Who To Test

Targeted tuberculin testing for latent TB infection (LTBI) is a strategic component of tuberculosis (TB) control for purposes of identifying persons at high risk for latent TB infection (LTBI) or TB disease who would benefit from treatment. Targeted tuberculin testing should be conducted only among groups at high risk and discouraged in those at low risk. **Public Health agencies in Colorado can only provide targeted testing as TB Program resources allow, or if the agency has alternate funding resources.** All testing activities should include a plan for follow-up care of persons with LTBI or disease and periodic program evaluation.

A local chief medical health officer may conduct required targeted screening programs of populations who are at increased risk of developing tuberculosis or having LTBI, as defined by the Centers for Disease Control and Prevention, and offer treatment as appropriate. Such screening programs shall not be implemented without the prior approval of the local board of health, state board of health and the state chief medical health officer.[1] Contact the TB Program for assistance with this process.

The Mantoux tuberculin skin test (TST), intradermal injection of purified protein derivative (PPD), is the standard method of identifying persons infected with *Mycobacterium tuberculosis* (MTB). Multiple puncture tests (MPTs), such as the Tine test, should not be used. The MPTs are not reliable because the amount of tuberculin injected intradermally cannot be precisely controlled. TB skin testing is both safe and reliable throughout the course of pregnancy and during breastfeeding.

If previous TST results cannot be provided (measured in mm, not “positive” or “negative”), repeat the test unless there was a severe reaction (e.g. blistering, ulceration, or necrosis) at the previous site of injection. TB skin retesting should NOT be done if there is appropriate documentation of a previous positive TST and/or previous treatment for LTBI or active TB.

In general, high-risk groups that should be tested for TB infection include:

- persons with HIV infection/AIDS
- recent close contacts to persons with infectious pulmonary TB disease
- persons with fibrotic lesions on chest x-ray consistent with healed TB
- persons who inject drugs or use other high risk substances, such as crack cocaine, and alcoholics

[1] State of Colorado Rules and Regulations Pertaining to Epidemic and Communicable Disease Control (6 CCR-1009-1). Regulation 4: Treatment and Control of Tuberculosis; K. (1-6).

- persons with medical conditions which increase the risk of TB disease[2]
- residents and employees of high risk congregate settings such as correctional institutions, long-term residential care facilities (nursing homes, mental institutions, etc.), hospitals and other health care facilities, and homeless shelters.
- health care workers and volunteers who serve high risk clients who undergo employment screening and cannot provide documentation of a previous TST or information about appropriate follow-up for a "positive" skin test
- mycobacteriology laboratory personnel
- foreign-born persons who have arrived within five years from countries that have a high TB incidence or prevalence (most countries in Africa, Asia, Latin America, Eastern Europe, and Russia)
- children less than 4 years of age, or children and adolescents exposed to adults in high risk categories
- adult contacts to children with TB infection (see "Contact Investigation")
- persons with a history of inadequately treated TB

NOTE: Colorado Department of Public Health and Environment (CDPHE) TB Program does not provide or pay for skin test products, chest x-rays, or chest x-ray interpretations for jail inmates, persons undergoing immigration examinations, or paid employees/volunteers of health care facilities, long term care facilities, drug treatment centers, correctional facilities, jails, homeless shelters, schools, and child care facilities. **The employer or facility is responsible for these costs and services.** Public health agencies in Colorado can only provide targeted testing for residents in these high-risk settings if TB Program resources allow or if the agency has alternate funding resources.

[2]Medical conditions which increase the risk of TB disease include diabetes mellitus, silicosis, recent infection with MTB (within the past 2 years), bone marrow and organ transplant recipients, prolonged high-dose corticosteroid therapy and other immunosuppressive therapy, chronic renal failure who are on hemodialysis, some hematological disorders (e.g., leukemias and Hodgkin's disease), other specific malignancies (e.g., carcinoma of the head or neck), chronic malabsorption syndromes, weight of 10% or more below ideal body weight, and intestinal bypass or gastrectomy.

How to Apply the Tuberculin Skin Test

1. Administer the tuberculin skin test using the Mantoux technique; intradermal injection of purified protein derivative (PPD). **NOTE: Some PPD vial stoppers contain 41.6% latex, which could pose a concern for those with latex allergy. For those persons who have a latex allergy, use vials without latex stoppers or remove the stopper prior to drawing up PPD.**

2. Mantoux test procedure

   - Equipment needed[3]: gloves, sharps container, PPD tuberculin (Tubersol or Aplisol), tuberculin syringe and safety needle, and alcohol pads. **NOTE: Opened PPD tuberculin vials must be dated and discarded after 30 days. Also see package insert for appropriate storage information.**

   - Obtain written consent as per agency requirements (See "Forms - Consent Form(s) – EXAMPLES").

   - Follow infection control procedures, including the use of gloves and a sharps container.

   - Clean the injection site, the upper, outer, lateral aspect of the left forearm 1-2 inches below the antecubital fossa, with an alcohol pad or alternative skin cleanser (for those allergic to alcohol). The left forearm is the standard site for TB skin testing.

   - Using a disposable safety needle and syringe, inject 0.1 ml of PPD tuberculin containing 5 TU between the layers of the skin (intradermally) with the needle bevel facing upward.

   - The injection should produce a discrete, pale elevation of the skin (a wheal) 6-10 millimeters (mm) in diameter. **NOTE: Repeat the test on the opposite arm or the same arm, 3 inches from the original site, if a 6-10 mm wheal is not produced.**

[3] See Administrative Issues, page 5-1, "How to Obtain Skin Testing Materials"

- Record the date and time of TST administration, location of injection site, dose, name of person who administered the test, name and manufacturer of tuberculin product used, lot number, expiration date, and the reason for testing.

How to Read/Measure/Record Test Results

1. Read the tuberculin skin test 48 to 72 hours after the injection.

   - If the individual fails to show up for the scheduled reading, positive reactions may still be measurable up to one week after testing.

   - If the results appear negative and more than 72 hours have passed, the test should be repeated. It can be repeated immediately, or after 1 week if two-step testing is required (see page 12, "Two Step Tuberculin Skin Testing").

   - TST results should be read by designated, trained personnel. Do not accept self-reading of TST results.

2. Measure the tuberculin skin test site crosswise to the axis of the forearm.

3. Measure only induration (swelling that can be felt) around the site of the injection. Do NOT measure erythema (redness). A tuberculin skin test with erythema but no induration is non-reactive.

4. Record the test result in mm, not as "positive" or "negative." An exact reading in mm may be necessary to interpret whether conversions occur on a subsequent test. Record a tuberculin skin test with no induration as "0 mm."

5. Adverse reactions to a TST (e.g. blistering, ulcerations, necrosis) should be reported to the Food and Drug Administration's Med Watch Program at 1-800-FDA-1088 or via the Internet at www.fda.gov/medwatch.

6. All licensed hospitals and nursing home facilities must maintain a register of the TST results of health care workers in their facility, including physicians and physician extenders who are not employees of the facility but provide care to or have face-to-face contact with patients in the facility. The facility must maintain such TST results as confidential.[4]

[4] State of Colorado Rules and Regulations Pertaining to Epidemic and Communicable Disease Control (6 CCR-1009-1). Regulation 4: Treatment and Control of Tuberculosis; J.

NOTE: CDPHE TB Program does not provide or pay for skin test products, chest x-rays, or chest x-ray interpretations for jail inmates, persons undergoing immigration medical examinations and paid or volunteer employees of health care facilities, long term care facilities, drug treatment centers, correctional facilities, jails, homeless shelters, schools, and child care facilities. **The employer is responsible for these costs and services.** Employers may purchase Purified Protein Derivative (PPD) through Adventis-Pasteur at 1-800-822-2463 (Tubersol PPD, 5 TU) or King Pharmaceuticals at 1-800-776-3637 (Aplisol PPD, 5 TU). Public Health agencies in Colorado can only provide targeted testing for residents in these high-risk settings if TB Program resources allow or if the agency has alternate funding resources.

How to Interpret Test Results

Use the chart below to interpret tuberculin skin test results:

5 or more mm	10 or more mm	15 or more mm
Induration of 5 or more mm is considered positive for: ▪ Persons with HIV infection/AIDS ▪ Recent close contacts to persons with infectious pulmonary TB disease ▪ Persons with fibrotic lesions on chest x-ray consistent with healed TB ▪ Persons with organ transplants or other immuno-suppressed persons (receiving the equivalent of ≥ 15mg/day of Prednisone for ≥ 1 month)	Induration of 10 or more mm is considered positive for: ▪ Foreign-born persons who have recently arrived (within five years) from countries that have a high TB incidence or prevalence (most countries in Africa, Asia, Latin America, Eastern Europe, Russia) ▪ Persons who inject drugs or use other high risk substances, such as crack cocaine, and alcoholics ▪ Residents and employees of high risk congregate settings such as correctional institutions, long-term residential care facilities (nursing homes, mental institutions, etc.), hospitals and other health care facilities, and homeless shelters. ▪ Mycobacteriology laboratory personnel ▪ Persons with other medical conditions which increase the risk of TB disease ▪ Children less than 4 years of age, or children and adolescents exposed to adults in high risk categories	Induration of 15 or more mm is considered positive for: ▪ Persons with no known risk factors for TB

In addition:

1. For persons previously skin tested, an increase in induration of 10 mm within a 2-year period is classified as a conversion to positive.

2. False negative reactions may be due to:
   - Anergy (see "Anergy Testing")
   - Recent TB infection (within the past 10 weeks)
   - Very young age (< 6 months of age-because their immune systems are not fully developed)
   - Overwhelming TB disease
   - Live virus vaccination (see below)
   - Some viral infections (measles, mumps, chickenpox, and HIV)
   - Corticosteroids and other immunosuppressive agents at doses of 2 mg/kg/day or greater for 2 or more weeks

3. False positive reactions may be due to:

   - Non-tuberculous mycobacteria
   - BCG vaccination
   - Local latex allergic reactions

4. Vaccination with live viruses (e.g. Measles, Mumps, Rubella, Varicella, Oral Polio, and Yellow Fever) may also interfere with TST reactivity and cause false negative reactions. TB skin testing should be done on either the same day as vaccination with live virus or 5-6 weeks after vaccination.

5. Call the TB Program regarding TST reactions for which interpretation and medical follow-up is unclear.

NOTE: Physicians, health care providers and health care facilities must report a TST result of 5 mm or more, if it occurs in a health care worker, correctional facility worker, or detention facility worker who has had close contact to a TB case. This must be reported within 7 days (see "Reporting Procedures").

BCG (Bacillus Calmette-Guerin) Vaccines

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis (M. bovis)*. Because their effectiveness in preventing infectious forms of TB is uncertain, they are not recommended as a TB control strategy in the U.S. except under rare circumstances (see below). They are, however, used commonly in other countries.

Tuberculin Skin Testing of an Individual with a History of BCG Vaccination

1. A history of BCG vaccination is not a contraindication to tuberculin skin testing if the person is at risk of exposure to TB.

2. A false positive reaction may occur in persons vaccinated with BCG. However, tuberculin reactivity caused by BCG vaccination wanes with time and is unlikely to persist > 10 years.

3. Consider treatment for LTBI in BCG-vaccinated persons who are infected with HIV and who are at risk for LTBI if they have a skin test reaction of $\geq$5 mm induration or with a nonreactive skin test if they have a history of contact to infectious TB.

4. A diagnosis of LTBI and the use of therapy should be considered for any BCG-vaccinated person who has a TST reaction of $\geq$10 mm induration, especially if:

    - the vaccinated person is exposed continually to populations in which the prevalence of TB is high (e.g., some health care workers, employees and volunteers at homeless shelters, and workers at drug-treatment centers)

    - the vaccinated person was born or has resided in a country in which the prevalence of TB is high; or

    - the vaccinated person is a contact of another person who has infectious TB, particularly if the infectious person has transmitted TB to others

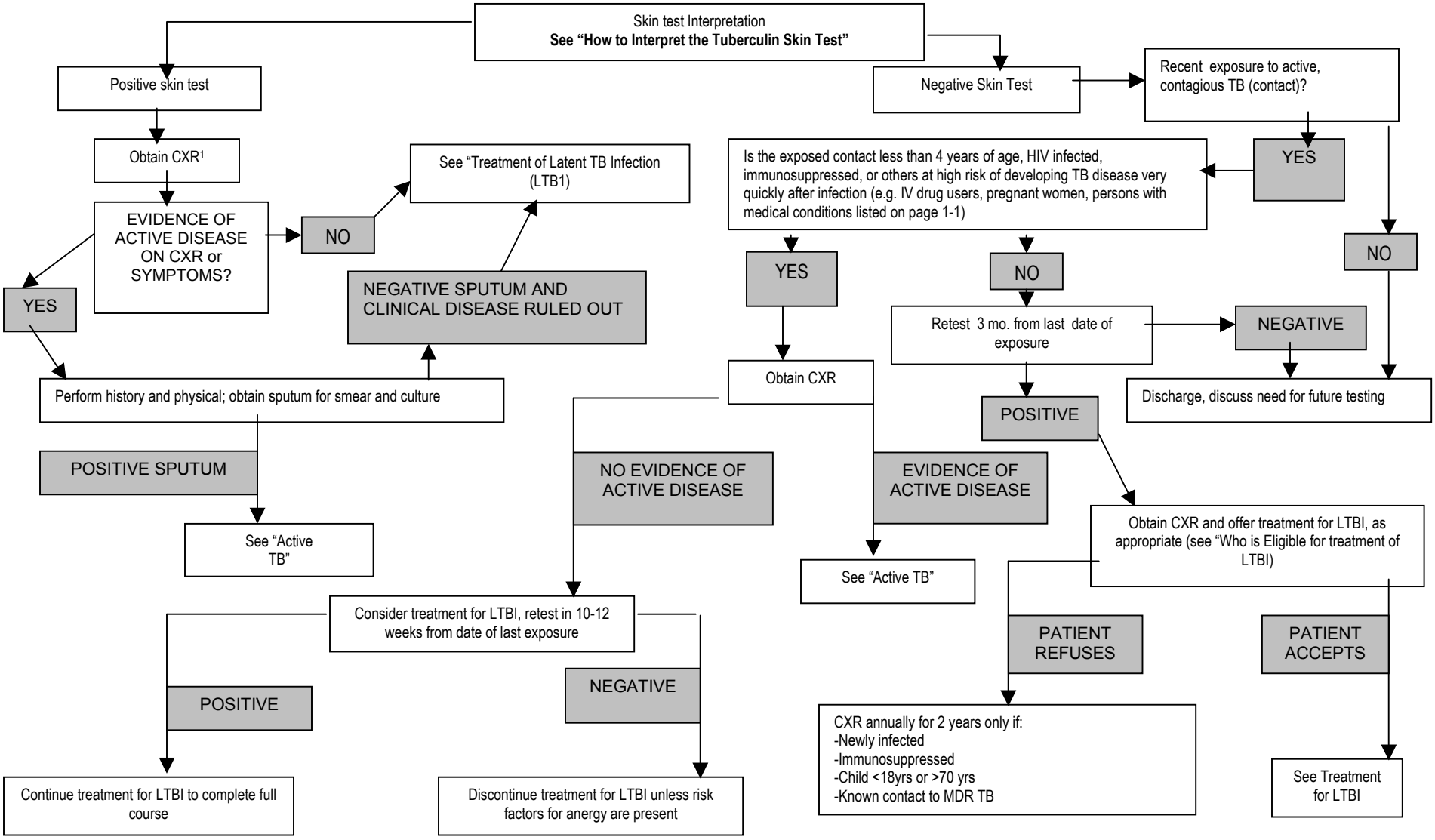
Use of BCG in the U.S. should be considered only in rare circumstances. One hypothetical example would be an infant or child who lives in a setting where the likelihood of TB transmission and subsequent infection is high, when no other prevention measures can be implemented (e.g., removing the child from the source of infection). For all practical purposes,

BCG should not be used in the United States since resources are available to stop the transmission of TB (e.g. effective therapy, resources for providing direct observed therapy and assistance of Social Services to ensure a safe environment for such a child). BCG vaccine should only be given in consultation with the TB Program at CDPHE.

What to do After Interpreting the Skin Test

The flow chart on the following page details the steps to take after interpreting whether a skin test is positive or negative.

What to Do After Interpreting The TB Skin Test



[1]Pregnant women found to have a positive TST should receive a chest x-ray after delivery or an immediate, shielded chest x-ray if:
-Symptoms of active disease are present
-They are likely to have been recently infected.
-They have high-risk medical conditions (e.g., HIV infection)

Two-Step Tuberculin Skin Testing (Booster Phenomenon)

Introduction

Delayed type hypersensitivity (a skin test reaction) may wane over the years in some people who are infected with TB. When these people are skin tested many years after infection, they may have a negative reaction. However, this negative skin test may stimulate (boost) their ability to react to tuberculin, causing a positive reaction to subsequent tests. This boosted reaction may be interpreted as new infection. Two-step testing is used to establish a true baseline skin test.

Thus, it is recommended that a baseline two-step tuberculin skin test be performed on workers in health care facilities, correctional institutions and jails, long term care facilities for the elderly, homeless shelters, drug treatment centers, residents of long-term care facilities, and other adults who will be re-tested periodically. Two-step tuberculin skin testing should be performed on these individuals who cannot document a history of a negative tuberculin skin test within the past year.

Protocol:

1. Apply the tuberculin skin test[5].

2. If the initial skin test is positive, consider person infected and refer to "What to do After Interpreting the Skin Test."

3. If the initial tuberculin skin test is negative:

    - It should be repeated within 1-3 weeks using the same dose and strength of tuberculin.

[5]An individual who can provide documentation of a TST by the Mantoux technique within the preceding year should have an initial skin test performed, and should be managed on the basis of that result. There is no need for a second test because the earlier test is, in effect, the first of a two-step test.

- If the second test is negative, the individual is classified as uninfected and retested at routine intervals (two-step testing is not required for subsequent tests unless one or more years have elapsed since the last test).

4. If the second test is positive, consider person infected and refer to "What to do After Interpreting the Skin Test".

Anergy Testing

Anergy testing is a diagnostic procedure used to obtain information regarding the competence of the cellular immune system. Persons with an impaired cellular immune system (e.g. HIV-infected persons, severe or febrile illness, measles or other viral infections, Hodgkin's Disease, sarcoidosis, live virus vaccination, corticosteroid or immunosuppressive therapy) may have suppressed reactions to a TST even if infected with TB. However, there are no simple skin testing protocols that can reliably identify persons as either anergic or nonanergic and that have been proven to be feasible for application in public health tuberculosis screening programs. Factors limiting the usefulness of anergy skin testing include:

- problems with standardization and reproducibility
- the low risk for TB associated with a diagnosis of anergy
- the lack of apparent benefit of treatment of LTBI for groups of anergic HIV-infected persons

The results of currently available anergy-testing methods in U.S. populations have not been demonstrated to make a useful contribution to most decisions about treatment of LTBI. **Therefore, the use of anergy testing in conjunction with TB skin testing is no longer recommended routinely for screening programs for TB infection conducted among HIV-infected persons in the United States.[6]**

[6] If a clinician elects to use anergy testing as part of a multifactorial assessment of a person's risk for TB, the two Food and Drug Administration-approved Mantoux-method tests (mumps and Candida), used together, with cut-off diameters of 5 mm of induration, are recommended. Efforts to apply the results of anergy testing to treatment of LTBI decision must be supplemented with information concerning the person's risk for infection with TB. CDPHE TB Program does not provide antigens for anergy testing. These must be obtained through a local pharmacy with a physician's order.

References

1. Centers for Disease Control and Prevention. Essential components of a tuberculosis prevention and control program; and screening for tuberculosis and tuberculosis infection in high-risk populations: recommendations of the Advisory Council for the Elimination of Tuberculosis: MMWR 1995;44(RR-11):18-34.

2. Colorado Medical Directors Association and Colorado Department of Public Health and Environment, Division of Disease Control and Environmental Epidemiology. Tuberculosis surveillance and screening for long term care facilities in Colorado. March 6, 2001.

3. Updated OSHA Tuberculosis Compliance Directive (CPL 2.106). Feb. 9, 1996.

4. Centers for Disease Control and Prevention. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13)

5. Centers for Disease Control and Prevention. The role of BCG vaccine in the prevention and control of tuberculosis in the United States. MMWR 1996;45(No. RR-4)

6. Centers for Disease Control and Prevention. Core curriculum on tuberculosis. Fourth Edition, 2000.

7. Colorado Revised Statutes; CRS 25-4-506(b).

8. Colorado Rules and Regulations Pertaining to Epidemic and Communicable Disease Control (6 CCR-1009-1).

9. Centers for Disease Control and Prevention. Anergy skin testing and preventive therapy for HIV-infected persons: revised recommendations: MMWR September 5, 1997; 46(No. RR-15).

10. Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations: MMWR October 30, 1998; 47 (No. RR-20).

11. Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection: MMWR June 9, 2000; 49 (No. RR-6).

Resources

For questions regarding tuberculin skin testing, call the TB Program (303) 692-2638.