% below ideal body weight
      - silicosis
      - gastrectomy, or jejunoileal bypass
   e. residents and staff of long-term care facilities
   f. health care personnel
   g. inmates in the Department of Corrections
   h. staff with direct inmate contact in the Department of Corrections and jails
   i. employees of HIV/AIDS adult daycare centers
   j. homeless shelter residents, employees and volunteers

k. individuals who increase their mm reading by 10mm or more within 2 years (converter)
l. mycobacteriology lab personnel
m. children and adolescents exposed to high-risk adults (homeless, substance abuse, incarcerated, HIV positive)
n. people who have resided in a medium- or high-prevalence area (Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands, or Eastern Europe) for 1 month or longer

3. A reaction of ≥ 15mm induration is considered positive for:

a. individuals who do not have any of the above risk factors

D. False Negative TST Reactions

An individual may be infected with *M. tuberculosis* but have little or no reaction to TST. False negative reactions may occur in any patient, but are more common in the following situations:

1. Recent (within 4-6 weeks) viral infections (rubella, mumps, influenza, measles, chicken pox) or live virus vaccinations (measles, mumps, rubella)
2. Overwhelming tuberculosis disease

Note: This means that a negative TST in the work-up of a possible case of TB does NOT rule out TB.

3. Immunosuppression associated with old age, debility, malnutrition, HIV infection, medications, and malignancy.

Note: Routine anergy testing is not recommended for use in identifying TB infection in immunosuppressed individuals due to the antigen tests' questionable validity and unpredictable variability over time.

4. Very recent tuberculosis infection (the individual may not have had time to develop the delayed hypersensitivity reaction, which can take up to 8-10 weeks after exposure)
5. High-dose steroids (≥15 mg of prednisone or its equivalent given daily for one month or longer) and other immunosuppressive agents
6. Infants younger than 6 months old (may have false-negative reactions because their immune systems are not fully developed)
7. Improper antigen storage, handling, technique in administration or error in reading

E. False Positive TST Reactions

An individual may not be infected with *M. tuberculosis*, but have a false positive reaction. False positive reactions may be caused by:

1. Cross reactions resulting from infection with nontuberculous mycobacteria
2. BCG (Bacille Calmette-Guérin) vaccine
3. Reading erythema (redness) rather than induration

Individuals at low epidemiologic risk for *M. tuberculosis* infection (for example, a person for whom a TST threshold of 15 mm or greater would be considered positive) with a positive TST (unexpected positive results) should have an IGRA performed if possible before considering LTBI treatment. Individuals at low epidemiologic risk with a positive TST and negative IGRA should generally not receive LTBI treatment.

F. TST Converters

An increase in reaction size of ≥ 10 mm within a period of 2 years should be considered a conversion

G. Two-Step TST (Booster Phenomenon)

1. In some individuals, the ability to react to the TST may gradually diminish over time. If skin tested at this point, these individuals may have a false negative reaction. However, if retested within 1 week to 1 year they may then demonstrate a positive reaction (the "booster" phenomenon). The booster phenomenon may occur at any age, but is more common in older people.
2. Two-step testing reduces the likelihood of interpreting a "boosted" reaction as a true conversion or a new infection; it is recommended in situations where there will be repeat testing on a regular basis. Two step testing is required for staff and residents of long-term care facilities as well as staff in adult day care centers that provide care for HIV/AIDS clients (see Chapter XI -10A NCAC 41A .0205 (c)1- 4. If the individual has had a documented TST within the last 12 months, that TST can be counted as the first step in 2 step testing.
3. If the reaction to the first test is positive, consider the individual infected and do not place a second test
4. If the reaction to the first test is negative a second test should be given 1 to 3 weeks later:
5. If the second test is positive, consider the individual infected
6. If the second test is negative, consider the individual not infected
7. Record reactions in mm and document dates of reading and signature(s) of person(s) reading the tests
8. Two step testing is not needed when using IGRA's instead of TST's

H. Bacille Calmette Guerin (BCG)

BCG is an attenuated or weakened form of tuberculosis, originally derived from M*ycobacterium bovis*, and is used in high-incidence countries to protect infants and young children against severe forms of TB disease (miliary and meningeal disease). BCG is also used as an intravesicular therapy (instilled into the bladder) for treatment of bladder cancer. BCG (identified as *M. bovis*) can frequently be isolated from the urine of people who have recently received intravesicular therapy, but this does not always require treatment. BCG type bovis is not generally communicable and should not be treated by the health department nor counted as a TB case.

Both BCG vaccination and intravesical BCG can cause a reactive TST; this effect seems to wane over time but can persist for years. IGRAs are therefore preferred for most people who have received the BCG vaccine.

I. Candidates for TST or IGRA

- TST of individuals and groups should be undertaken only if the diagnostic evaluation and a course of preventive therapy can be completed
- **routine testing of low-risk individuals is not recommended; locally purchased PPD must be used for all low-risk testing, e.g., job-related**

- ***state supplied PPD may be used only for people in categories #1-7 as follows (high-risk for infection or disease)***

1. The following children and adults are legally required (10A NCAC 41A.0205) to receive a TST or IGRA:

    a. household and other close contacts of active cases of pulmonary and laryngeal tuberculosis
    b. people reasonably suspected of having tuberculosis disease
    c. inmates in the custody of, and staff with direct inmate contact, in the Department of Correction upon incarceration or employment, and annually thereafter
    d. patients and staff in long term care facilities upon admission or employment, using the two-step skin test method

e. staff in adult day care centers providing care for people with HIV infection or AIDS upon employment, using the two-step skin test method
f. people with HIV infection or AIDS

2. The following children and adults should receive a baseline TST or IGRA when they initially present for health care:

   a. foreign-born individuals from high incidence areas, such as, Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe
      Low-prevalence countries for TB disease are USA, Canada, Japan, Australia, Western Europe and New Zealand
   b. individuals who inject illicit drugs or use crack cocaine
   c. migrants, seasonal farm workers, and the homeless (if unable to ensure completion of evaluation and treatment of LTBI, screen for disease)
   d. people who have traveled outside the US and stayed with family and friends who live in high incidence areas, for greater than 1 month cumulatively
   e. children and adolescents exposed to high-risk adults (homeless, substance abuse, incarcerated, HIV positive)

   A subsequent TST/IGRA is not necessary unless there is a continuing risk of exposure to people with tuberculosis disease

3. People taking or considering taking tumor necrosis factor (TNF) inhibitors (e.g., etanercept, infliximab, adalimumab or anakinra) or other biologics which can suppress the immune system are at high risk for TB disease if infected. Before starting these drugs, a TST or IGRA should be done (preferably a 2-step test if the TST is used) and treatment for LTBI started if the TST reading is 5 mm or greater or the IGRA is positive. If there is a credible history of exposure to TB, LTBI treatment should be initiated regardless of TST result.

4. Clinically assess all household members in the immediate environment of a child $\leq$ 2 years of age with a newly identified positive TST or IGRA to rule out an undiagnosed case of tuberculosis. An assessment should include an evaluation of symptoms for TB disease and may include a TST or IGRA, bacteriological examination and chest X-ray, if indicated.

5. Clinically assess all household members in the immediate environment of a pregnant woman with a newly identified positive TST to rule out TB exposure in the immediate environment that the newborn infant will be entering. An assessment should include an evaluation of symptoms for TB disease and may include a TST or IGRA, bacteriological examination and chest X-ray, if indicated.

6. Homeless shelters

    a. staff and volunteers should be educated regarding the symptoms of tuberculosis disease. Those clients with symptoms suggesting TB disease should be promptly evaluated for active disease.
    b. staff and volunteers should receive a two-step TST or IGRA on employment
    c. routine TST or IGRA of clients should be undertaken only if the diagnostic evaluation and course of LTBI therapy can be initiated and completed

7. Local jails and detox units

    a. All jail facilities must conduct a facility specific risk assessment; for additional guidance see: prevention and Control of Tuberculosis in Correctional and Detention Facilities: Recommendations from CDC. MMWR 2006;55 (No RR-9)
    b. Test staff with a TST (using the two-step method) or IGRA upon employment. Annual TST or IGRA is based on the facility's current risk level.
    c. Verbally screen all inmates for symptoms of TB on admission. Inmates with symptoms suggesting TB disease should be evaluated for active disease

8. Staff and residents in occupational settings where TST is required by regulatory and/or agency policy

    a. two-step TST [upon admission or employment] individuals who cannot provide a documented negative TST within the preceding 12 months:
        - individuals who can provide a documented negative TST within the preceding 12 months should receive a single TST and use this result as the second part of the two-step test
        - individuals who can provide a documented positive TST should have a Record of Tuberculosis Screening (DHHS 3405) completed using the most recent chest X-ray report

b. **individuals with a previously documented positive TST should be re-X-rayed only when symptoms of tuberculosis disease are present**

J. Chest X-rays

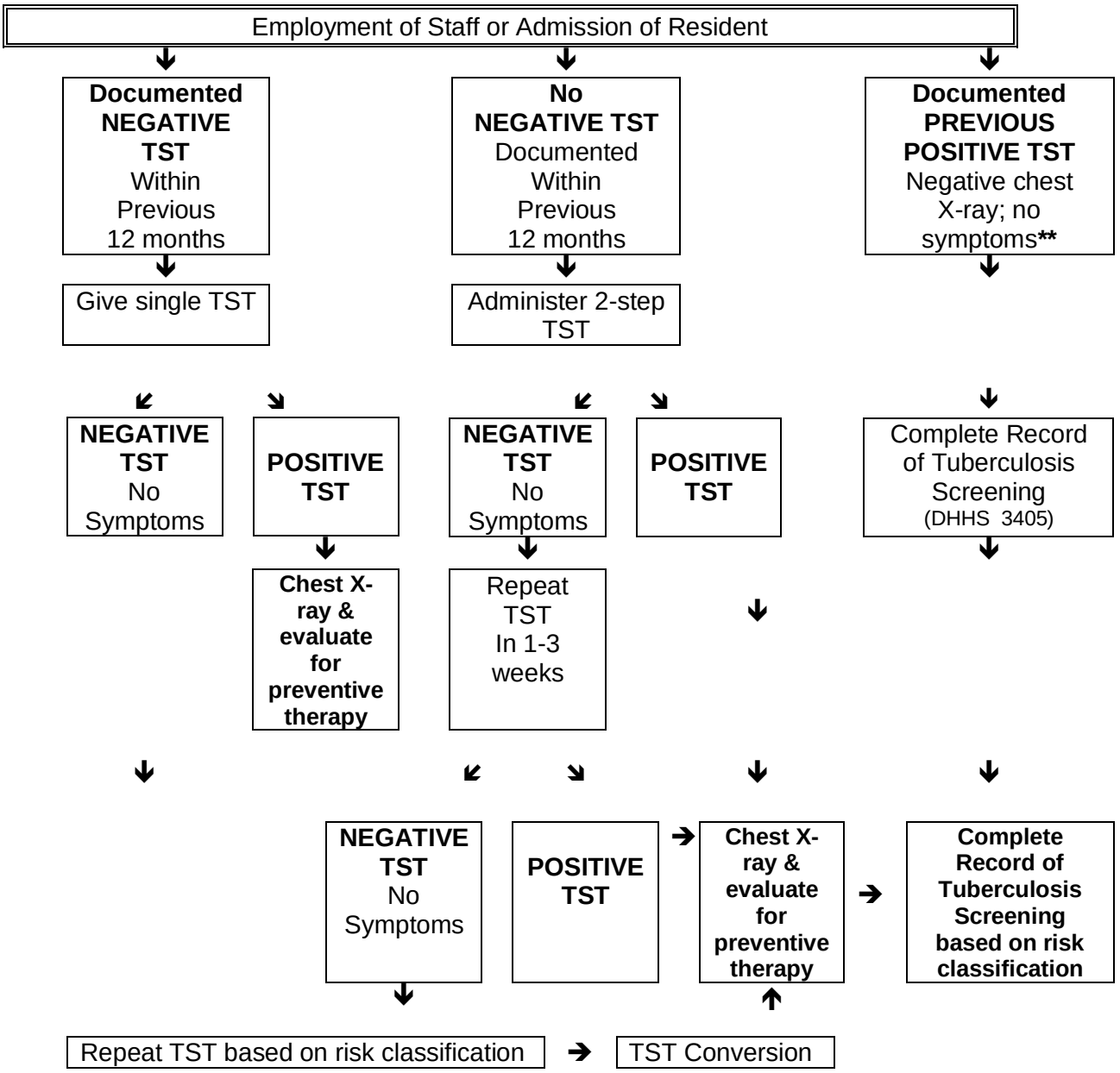
1. A posterior-anterior view of the chest should be obtained on all adults:
   a. with a newly identified positive TST or IGRA
   b. with symptoms suggestive of TB disease regardless of TST/IGRA results
   c. with suspected extrapulmonary TB disease
   d. with negative TST/IGRA and starting treatment for LTBI, i.e. close contact

2. A posterior-anterior and lateral view of the chest should be obtained on children under 5 years of age:
   a. with a newly identified positive TST/IGRA
   b. with symptoms suggestive of TB disease regardless of TST/IGRA results
   c. with suspected extrapulmonary TB disease
   d. with negative TST/IGRA and starting latent TB treatment, i.e. close contact

3. Due to the risk of progressive and/or congenital TB, **pregnant women** should have a PA view of the chest (with appropriate shielding) as soon as possible, even during the first trimester of pregnancy, if they have a positive TST or IGRA

4. Individuals with a previously documented positive TST/IGRA and a negative chest X-ray should have a repeat X-ray only when symptoms for tuberculosis disease are present (see Chapter III for chest X-ray recommendations when starting treatment for LTBI for someone with a remote or prior positive TST/IGRA)

K. Two-Step Tuberculin Skin Testing (TST)*



***Initial two-step TST is required for employees and residents of long-term care facilities and facilities providing adult day care for HIV positive individuals. Other agency/institution requirements may vary.**

****Repeat X-ray ONLY if signs and symptoms of tuberculosis disease are present. Obtain sputums and X-ray individuals with symptoms regardless of TST result.**

L. Interferon Gamma Release Assays (IGRAs)

Background

Interferon gamma release assays (IGRAs) are tests for tuberculosis (TB) infection. These tests measure the patient's immune response (interferon gamma release) after stimulation of white blood cells in a test tube with relatively TB-specific antigens. In contrast to the tuberculin skin test, which requires two separate visits for placement and reading, IGRAs offer the possibility of testing for TB infection with a single blood draw at a single visit. In addition to the logistical advantage of requiring a single visit, IGRAs may have other advantages over the tuberculin skin test. The antigens used for the IGRA tests are not present in the Bacille Calmette-Guerin vaccine (BCG), so false positive tests due to BCG are unlikely to occur. The IGRA antigens are also not present in most nontuberculous mycobacteria, so false positive tests due to nontuberculous mycobacterial exposure or infection are less likely to occur with IGRAs than with tuberculin skin testing.

Despite these potential advantages, the IGRAs are imperfect tests for TB diagnosis. Large, prospective studies have demonstrated that both the TST and IGRAs fail to identify people who will develop active TB in the future, and most people with positive TSTs or IGRAs will never develop active TB. Additionally, every study comparing the two available IGRA tests has demonstrated a significant proportion of discordant results, the significance of which is unknown. This discordance means that the IGRAs are not interchangeable; switching among the IGRAs (or for that matter, between an IGRA and tuberculin skin testing) in the setting of serial testing may result in false "conversions" caused by discordance between the different tests used (as opposed to new TB infection). Furthermore, the cost of an IGRA is significantly greater than the cost of a tuberculin skin test.

Currently two IGRAs are approved for use in the United States by the Food and Drug Administration. The QuantiFERON Plus® is an enzyme-linked immunosorbent assay-based test. The test measures the concentration of interferon gamma in whole blood in four separate tubes: a nil tube (negative control), two tubes containing peptides derived from two TB antigens (ESAT-6 and CFP-10), and a tube containing phytohemagglutinin (a mitogen used as a positive control). Blood is either drawn from the patient directly into each tube (about 1 ml of blood each) or into a single lithium heparin tube and subsequently aliquoted into each of the four tubes. If blood is drawn directly from the patient into the QuantiFERON tubes, the tubes must be gently shaken and placed into an incubator at 37 C within 16 hours of the blood draw and are then incubated for 16-24 hours. If blood is drawn from the patient into a lithium heparin tube, the tube may be stored refrigerated or at room temperature for up to 53 hours before aliquoting into the four QuantiFERON tubes and incubating. After incubation, a machine is used to measure the concentration of interferon gamma in each tube. The criteria for test interpretation are listed in the package insert, available at https://www.quantiferon.com/us/wp-

content/uploads/sites/13/2019/07/L1095849-R05-QFT-Plus-ELISA-IFU-USCA.pdf.

The T-SPOT.TB® is an enzyme-linked immunospot test. The test measures the number of spots on a plate containing four different antigens: nil (negative control), two TB antigens (ESAT-6 and CFP-10, also called Panel A and Panel B), and phytohemagglutinin (positive control). Each spot theoretically represents a white blood cell that is secreting interferon gamma. Blood is drawn from the patient (8 mL for adults, 4 mL for children 2-9 years old, and 2 mL for children under 2 years) and then must be processed in the laboratory within 8 hours. The white blood cells are separated from the rest of the blood, and a standard number of white cells is placed into each plate. The cells are incubated with the antigens for 16-20 hours, and then further steps are used to develop the spots for each plate. The criteria for test interpretation are described in the package insert, available at www.tspot.com.

A brief comparison of the tuberculin skin test and the two IGRAs follows in the Table.

	Tuberculin skin test	QuantiFERON Plus	T-SPOT.TB
Number of visits required	2*	1	1
Time frame to get blood to lab	N/A	<16 hours if drawn directly into tubes <53 hours if drawn into single tube	<33 hours
Result format	mm of induration	Concentration of interferon gamma (IU/mL)	Number of spots on a plate
Reliability among observers	+/-	++	++
Test-retest variability	Moderate	High	High
Potential as a “send out” test to distant labs	N/A	Yes	Yes (always done this way)
Cost to health department or healthcare facility	Reagent inexpensive, labor somewhat more	Moderately expensive	Moderately expensive
Cross-reacts with BCG, nontuberculous mycobacteria	Yes (mostly an issue in foreign-born populations)	No	No

* 4 visits may be necessary if 2-step testing is performed

Reporting of IGRA results
Reporting of IGRA results as “Positive,” “Negative,” or “Indeterminate” is clinically useful, but may be suboptimal in certain circumstances. Both clinically available IGRAs have a certain amount of test-retest variability (“wobble” — for example see Pai M et al., American Journal of Respiratory and Critical Care Medicine 2006 174: 349). Particularly when results are near the threshold for a positive test, repeat testing has a significant probability of producing a result on the other side of the threshold. This problem is of particular concern in the setting of repeat testing, when a patient may test negative at just below the threshold on one occasion, and then test positive at just above the threshold on another occasion solely due to inter-test variability.

To assist with test interpretation, the NC Tuberculosis Control Program recommends that laboratories report the following information:

QuantiFERON Plus®
- Nil tube interferon gamma concentration (IU/mL)
- TB1 antigen tube interferon gamma concentration (IU/mL)
- TB2 antigen tube interferon gamma concentration (IU/mL)
- TB1-Nil and TB2-nil values (difference, IU/mL)
- Criteria for a positive value (i.e. difference of ≥35 IU/mL and >25% of nil)
- Interpretation (“Positive,” “Negative,” “Indeterminate,” ”Invalid”)

T-SPOT.TB®
- Nil plate spots (number)
- TB antigen plate spots (number, both plates)
- Highest difference (TB antigen-nil)
- Criteria for a positive value (i.e. difference of ≥8 spots)
- Interpretation (“Positive,” “Negative,” “Borderline”,”Invalid”)

Management of indeterminate results
Both IGRAs may yield indeterminate/invalid results, either due to high Nil background or an inadequate interferon gamma response to mitogen. Indeterminate results are more common in the setting of immunosuppression, but can also occur in apparently immunocompetent hosts. However, a significant proportion of people with indeterminate results on one occasion will have a non-indeterminate result on repeat testing. Similarly, while an indeterminate result is associated with an anergic response to the tuberculin skin test, not all people with an indeterminate response from an IGRA will have anergy in response to the tuberculin skin test.

Recommendations:
- If an indeterminate result is obtained from IGRA testing, repeating the same IGRA test should be considered.
- If an indeterminate result is obtained from one IGRA test (outside the setting of serial testing) performing a different IGRA test (if available) or a tuberculin skin test can be considered

- No data exist on the effect of MMR vaccine (or infection with measles, mumps, or rubella) on IGRAs, but it is advisable to delay performing an IGRA until at least four weeks after MMR is administered. If an indeterminate or negative result is obtained from a patient who had MMR or infection with one of these viruses within the past four weeks, repeating the test is advisable if the patient has epidemiologic risk for TB exposure

Unexpected positive results

- A positive IGRA result in a patient with low risk for TB infection has a high probability to be a false-positive result
- Consistent with CDC guidelines, NC TB Control recommends repeating the same IGRA (or performing an IGRA in the case of an unexpected positive TST) when an unexpected positive result is obtained
- A person with an initial unexpected positive result and subsequent negative IGRA should generally not be offered LTBI treatment

Diagnosis of active tuberculosis

Like the tuberculin skin test, IGRAs are at best imperfect tools in the diagnosis of active TB. A recent meta-analysis estimated that the sensitivity of the tuberculin skin test among people with active tuberculosis was 77%, the sensitivity of the QuantiFERON Gold in-tube® was 70%, and the sensitivity of the T-SPOT.TB® was 90% (Pai M et al., Annals of Internal Medicine 2008; 149: 177). IGRAs will therefore be falsely negative in a significant proportion of people with active TB. Also, IGRAs cannot discriminate between latent TB infection and active TB disease in a given patient. However, one study did demonstrate that IGRAs were useful in distinguishing children with TB cervical lymphadenitis from children with nontuberculous mycobacterial lymphadenitis (Clin Infect Dis. 2007; 45(3):322) in a low-incidence area.

Recommendations:

- Like the tuberculin skin test, IGRAs should not be relied upon to make or disprove the diagnosis of active TB in adults.
- IGRAs may be used in children as part of diagnostic algorithms for TB diagnosis, keeping in mind their imperfect test characteristics.
- Microbiologic diagnosis (culture) is the gold standard and should be aggressively pursued in both adults and children.

M. Use of Interferon Gamma Release Assays in Children <2 Years Old

Background

In the United States, interferon gamma release assays (IGRAs) are the preferred tests for latent tuberculosis (LTBI) in most populations ages two and older, primarily because the IGRAs are more specific than the tuberculin skin test (TST). However, current guidelines from the American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention (ATS/IDSA/CDC) and American Association prefer the TST for young children (under 5 years of age in the ATS/IDSA/CDC guidelines(1) and under 2 years of age in the Red Book(2)). This preference arises from concerns regarding the sensitivity of IGRAs for tuberculosis infection in young children.

Evidence supporting use of IGRAs in children <2 years old

In most countries where the Bacille Calmette-Guérin (BCG) vaccine is administered, it is administered at birth. Older studies suggested that the effect of BCG on the tuberculin skin test was most pronounced in children under 5 years of age. More recent studies have supported this contention; for example, a prospective study of children in South Africa demonstrated that positive IGRAs were more strongly associated with contact with an infectious tuberculosis case than the TST (3). In the subset of children <2 years old in this study, IGRAs were even more strongly associated with tuberculosis exposure than in older children. A meta-analysis examining LTBI screening in children <2 reported an average LTBI prevalence of 5% using IGRAs compared with 15% using TST, suggesting significant overdiagnosis of LTBI in children <2 when the TST is used (4).

The major concerns regarding the use of IGRAs in children <2 are that 1) IGRAs may be less sensitive for LTBI diagnosis in this population, leading to missed opportunities for tuberculosis prevention and 2) IGRAs are more logistically challenging than the TST in young children because of the need to draw blood for the former but not the latter. Studies of the sensitivity of IGRAs for active TB in young children have yielded mixed results, but in general have not demonstrated major differences in performance between the IGRAs and the TST for active TB diagnosis (5). Data supporting the use of IGRAs for LTBI diagnosis in young children are summarized in Tables 1-3. While the data are limited, they support three broad contentions. First, all available tests (TST and both IGRAs) are imperfectly sensitive for LTBI. Second, there is no clear difference between the sensitivity of TST and the sensitivity of IGRAs for LTBI diagnosis. Third, and perhaps most importantly, the greater specificity of IGRAs, particularly in the setting of recent BCG vaccination (which is by definition the case for children <2 who received the vaccine at birth), permits treatment of fewer children for LTBI, optimizing use of available resources. For example, reference (6) reports a positive predictive value of only 10% for the TST in children <5 versus 73-79% for the IGRAs; this suggests that about 9 of 10 children with a positive TST are being unnecessarily treated for LTBI versus 2-3 of 10 unnecessarily treated when an IGRA is used. Programmatic data support this contention; the Harris County, Texas refugee program reported that children were more likely to have positive TST than IGRAs, and 95% of discordant test results were TST+/IGRA- (7). Furthermore, several studies (Table 3) support the contention that children with a positive TST but negative IGRA are at very low risk to progress to active tuberculosis without treatment.

Concerns about the ability to successfully obtain IGRAs from young children are valid; clinical settings in which young children at risk for tuberculosis exposure are seen may not have phlebotomists experienced in drawing blood from young children and parents may be reluctant to have this done. However, in at least one US programmatic setting (Denver Health), obtaining IGRAs from children <2 was routinely successful, with only 1/116 (0.9%) failed phlebotomy and 2 (17%) parental refusals (8).

Recommendations for use of IGRAs in children <2 years old

- **Neither the TST nor the IGRAs are perfectly sensitive for diagnosis of latent or active tuberculosis in any population. Clinical judgment, including assessment of exposure risk as well as likelihood to progress to disease, is vital regardless of which test is used. A negative IGRA or TST should not delay appropriate evaluation and treatment for active tuberculosis.**
- **IGRAs are acceptable alternatives to the TST for LTBI screening in children <2 years**
- **Local logistical factors including the availability of phlebotomists experienced in drawing blood from young children and reliable courier services should be considered when deciding which test (TST or IGRA) is most appropriate for a given clinical setting.**

Table 1. Studies evaluating the performance of IGRAs in children <2 years old.

Reference	Population Studied	Main Outcome
Bakir 2008 (9)	Contacts to smear-positive TB (n=908, all ≤16 years old) Mean age 7.5 yrs (range 1 month-16 years)	Active TB (n=15, 9 in children <5, 4 in children <2)
Diel 2011 (10)	Contacts to smear-positive TB (n=1414) 24 children 1-5 years old with both TST and QFT-GIT done	Active TB (n=3 in children <6)
Grinsdale 2016 (11)	Children <15 years (n=1092) 236 < 2-4 years old 56 < 2 years old US Presenting for TB screening (78% non-US-born, 12% contacts)	Active TB (n=0)
Stout 2018 (6)	Children < 5 years (n=464) Median age 3.1 US Non-US-born from TB-endemic area	Latent TB (assessed by latent class analysis)
Velasco-Arnaiz 2018 (12)	Children <5 years (n=383) 141 < 2 years old Spain 67% contacts, 10% TB suspects	Active TB (n=1 incident)
Ahmed 2020 (13)	Children <15 years (n=3593)	Active TB (n=4)

	681 2-4 years old 219 <2 years old US High risk for LTBI	
Wendorf 2020 (14)	Refugees <5 years old (n=3371) 1204 < 2 years old	Active TB (n=0)
Gaensbauer 2020 (8)	Children <2 tested with QFT US	Active TB (n=0)

Table 2. Summary of test characteristics for tuberculin skin tests and IGRAs in young children from studies in which these data were available.

Reference	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Bakir 2008 (9) TST ELISPOT (T-SPOT like test)	 80 (52-96) 73 (45-92)	 27 (25-31) 59 (55-62)	 1.6 (0.8-3.0) 2.9 (1.5-5.1)	 98.4 (96.0-99.6) 99.2 (98.1-99.8)
Diel 2011 (10) TST QFT-GIT	 100 (29-100) 100 (29-100)	 67 (45-84) 71 (49-87)	 37.5 (9-76) 43 (10-82)	 100 (79-100) 100 (80-100)
Stout 2018 (6) TST QFT-GIT T-SPOT	 69.1 (58.5-79.7) 71.2 (55.3-86.5) 58.9 (42.7-76.2)	 73.9 (69.6-77.9) 98.9 (97.4-99.9) 99.4 (98.4-99.9)	 10.0 (4.8-16.5) 73.1 (41.3-95.3) 79.2 (52.0-96.3)	 98.3 (96.7-99.3) 98.8 (97.4-99.6) 98.3 (96.5-99.4)
Ahmed 2020 (13) TST QFT-GIT T-SPOT	 50.0 (15.0-85.0) 75.0 (30.1-95.4) 50.0 (15.0-85.0)	 73.4 (71.9-74.8) 90.1 (89.1-91.1) 92.9 (92.0-93.7)	 0.2 (0.1-0.8) 0.9 (0.3-2.5) 0.8 (0.2-2.9)	 99.9 (99.7-100) 100.0 (99.8-100) 99.9 (99.8-100)

Table 3. Comments on selected studies examining the performance of IGRAs in young children.

Reference	Notes
Bakir 2008 (9)	Testing performed only at baseline and then after 6 months; 1/15 incident cases converted TST to positive at 6 months and 2/15 incident cases converted ELISPOT to positive at 6 months 10/15 incident cases had received isoniazid preventive therapy
Grinsdale 2016 (11)	146/906 children were TST+/QFT- 59/906 were QFT-indeterminate (5 with +TST, 14 with negative TST, 40 not done) 0/146 TST+/QFT- untreated children progressed to active TB
Stout 2018 (6)	Latent class analysis based on test pattern combinations used to estimate LTBI prevalence and test characteristics Children were a subset of the cohort reported in Ahmed 2000
Velasco-Arnaiz 2018 (12)	Children with +TST/-QFT categorized as not having LTBI, not offered LTBI treatment 0/47 TST+/QFT- untreated children developed active TB during follow up The single incident case had -TST/-QFT but subsequently spent 2 months in Pakistan
Ahmed 2000 (13)	2 children <2 developed active TB; both had negative TST/negative T-SPOT, 1 had negative QFT-GIT and the other positive; both were on isoniazid prophylaxis at time of diagnosis 0/54 untreated children <2 with +TST/-IGRA developed disease
Wendorf 2020 (14)	TST and QFT-GIT done on different groups of children TST positive in 13% vs. QFT positive in 1.4%

	0/1830 children with negative IGRAs developed TB during about 3 years median follow up 0/425 children <2 with negative IGRAs developed TB during about 3 years median follow up
Gaensbauer 2020 (8)	0/108 children <2 with negative QFT-GIT developed active TB after median about 3 years follow up Only 1 failed phlebotomy and 2 parental refusal of 116 patients; 3/116 (2.8%) indeterminate

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Appendix F
Quality Control Procedural Observation Checklist (from MMWR2 2005;54 (RR-17))

Appendix F. Quality control (QC) procedural observation checklists

Quality Control (QC) Procedural Observation Checklist for Placing Tuberculin Skin Tests (TSTs) — Mantoux Method

Date _____ **Trainer (QC by)** _____ **Trainee (TST placed by)** _____

Scoring: ✓ or Y = Yes X or N = No NA = Not Applicable

1. Preliminary

_____ Uses appropriate hand hygiene methods before starting.
_____ Screens patient for contraindications (severe adverse reactions to previous TST).*
_____ Uses well-lit area.

2. Syringe† filled with exactly 0.1 mL of 5 tuberculin units (TU) purified protein derivative (PPD) antigen§

_____ Removes antigen vial from refrigeration and confirms that it is 5 TU PPD antigen.¶
_____ Checks label and expiration date on vial.
_____ Marks opening date on multidose vial.
_____ Fills immediately after vial removed from refrigeration.
_____ Cleans vial stopper with antiseptic swab.
_____ Twists needle onto syringe to ensure tight fit.
_____ Removes needle guard.
_____ Inserts needle into the vial.
_____ Draws slightly over 0.1 mL of 5 TU PPD into syringe.
_____ Removes excess volume or air bubbles to exactly 0.1 mL of 5 TU PPD while needle remains in vial to avoid wasting of antigen.
_____ Removes needle from vial.
_____ Returns antigen vial to the refrigerator immediately after filling.

3. TST administration site selected and cleaned

_____ Selects upper third of forearm with palm up ≥2 inches from elbow, wrist, or other injection site.**
_____ Selects site free from veins, lesions, heavy hair, bruises, scars, and muscle ridge.
_____ Cleans arm site with antiseptic swab using circular motion from center to outside.
_____ Allows site to dry thoroughly before administering antigen.

4. Needle inserted properly to administer antigen

_____ Rests arm on firm, well-lit surface.
_____ Stretches skin slightly.††
_____ Holds needle bevel-up and tip at 5°–15° angle to skin.
_____ Inserts needle in first layer of skin with tip visible beneath skin.
_____ Advances needle until entire bevel is under the first layer of skin.
_____ Releases stretched skin.
_____ Injects entire dose slowly.
_____ Forms wheal, as liquid is injected.
_____ Removes needle without pressing area.
_____ Activates safety feature of device per manufacturer's recommendations, if applicable.
_____ Places used needle and syringe immediately in puncture-resistant container without recapping needle.
_____ Immediately measures wheal to ensure 6–10 mm in diameter (Actual wheal measurement _____mm).
_____ If blood or fluid is present, blots site lightly with gauze or cotton ball.
_____ Discards used gauze or cotton ball according to local standard precautions.
_____ If the TST is administered incorrectly (too deeply or too shallow) and the wheal is inadequate (<6 mm), a new TST should be placed immediately. Applying the second TST on the other arm or in a different area of the same arm (at least 2 inches from the first site) is preferable so that the TST result will be easier to read.
_____ Documents all information required by the setting (e.g., date and time of TST placement, person who placed TST, location of injection site and lot number of tuberculin).
_____ Uses appropriate hand hygiene methods after placing TST.

5. Explanation to the client regarding care instructions for the injection site

_____ The wheal (bump) is normal and will remain about 10 minutes.
_____ Do not touch wheal; avoid scratching.
_____ Avoid pressure or bandage on injection site.
_____ Rare local discomfort and irritation does not require treatment.
_____ May wash with soap and water (without pressure) after 1 hour.
_____ No lotions or liquids on site, except for light washing, as above.
_____ Keeps appointment for reading.

* Severe adverse reactions to the TST are rare but include ulceration, necrosis, vesiculation, or bullae at the test site, or anaphylactic shock, which is substantially rare. These reactions are the only contraindications to having a TST administered.

† Use a ¼–½-inch 27-gauge needle or finer, disposable tuberculin (preferably a safety-type) syringe.

§ Prefilling syringes is not recommended. Tuberculin is absorbed in varying amounts by glass and plastics. To minimize reduction in potency, tuberculin should be administered as soon after the syringe has been filled as possible. Following these procedures will also help avoid contamination. Test doses should always be removed from the vial under strictly aseptic conditions, and the remaining solution should remain refrigerated (not frozen). Tuberculin should be stored in the dark as much as possible and exposure to strong light should be avoided. **SOURCE:** American Thoracic Society, CDC, Infectious Disease Society of America. Diagnostic standards and classification of tuberculosis in adults and children. Am J Respir Crit Care Med 2000;161:1376–95.

¶ Preventing tuberculin antigen and vaccine (e.g., Td toxoid) misadministration is important. Measures should include physical separation of refrigerated products, careful visual inspection and reading of labels, preparation of PPD for patient use only at time of testing, and improved record keeping of lot numbers of antigens, vaccines, and other injectable products. **SOURCE:** CDC. Inadvertent intradermal administration of tetanus toxoid–containing vaccines instead of tuberculosis skin tests. MMWR 2004;53:662–4.

** If neither arm is available or acceptable for testing, the back of the shoulder is a good alternate TST administration site. **SOURCE:** National Tuberculosis Controllers Association, National Tuberculosis Nurse Consultant Coalition. Tuberculosis nursing: a comprehensive guide to patient care. Smyrna, GA: National Tuberculosis Controllers Association; 1997.

†† Stretch skin by placing nondominant hand of health-care worker (HCW) on patient's forearm below the needle insertion point and then applying traction in the opposite direction of the needle insertion. Be careful not to place the nondominant hand of the HCW opposite the administration needle if the patient is likely to move during the procedure, which might cause an accidental needle-stick injury. In children and others who are likely to move during the procedure, certain trainers prefer stretching the skin in the opposite direction of the needle insertion by placing the nondominant hand of the HCW under the patient's forearm. This method should not be used for persons with poor skin turgor.

Quality Control (QC) Procedural Observation Checklist for Reading Tuberculin Skin Test (TST) Results — Palpation Method

Date _____ **Trainer (QC by)** _____ **Trainee (TST placed by)** _____

Scoring: ✓ or Y = Yes X or N = No NA = Not Applicable

1. Preliminary

_____ Uses appropriate hand hygiene methods before starting.
_____ Keeps fingernails shorter than fingertips to avoid misreading TST result.
_____ Keeps TST reading materials at hand (eyeliner pencil or ballpoint pen,* and ruler).
_____ Uses well-lit area.
_____ Inspects for the site of the injection.

2. Palpate — finding margin ridges (if any)

_____ Palpates with arm bent at elbow at a 90° angle.
_____ Lightly sweeps 2-inch diameter from injection site in four directions.
_____ Uses zigzag featherlike touch.
_____ Repeats palpation with arm bent at elbow at a 45° angle to determine presence or absence of induration.

If induration is present, continue with these steps†:

3. Placing marks

_____ Holds palm over injection site.
_____ Uses fingertips to find margins of the induration.
_____ Marks the induration by placing small dots on both sides of the induration.
_____ Inspects dots, repeats finger movements toward indurated margin, and adjusts dots if needed.
_____ Marks dots transverse (perpendicular) to long axis of forearm.

4. Placing and reading ruler

_____ Places the "0" ruler line inside the edge of the left dot. Reads the ruler line inside right dot edge (uses lower measurement if between two gradations on millimeter scale) (see Figure 1).
_____ Uses appropriate hand hygiene methods after reading TST.

5. Documenting results

_____ Records all TST results in millimeters, even those classified as negative. Does not record only as "positive" or "negative." Records the absence of induration as "0 mm."
_____ Correctly records results in mm; only a single measured induration in mm should be recorded.
Trainee's measurement _____ mm.
Trainer's (gold standard) measurement _____ mm.
Trainee's result within 2 mm of gold standard reading?§
Yes _____ No _____

NOTE: In rare instances, the reaction might be severe (vesiculation, ulceration, or necrosis of the skin). Report severe adverse events to the FDA MedWatch Adverse Events Reporting System (AERS), telephone: 800-FDA-1088; fax: 800-FDA-0178; http://www.fda.gov/medwatch report form 3500, Physicians' Desk Reference.

* A fine-tipped eyeliner pencil or ballpoint pen can be used as a marker. An eyeliner pencil is useful for TST training and for blinded independent duplicate readings (BIDRs) because the dots are easy to remove with a dot of lubricant (e.g., baby oil). Alternative TST result reading methods have been described, including the pen method.
† If induration is not present, record the TST result as 0 mm and go to the end of this form (Documenting results).
§ For example, if the TST trainer reads the TST result (the gold standard reading) as 11 mm, the trainee's TST reading should be between 9–13 mm to be considered correct. Only a single measured induration in millimeters should be recorded.

Sample Standing Order: Purified Protein Derivative (PPD) Placement

Assessment: This standing order shall be initiated to place a PPD if the PHN has completed a TB program orientation which includes training on the administration and reading of PPD's in any of the following situations and if the following subjective and objective findings exist:

- when an individual is a contact to active tuberculosis (TB)
- in individuals with signs and or symptoms of active tuberculosis (abnormal chest X-ray, positive AFB smear or culture, productive cough, fever, night sweats, shortness of breath, chest pain, unexplained appetite loss, unexplained weight loss, or unexplained fatigue), or
- Individual has a new positive HIV test

Subjective findings:
Screening for Mycobacterium tuberculosis is:

- Requested by patient, or
- Requested by medical provider, or
- Required by communicable disease/TB rules

Objective findings:
. Medical record indicates:

- The patient has not recently had (within 4-6 weeks) viral infections (rubella, mumps, influenza, measles, chicken pox) or live virus vaccinations (measles, mumps, rubella)
- The patient has no documentation of a positive Interferon Gamma Release Assay (IGRA) or PPD.

Implementation:

Administering a PPD

1. Tuberculin skin test (TST) shall be performed using 0.1 cc of 5TU Purified Protein Derivative (PPD).
2. Use tuberculin syringe with 3/8-inch, 26-27 gauge needle
3. Clean volar or flexor surface of left forearm approximately 2-4 inches below the elbow: allow to dry completely
4. Give intradermal injection with needle bevel up. A tense white wheal 6-10 mm in diameter should be produced when the TST is accurately administered.
5. Repeat injection at another site at least 2 inches from original site if antigen is lost or injection is given too deeply. Specify location of the retest in the record.
6. If the use of the left arm is not feasible due to injury, deformity, etc., the PPD may be administered in the volar or flexor region of the right forearm and a notation of the site change recorded on the client's chart.
7. Administer TST prior to or simultaneously with live virus vaccines. Client may not receive another TST for 4-6 weeks after live virus vaccines

Reading a PPD

1. Read TST 48 – 72 hours after placement, preferably at 72 hours

a. Instruct patient to return to the health department if induration occurs after the TST is read
b. Positive TST reactions occurring after 72 hours are considered valid.
c. Negative TST reactions should be repeated when individuals fail to return to return within 72 hours.

2. Locate induration (not redness) by palpating in a crosswise motion. Measure transversely to the long axis of the forearm and record this as a single measurement.
3. Record reaction in mm (example: 0 mm, 16 mm) and document date of reading and signature of the person reading the test.

Interpretation of PPD results: A skin test is considered positive based on the risk factors of the patient.

1. A reaction of ≥ 5 mm induration is considered positive for:
    a. Close contacts to an individual with known or suspected infectious tuberculosis within the past 2 years.
    b. Those suspected of having active TB disease based on clinical and/or chest X-ray evidence.
    c. Individuals with HIV infection.
    d. Individuals with fibrotic changes on chest X-ray consistent with prior TB who have received no or inadequate prior treatment for active TB
    e. Immunocompromised individuals, e.g., receiving > 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or people taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel ®), infliximab (Remicade ®) or anakinra (Kineret™) or adalimumab (Humira ®)
    f.
2. A reaction of ≥ 10 mm induration is considered positive for:
    a. Children younger than 4 years of age
    b. Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe. *Low-prevalence countries for TB disease are USA, Canada, Japan, Australia, Western Europe and New Zealand*
    c. Individuals who inject illicit drugs or use crack cocaine
    d. Individuals with medical conditions that have been reported to increase the risk of tuberculosis disease once infected:
        i. diabetes mellitus
        ii. chronic malabsorption syndrome
        iii. chronic renal failure
        iv. leukemia, lymphomas, Hodgkin's disease
        v. cancer of the head or neck
        vi. weight loss of > 10% below ideal body weight
        vii. silicosis
        viii. gastrectomy, or jejunoileal bypass
    e. Residents and staff in long-term care facilities.
    f. Health care personnel
    g. Inmates in the Department of Corrections
    h. Staff with direct inmate contact in the Department of Corrections and jails
    i. Employees of HIV/AIDS adult daycare centers
    j. Homeless shelter residents

k. Individuals who increase their mm reading by 10mm or more within 2 years (converter)
l. Mycobacteriology lab personnel
m. Children and adolescents exposed to high-risk adults (homeless, substance abuse, incarcerated, HIV positive)
n. People who have traveled outside the US and stayed with family and friends who live in high incidence areas, for greater than 1 month cumulatively

3. A reaction of $\geq$ 15 mm induration is considered positive for:
    a. Individuals who do not have any of the above risk factors.

Nursing Action:

1. Store the tuberculin skin test solution in the vaccine refrigerator. Tuberculin solution can be adversely affected by exposure to light or temperature extremes
2. Advise the patient to return to the health department between 48 and 72 hours to have the PPD read.
3. Instruct the patient not to scratch the PPD site or place a Band-Aid over the site of injection.

Criteria for calling physician:

1. Contact physician if there is any question about whether to carry out any part of this standing order.
2. Contact physician if the individual has an allergic reaction to the PPD.

Follow-up requirements:

If the PPD result is positive:

1. Obtain a posterior/anterior view chest X-ray for individuals 5 years or older and add a lateral view chest X-ray for children less than 5 for all individuals with an induration considered positive based on the above criteria. Appropriate shielding should be used for all pregnant women,
2. Complete a TB Epidemiological form (DHHS 1030).
3. Obtain a HIV test unless the individual refuses.
4. Notify the health department TB nurse about all patients determined to have a positive PPD for further follow-up. (This may be modified if the local health department has a different procedure for positive PPD follow-up.

Resources:

- North Carolina TB Control Manual 2012 edition.

Legal Authority:

- Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written:_____

Approved by: _____ Date:_____

Approved by: _____ Date:_____

Approved by: _____ Date:_____

Sample Standing Order: Obtaining an Interferon Gamma Release Assay (IGRA)

Assessment:
This standing order shall be initiated by a PHN who has completed a TB program orientation. This standing order will be used to obtain an IGRA in any of the following situations and if subjective and objective findings exist:

- when an individual is a contact to active tuberculosis (TB), or
- in individuals with signs and or symptoms of active tuberculosis (abnormal chest X-ray, positive AFB smear or culture, productive cough, fever, night sweats, shortness of breath, chest pain, unexplained appetite loss, unexplained weight loss, or unexplained fatigue), or
- Individual has a new positive HIV test

Subjective findings:
Screening for Mycobacterium tuberculosis is:

- Requested by patient, or
- Requested by medical provider, or
- Required by communicable disease/TB rules

Objective findings:
Medical record indicates:

- The patient has not recently had (within 4-6 weeks) viral infections (rubella, mumps, influenza, measles, chicken pox) or live virus vaccinations (measles, mumps, rubella)
-
- The patient has no documentation of a positive Interferon Gamma Release Assay (IGRA).

Implementation:
Refer to or insert the lab test procedure for drawing the blood/shipping to reference lab, etc.

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Nursing Action:

- Review the IGRA lab result.
    - If positive, give results to the patient and proceed with the follow-up requirements below.
    - If results are negative, provide results to the patient.
    - If results are indeterminate, or inconclusive, repeat the IGRA as soon as possible.

Criteria for calling physician:

- Call the physician if there is any question about whether to implement the standing order.
- Call the physician for further guidance if an IGRA is repeated because the results are indeterminate and the second result is also indeterminate.

Follow-up requirements:
If the IGRA result is positive:

5. Obtain a posterior/anterior view chest X-ray for individuals 5 years or older and add a lateral view chest X-ray for children less than 5. Provide appropriate shielding for pregnant women.
6. Complete a TB Epidemiological form (DHHS 1039).
7. Obtain a HIV test unless the individual refuses.
8. Notify the health department TB nurse about all patients determined to have a positive IGRA for further follow-up. (This may be modified if the local health department has a different procedure for positive IGRA follow-up.

Resources:

- North Carolina TB Control Manual 2018 edition.

Legal Authority:

- Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written: _____

Approved by: _____ Date:_____

Approved by: _____ Date:_____

Approved by: _____ Date:_____