Tuberculosis Control
Program Manual

UTAH DEPARTMENT OF
HEALTH

October 2017

Tuberculosis Control
Physical Address: 288 North 1460 West Salt Lake City, Utah 84116
Mailing Address: Box 142104 Salt Lake City, UT 84114-2104
Phone: (801) 538-6191
Fax: (801) 538-9913
Website: http://health.utah.gov/epi/diseases/TB/

Contents

Introduction 3
2017 Program Goals and Objectives 4
Testing for Tuberculosis Infection 7
Treatment of Tuberculosis Infection 14
Active Tuberculosis Disease (ATBD) Initial Evaluation 19
Basic Guidelines for Treating Active Tuberculosis Disease 23
Contact Investigation 27
Interjurisdictional Referrals 42
Isolation Considerations 43
Transmission Prevention & Infection Control Planning 45
Improving Adherence with Therapy 49
Isolation of Non-Adherent Individuals with ATBD 51
Travel Restrictions 53
Utah Public Health Laboratory/ Mycobacteriology Laboratory 58
Utah Public Health Laboratory Specimen Collection and Transport 61
Confidentiality in TB Control 67
Criteria for Hospitalization in Secure TB Unit at UUMC 68
TB Evaluation for Class B Refugees/Immigrants 69
Tuberculin Skin Testing in Schools 72
Tuberculin Skin Testing in Post-Secondary Schools 73
Tuberculin Skin Testing in Dialysis Centers 74
Screening for TB in Health Care & other High-Risk Congregate Settings 76
Disease Reporting 78
Managing a TB Outbreak 80
Program Resources 81
QFT Testing and CXR 82
Ordering Anti-tuberculosis Medication 83
TB Control Program: Use of State PPD 84
Incentives and Enablers 85
Required Reports and Forms 86
Site Visits 87
Medical Interpreters/Translators 88
State Consultants 89
Classification System for TB 90
TB Medicaid Program 91

Introduction

The Tuberculosis (TB) Control Program at the Utah Department of Health (UDOH) in partnership with local health departments (LHDs) and health care providers is responsible for the implementation of the Utah Administrative Code Communicable Disease Rule (R388-804), which outlines a multidisciplinary approach to communicable and infectious disease control. The Special Measures for the Control of Tuberculosis (Rule R388-804) gives the Program the authority to write rules to control TB. The purpose of this rule is to focus the efforts of TB control on disease elimination. The rule also establishes standards for control and prevention of TB as required by the Utah Communicable Disease Act and Communicable Disease-Treatment, Isolation and Quarantine Procedures (Utah Health Code 26-6B). The standards outlined in this rule constitute the minimum expectations in the care and treatment of individuals diagnosed with, suspected to have, or exposed to TB.

While Utah is a low incidence state, the burden of identifying, evaluating and treating TB remains significant. TB morbidity is widely distributed throughout the state involving urban and rural areas. While urban areas experience TB more frequently, rural areas may not have sufficient capacity and capital to address cases in their area. Cases among foreign born persons continue to account for the majority of cases in Utah. Treating TB among refugee and immigrant populations presents cultural and linguistic challenges that can complicate the treatment of TB.

The Program will prevent, control and eliminate TB in Utah by ***fostering community health partnerships with those who serve high risk populations through culturally aware identification, evaluation, treatment and education***. Through Human Resource Development activities, the Program works closely with local health departments, throughout the thirteen health districts in Utah to provide resources and expertise to ensure that individuals with active TB disease are treated to completion. The Program continues to support the Utah Public Health Laboratory in order to strengthen capacity to provide timely and reliable TB laboratory services.

This manual describes policies, protocols, and recommendations for the State of Utah. The protocols cover common as well as complex clinical issues that arise in the control of TB. These protocols are based on recommendations of the Centers for Disease Control and Prevention (CDC), the American Thoracic Society (ATS), the Infectious Disease Society of America (IDSA), and the opinions of local and national experts in TB diagnosis, treatment, and control.

Although an attempt has been made to design a comprehensive manual, protocols cannot and should not be substituted for clinical judgment. For most individuals however, strict adherence to clinical protocols will result in improved care and the control of TB. Clinicians are strongly encouraged to seek consultation for issues related to individual cases that may not be fully discussed in this manual.

2017 Program Goals and Objectives

IMPROVED TB CASE DETECTION AND MANAGEMENT

Program Objectives:

- Objective 1.1: Ensure that at least 92% of individuals with a high-likelihood of having TB receive a medical evaluation within 14 days for active TB disease.
- Objective 1.2: Increase the proportion of TB cases with a pleural or respiratory site of disease in individuals ages 12 or older that have sputum-culture results reported to 92%.
- Objective 1.3: Ensure that 92% of sputum-smear positive individuals initiate treatment within 7 days of specimen collection.
- Objective 1.4: Ensure that 94% of individuals with active TB disease are placed on appropriate therapy following CDC/ATS guidelines.
- Objective 1.5: Ensure that at least 92% of individuals with active TB disease are provided directly observed therapy.
- Objective 1.6: Ensure that at least 77% of individuals with positive sputum-culture results convert to sputum culture-negative within 60 days of initiating treatment.
- Objective 1.7: Ensure that at least 92% of individuals with newly diagnosed active TB disease, for which therapy for one year or less is indicated, complete therapy within 12 months.

CONTACT INVESTIGATION

Program Objectives:

- Objective 2.1: Contacts will be identified for at least 90% of newly reported sputum AFB-smear positive TB cases.
- Objective 2.2: At least 85% of contacts of newly reported sputum AFB-smear positive TB cases will be evaluated for TB infection and disease.
- Objective 2.3: At least 80% of contacts to sputum AFB-smear positive TB cases who are newly diagnosed with TB infection will start treatment.
- Objective 2.4: At least 74% of infected contacts to sputum AFB-smear positive TB cases who are started on treatment for TB infection will complete therapy.

EVALUATION OF IMMIGRANTS AND REFUGEES

Program Objectives:

- Objective 3.1: Ensure that local health departments locate and initiate medical evaluation for at least 80% of refugees and immigrants with abnormal chest x-rays read overseas as consistent with TB, classified as A or B/TB for active TB disease, within 30 days of being notified of A or B/TB classification.

- Objective 3.2: Ensure that local health departments complete the medical evaluation for at least 85% of refugees and immigrants with abnormal chest x-rays read overseas as consistent with TB, classified as A or B/TB for active TB disease, within 90 days of being notified of A or B/TB classification.

- Objective 3.3: Ensure that local health departments initiate treatment for at least 65% of refugees and immigrants with abnormal chest x-rays read overseas as consistent with TB, classified as A or B/TB for active TB disease, upon diagnosis of TB infection during the medical evaluation.

- Objective 3.4: Ensure that local health departments complete treatment for at least 60% of refugees and immigrants with abnormal chest x-rays read overseas as consistent with TB, classified as A or B/TB for active TB disease, upon diagnosis of TB infection during the medical evaluation who begin treatment.

- Objective 3.5: Ensure 80% completeness of Electronic Disease Notification data.

SURVEILLANCE OF TB CASES AND TB REPORTING

Program Objectives:

- Objective 4.1: Decrease the TB case rate for foreign-born persons to less than 14.0 cases per 100,000.

- Objective 4.2: Decrease the TB case rate for children younger than 5 years of age to less than 0.8 cases per 100,000.

- Objective 4.3: Ensure that all verified cases of TB are reported with at least 95% of core data items being complete.

- Objective 4.4: Drug susceptibility results will be reported for 100% of all newly reported culture-positive TB cases.

- Objective 4.5: Genotyping results will be reported for at least 90% of all culture-confirmed TB cases.

- Objective 4.6: A positive or negative HIV test result will be reported for at least 90% of all newly reported TB cases.

HUMAN RESOURCE DEVELOPMENT

Program Objectives:

- Objective 5.2: Provide at least 150 hours of Tuberculin Skin Test (TST) training.
- Objective 5.3: Provide at least 350 of non-TST, TB-related training.
- Objective 5.4: Post at least 24 postings to the TB Listerv.

Other Resources

Centers for Disease Control and Prevention National TB Program Objectives and Performance Targets for 2020

Testing for TB Infection

Targeted testing for TB infections is a strategic component of tuberculosis (TB control. It identifies persons at high risk for developing TB disease who would benefit from treatment, if detected. Persons with increased risk for developing TB disease include those recently infected with *Mycobacterium tuberculosis* and those who have clinical conditions that are associated with an increased risk for progression of TB infection to active TB disease (ATBD). Infected persons who are at high risk for developing ATBD should be considered for treatment of TB infection regardless of age.

Targeted testing programs should be conducted only among high-risk persons. Persons administering/reading the Tuberculin Skin Test (TST) or drawing blood for an Interferon Gamma Release Assay (IGRA) should be properly trained. **The decision to test should be a decision to assess the individual and consider treatment of TB infection if the person has a positive result.** Screening persons at low risk for TB is discouraged because this test has poor predictive value in unselected (low risk) populations and diverts resources away from higher priority TB control activities such as the identification and treatment of ATBD cases and contact investigation.

It is recommended that the following groups be considered for screening:

- Close contacts of persons known or with a high-likelihood of having TB
- Foreign-born persons, including children, who have recently arrived from areas that have a high incidence of TB
- Health care workers who serve high-risk individuals
- Some medically under-served, low-income populations as defined locally
- Employees or residents of high-risk congregate settings such as hospitals, correctional facilities, homeless shelters, nursing homes, or drug treatment centers
- High-risk populations, defined locally as having increased prevalence of TB. In Utah this includes: Asians, Africans, Pacific Islanders, Hispanics, Native Americans, migrant farm workers, people experiencing homelessness, and Latter Day Saints (LDS) returned from missions
- Mycobacterial laboratory personnel
- Intravenous or other high-risk drug users
- Infants, children, and adolescents exposed to adults in high-risk categories

The following persons are at higher risk for ATBD once infected and testing should be considered if they have risk of exposure:

- Persons who are HIV-positive
- Persons who have medical conditions known to increase the risk for ATBD if infection occurs (diabetes, silicosis, prolonged corticosteroid therapy, cancer of the head and neck, hematologic and reticuloendothelial diseases, end-stage renal disease, intestinal bypass or gastrectomy, chronic malabsorption syndromes, low body weight [10% or more below ideal])
- Persons with rheumatoid arthritis being treated with TNF-alpha antagonists or other immunosuppressive drug.

Procedure: Use the UDOH TB Screening Form, and do not routinely repeat the TST or IGRA if documentation of previous positive results exists.

Tuberculin Skin Test (TST)

a. The TST should be administered by the Mantoux technique as described in the CDC Core Curriculum. **Multiple puncture tests (e.g., the Tine Test) should not be used**. Purified protein derivative (PPD), the antigen used in the TST, should be stored between 2 and 8°C (35 and 46°F) and protected from light. Vials in use more than 30 days should be discarded due to possible oxidation and degradation, which may affect potency. Syringes should not be pre-filled and the use of safety syringes is recommended. Care should be taken to avoid inserting air directly back into the serum remaining in the vial. Gloves are optional; consult the infection control requirements of your facility. An informed consent to administer the TST is recommended.

b. Reading of the TST should only be done by a trained health care worker; individuals should **never** be allowed to read their own reaction. Measure only the **hard**, swollen area known as the induration and record the size of the induration (between palpable borders laterally) in millimeters (mm), not as "positive" or "negative." Results are read 48-72 hours after administering the test. If the individual fails to return for the scheduled reading but returns up to a week after the test administration, examine the test site and measure any induration present. If there is no reaction or it is too small to be classified as positive, repeat the test.

c. Classifying the results should be done using UDOH's Tuberculosis Provider Guide - Testing for TB Infection & Guidelines for Post-Test Referral.

d. Tuberculin skin testing **is not contraindicated** for persons who have been vaccinated with Bacillus Calmette-Guérin (BCG), and the skin test results of such persons are used to support or exclude the diagnosis of TB infection. The booster phenomenon may occur among persons who have had a prior BCG vaccination. An IGRA might be a better choice for assessing TB infection, since it will not falsely react in a person with a history of BCG vaccination. A diagnosis of TB infection and the use of treatment for infection should be considered for any BCG-vaccinated person using the same guidelines as described in procedure 'c' above, especially if any of the following circumstances are present:
   - The vaccinated person is a contact of a person who has ATBD, particularly if the person is infectious and has transmitted *M. tuberculosis* to others.
   - The vaccinated person was born or has resided in a country in which the prevalence of TB is high.
   - 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 employees at drug-treatment centers).

e. The absence of a reaction to a TST does not rule out the diagnosis of ATBD or TB infection. In immunosuppressed persons, delayed-type hypersensitivity responses such as tuberculin reactions may decrease or disappear. This condition, known as anergy, may be caused by many factors, such as HIV infection, severe or febrile illness, measles or other viral infections, Hodgkin's disease, sarcoidosis, live-virus

vaccination, or the administration of corticosteroids or immunosuppressive drugs. On average, 10% to 25% of individuals with ATBD have negative reactions when given a TST. **Do not rule out diagnosis based on a negative TST result. Consider anergy in persons with no reaction if they:**

- are HIV-positive
- have overwhelming TB disease
- have severe or febrile illness
- have viral infections
- received a live-virus vaccination in the 30 days previous to testing
- are receiving immunosuppressive therapy/disease

Note: Anergy skin testing is no longer routinely recommended.

f. In some people who are infected with *M. tuberculosis*, delayed-type hypersensitivity to tuberculin may wane over the years. When these people are given a TST many years after infection, they may have a negative reaction. However, this skin test may stimulate (boost) their ability to react to tuberculin, causing a positive reaction to subsequent tests. This booster reaction may be misinterpreted as a new infection. The booster phenomenon may occur at any age; its frequency increases with age and is highest among older persons. Boosted reactions may occur in persons infected with nontuberculous mycobacteria or in persons who have had a prior BCG vaccination.

Two-step testing is used to reduce the likelihood that a boosted reaction will be misinterpreted as a recent infection. If the reaction to the first test is classified as negative, a second test should be done 1-3 weeks later. A positive reaction to the second test probably represents a boosted reaction (past infection or prior BCG vaccination). On the basis of this second test result, the person should be classified as previously infected and cared for accordingly. This would not be considered a skin test conversion. If the second test result is also negative, the person should be classified as uninfected. In these persons, a positive reaction to any subsequent test is likely to represent new infection with *M. tuberculosis* (skin test conversion). Two-step testing should be used for **initial** skin testing of adults who will be retested periodically, such as health care workers and correctional staff. (If the individual has record of a negative PPD within the past 12 months, then the test done upon hire may be considered the second test.)

g. *False **negative** TST or IGRA reactions* may be due to:

- Anergy
- Recent TB infection or overwhelming TB disease
- Very young age (< 6 months age)
- Live virus vaccinations* • Some viral infections (measles, mumps, chickenpox, and HIV)
- Corticosteroids and other immunosuppressive agents at doses of 2mg/kg/day or greater for 2 or more weeks

*Vaccination with live viruses (e.g. measles, mumps, rubella, varicella, typhoid oral, polio oral and yellow fever) may interfere with TST reactivity and cause false

negative reactions. TST should be done on either the same day as vaccination with live virus or 4-6 weeks after vaccination.

h. *False **positive** TST reactions* may be due to:
   - Nontuberculous mycobacteria
   - BCG vaccination

i. Tuberculin skin testing in pregnant women is safe and reliable. Routine TST screening among pregnant women is not indicated because pregnancy itself does not increase the risk for TB infection. However, pregnant women at high-risk for TB infection or disease should be tested.

j. Adverse reactions to a TST (e.g. severe 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.

k. In most cases, an IGRA (QFT or T-Spot) blood assay can be substituted for a TST. Usefulness would be most evident in identifying infection in those with a history of BCG vaccination (BCG will not cause a false positive). Two-step testing is not necessary or recommended. Sensitivity is comparable to a TST, and specificity appears superior. The QFT is available through the Utah Public Health Laboratory, as well as private labs. Cost varies, and will not routinely be reimbursed by the TB Control Program. Contact the Utah Public Health Laboratory, 801- 965-2400 for more information. For technical assistance, contact the manufacturer at: http://www.cellestis.com/ T-Spot may also be an option. Consult with the UDOH TB Control Program for more information.

QuantiFERON®-TB Gold In-Tube

Test Principle

The QuantiFERON®-TB Gold In-Tube assay is an in vitro diagnostic laboratory test that aids in the detection of infection with *Mycobacterium tuberculosis*. It uses human whole blood, with patented assay technology based on the measurement of Interferon-gamma (IFN-γ) secreted from stimulated T-cells previously exposed to *Mycobacterium tuberculosis*. The QuantiFERON®-TB Gold In-Tube assay is a straightforward laboratory test that involves simple steps. There are several options available for your facility depending on your resources and preferences. Most facilities choose to simply draw blood and send it to the Utah Public Health Laboratory within 15 hours, but if distance or schedule do not allow for arrival at the laboratory within the 15-hour limit, samples may be incubated and centrifuged at your facility. The following steps outline the procedures for these three different options:

Option 1 (*preferred*): On-Site Collection (15 hour time constraint)

1. Collect 1 mL blood into each of the three blood collection tubes (gray, red, and purple).
2. After blood collection, mix the tubes thoroughly by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).

3. Transport tubes at room temperature. Tubes need to arrive at the laboratory within 15 hours of collection, and by 4:00 p.m. Monday through Friday.

<u>Option 2</u> (*not recommended*): On-Site Collection and Incubation (70 hour time constraint, upright transport)

1. Collect 1 mL blood into the three blood collection tubes (gray, red, and purple).
2. After blood collection, mix the tubes thoroughly by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).
3. As soon as possible, and within 16 hours of collection, incubate tubes upright at 37°C for 16-24 hours. Be certain to document the date and time for each step.
4. Tubes need to arrive at the laboratory within 72 hours of incubation completion, and by 4:00 p.m. Monday through Friday.

<u>Option 3</u> (*discouraged)*: On-Site Collection, Incubation, and Centrifugation (refrigerated transport)

1. Collect 1 mL blood into the three blood collection tubes (gray, red, and purple).
2. After blood collection, mix the tubes thoroughly by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).
3. As soon as possible, and within 16 hours of collection, incubate tubes upright at 37°C for 16-24 hours. Be certain to document the date and time for each step.
4. As soon as possible, and within 72 hours of incubation, centrifuge tubes at 2000-3000 g (RCF) for 15 minutes. Be certain to document date and time for each step.
5. After centrifugation, tubes must maintain a temperature of 2-8°C.
6. Tubes need to arrive at the laboratory within a week of centrifugation, and by 4:00 p.m. Monday through Friday. Tubes must be maintained at a temperature of 2-8°C during transport.

Some of the frequently asked questions relating to the QFT are listed below. The answers provided act as a guide only.

Blood Collection

The blood hasn't reached the black mark on the side of the blood collection tube. Is this important?

The mark on the side of the tubes indicates the 1 mL fill volume. QFT tubes have been validated for volumes ranging from 0.8 to 1.2 mL. If the level of blood in any tube is not close to the indicator mark, it is recommended to obtain another blood sample.

How important is the tube mixing process?

The antigen mixing process ensures even distribution of stimulating antigens to allow white blood cells to ingest and process antigen for presentation to T-cells, thus leading to IFN-secretion. It is a very important step in the process and poor mixing will lead to low and incorrect results. Mix the tubes by vigorously shaking for at least 5 seconds, ensuring that the entire surface of the tube has been coated with blood. Thorough mixing is required to ensure complete mixing of the blood with the tube's contents. Causing the blood to froth will not adversely affect the performance of the test.

Universal blood handling precautions should be used. A demonstration video can be at: www.cellestis.com.

Can the blood collection tubes be transported lying down?

Yes and No.

(Option 1)-- Tubes can be transported lying down only after the tube-mixing step has been done and prior to incubation.

(Option 2)-- If tubes are transported after incubation, but prior to centrifugation, care should be taken to ensure that tubes remain upright during transport.

(Option 3)-- Tubes transported after centrifugation, may be transported lying down if necessary.

At what temperature can the blood be transported to another site, or held prior to incubation at 37°C?

(Option 1, Option 2)-- Blood should be held and transported at room temperature (17°C to 27°C). Do not refrigerate the blood or place on ice.

(Option 3)-- Blood should be held and transported at (2°C to 8°C), refrigerated or placed on ice.

Blood Incubation and Centrifugation

What if 37°C incubation starts more than 16 hours after the time of blood collection?

The package insert specifies that the 37°C blood incubation must commence within 16 hours of collection. Blood samples incubated more than 16 hours after collection are likely to exhibit a decreased IFN-γ response due to cellular breakdown (death), leading to loss of sensitivity and inaccurate results.

Can I incubate the blood collection tubes lying down?

QFT tubes must be kept upright during incubation at 37°C.

Do I have to centrifuge the tubes immediately after removal from incubator?

QFT tubes may be held between 2°C and 27°C for up to 3 days before centrifugation or harvesting.

The gel plug hasn't moved during centrifugation. What should I do?

After incubation of tubes at 37°C, the plasma is separated from the cells by centrifuging for 15 minutes at 2000 - 3000 RCF (g). The gel plug should move to separate the cells from the plasma. If this does not occur, the tubes should be recentrifuged at a higher speed.

The plasma doesn't appear the color it normally does. Is this OK?

Plasma from QFT tubes can appear more red than usual but this is normal. It should be noted that the color of plasma, even those without any red blood cell contamination, can vary from almost colorless to shades of yellow/pale brown; some plasma samples even have an opaque character. These qualities have not been found to affect QFT results.

Other Resources

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children

Tuberculosis Associated with Blocking Agents Against Tumor Necrosis Factor

Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection --- United States, 2010. *Recommendations and Reports*. June 25, 2010 / 59(RR05);1-25

Treatment of TB Infection

Individuals found to have a positive Tuberculin Skin Test (TST) or Interferon Gamma Release Assay (IGRA) blood assay should be carefully evaluated to rule out active TB disease (ATBD). An IGRA may be used in all instances where a TST would be used, with the exception that an IGRA is not recommended in children younger than 5 years old. For CDC specific recommendations, see the Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium Tuberculosis Infection. If no evidence of ATBD is found, then evaluate for treatment of TB infection. Targeted testing programs should be designed to identify persons who are at higher risk for TB and who would benefit from treatment of TB infection. **The decision to test is a decision to evaluate for treatment!**

Procedure

Medical evaluation should include a history of:

- Symptoms of disease
- Chest x-ray within past 3 months,
- History of TB exposure, infection, or disease
- Past TB treatment
- Demographic risk factors for TB
- Medical conditions that increase risk for TB
- Bacteriologic or histologic exam
- Medical contraindications for treatment of TB infection
- Current medications that may be affected by use of isoniazid (INH) or Rifampin

Classification of a positive TST is found in A Tuberculosis Provider Guide - Testing for TB Infection & Guidelines for Post-Test Referral. IGRA results are not classified according to risk; simply positive or negative.

All individuals being considered for treatment should undergo a chest x-ray to rule out active pulmonary TB disease. Children younger than 10 years old should undergo both a posterior-anterior and a lateral chest x-ray. All other individuals should receive a posterior-anterior chest x-ray only; additional x-rays should be done at the clinician's discretion. Consultation with the Utah State Pulmonologist and/or Utah State Pediatric Consultant is available through the UDOH TB Control Program. A chest x-ray should be given **even during the first trimester**, to pregnant women who:

- Have symptoms that are highly suggestive of ATBD (cough, fever, night sweats, chest pain etc.), **or**
- Are HIV seropositive and are (1) TST or IGRA positive or (2) TST or IGRA negative but have been in close contact with a person who has pulmonary or laryngeal TB disease, **or**
- Are TST or IGRA positive and have been in close contact with a person who has pulmonary or laryngeal TB disease.

Other pregnant women who have a positive TST or IGRA should be advised to obtain a chest x-ray after the end of the first trimester. **An appropriate lead shield should be used for chest x-rays in pregnant women. (A doctor's order is required for a shielded chest x-ray.)**

Persons in the following high-risk groups should be given the highest priority for treatment of TB infection if they have positive skin test results ≥5 mm of induration, or their IGRA is positive:

- HIV-positive persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Individuals with organ transplants
- Other individuals who are immunosuppressed

In addition, persons in the following high-risk groups should be considered for treatment of TB infection if their reaction to the TST is ≥10 mm of induration, or their IGRA is positive:

- Recent arrivals from high-prevalence countries
- Intravenous drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that make them high-risk
- Children younger than 5 years of age, or children and adolescents exposed to adults in high-risk categories
- Latter Day Saint (LDS) missionaries returning from countries with a high-prevalence of TB

Persons with no known risk factors for TB may be considered for treatment of TB infection if their reaction to the tuberculin test is ≥15 mm of induration or their IGRA is positive. This group should be given the lowest priority for treatment efforts.

Some contacts of persons with ATBD that have a negative TST (<5 mm of induration) or IGRA should be evaluated for treatment of TB infection, after ATBD has been ruled out. These contacts include children younger than 5 years of age, individuals who are immunosuppressed, and others who may develop ATBD quickly after infection.

Close contacts of a person with ATDB that have a negative reaction to an initial TST or IGRA should be retested 8 - 10 weeks after they were last exposed to TB. Treatment for TB infection may be discontinued if the TST or IGRA result is again negative **and** if the person is no longer exposed to TB. However, persons known to have or who may be HIV-positive and other individuals who are immunocompromised should be given treatment for TB infection regardless of their test result.

Because of their age, infants and young children with TB infection are known to have been infected recently, and thus are at a high risk of their infection progressing to disease. Infants and young children are also more likely than older children and adults to develop life-threatening forms of TB. Children younger than 5 years of age who are close contacts of person with ATBD should receive treatment for TB infection even if their TST and chest x-ray do not suggest infection. A second TST should be placed 8 - 10 weeks after their last exposure to infectious TB. Treatment for TB infection can be discontinued if their second test placed at least 8 weeks after exposure was also negative and the infant is at least 6 months of age (a false negative is more likely to occur in a child less than 6 months old due to an underdeveloped immune system).

Before treatment for TB infection is initiated and after ATBD is ruled out, the clinician should discuss the risks and benefits of treatment with the individual, determine contraindications to treatment and check for adverse reactions to current drugs which have known interactions with drugs used for TB infection. Medication adherence issues should also be discussed with the individual. Written consent to begin therapy must be obtained and maintained in the individual's health record. Commitment to complete the 6 to 9 month course of treatment should be obtained.

Medication used for the treatment of TB infection in adults is described in detail in the Core Curriculum on Tuberculosis, What the Clinician Should Know, and Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection.

Drugs	Duration	Interval	HIV-	HIV+
Isoniazid** (INH)	9 months	Daily	A (II)	A (II)
		Twice Weekly****	B (II)	B (II)
Isoniazid** (INH)	6 months	Daily	B (I)	B (I)
		Twice Weekly****	B (II)	B (II)
Rifampin***£ (RIF)	4 months	Daily	B (II)	B (II)

*A – Preferred; B - Acceptable alternative
* I - Randomized clinical trial data; II - Data from clinical trials that are not randomized or were conducted in other populations; III - Expert opinion
** Pregnancy is not an absolute contraindication, but risk vs gain should be carefully assessed as there is an increased risk of hepatotoxicity with INH during pregnancy and up to 3 months post-partum.
*** Do not use Rifampin during pregnancy
****Intermittent therapy requires DOT
£ Caution: there are many drug-drug interactions with Rifampin; check carefully before proceeding.

The recommended regimen for treatment of TB infection in children and people with HIV is INH for 9 months. If INH cannot be tolerated, Rifampin (RIF) can be used for 4 months, preferably only for HIV-negative patients.

In addition, CDC recommends INH and Rifapentine once weekly for 12 weeks by directly observed therapy (DOT) only, for specified risk groups. Follow this link to access UDOH protocol.

Completion of therapy should be based on the total number of doses administered, not duration of therapy. If treatment is interrupted the recommended number of doses of the regimen should be provided within a certain time frame. A 6-month regimen consisting of 180 doses of INH can be given over 9-months. A 9-month regimen consisting of 270 doses of INH can be given over 12-months.A 4-month regimen consisting of 120 doses of RIF can be given over 6-months.

The entire regimen should be restarted if interruptions were frequent or prolonged enough to preclude completion of doses in the time frames specified. When therapy is

restarted after an interruption of more than 3 months a medical examination should be conducted and chest x-ray repeated to exclude active disease is indicated.

Individuals who are at high risk of developing ATBD, and who are prescribed treatment for TB infection but have interruptions in treatment, should be encouraged to complete the regimen. However, if the individual has failed three attempts to complete treatment, no further efforts should be made. Incentives and enablers may be used to encourage completion in high-risk individuals such as contacts, young children and HIV-positive individuals.

Monitoring for side effects may include baseline laboratory testing for individuals whose initial evaluation suggests a liver disorder, who use alcohol regularly and others who are at risk of chronic liver disease. Baseline testing is also indicated for individuals who are HIV-Positive, as well as women who are pregnant or less than 3 months post-partum. Testing should be considered on an individual basis, particularly for individuals who are taking other medications for chronic medical conditions. See the Core Curriculum on Tuberculosis, What the Clinician Should Know, and Management of Common Side Effects of INH, RIF, PZA, and EMB for more details.

Monthly monitoring is required for adherence to the prescribed regimen, signs and symptoms of ATBD, and signs and symptoms of hepatitis or other side effects. Face-to-face visits and assessments are required. Consultation with the individual's primary care physician and/or the State Pulmonologist Consultant, Pediatric Consultant or Nurse Consultant is recommended when adverse reactions occur.

Peripheral neuropathy is associated with the use of INH but is uncommon at doses of 5mg/kg. Persons with conditions in which neuropathy is common, e.g., diabetes, uremia, alcoholism, malnutrition, HIV-positive, pregnant women and persons with a seizure disorder, may be given pyridoxine (vitamin B6) 10-50mg/day with INH.

Health care providers often do not realize that their patients are not following recommendations. It is very important to determine that individuals are taking medications as prescribed, and to have a high index of suspicion of non-adherence. There are several methods for assessing adherence:

- Ask the individual directly
- Communicate effectively
- Help the individual to remember
- Listen carefully and ask the individual to report any problems with taking the medications
- Monitor appointment keeping, medication refill, and pick-up
- Monitor pills (perform pill counts); if Rifampin, urine may be examined for characteristic rust color
- Directly observe the individual swallowing each dose of medication

DOT is recommended for individuals who are at high risk for progression to disease and whose adherence is questionable (e.g. intravenous drug users, persons experiencing homelessness, children, contacts to people with drug resistant TB and persons with a history of non-adherence with any medical treatment regimen). DOT is required for all intermittent regimens.

A physician or primary care provider must decide the appropriate duration of treatment for TB infection. Both the 6 month and 9 month regimens of INH are acceptable for adults, but only 9 months is acceptable for children or people with HIV. Individuals should be advised to return to report to their clinician or a public health nurse any time they develop symptoms suggestive of ATBD.

Upon completion of therapy, the individual should be informed that repeat chest x-rays are not necessary and **repeat TSTs are not advised**. Individuals should be given documentation of completion of TB infection treatment. Selected high-risk individuals such as HIV-positive persons who cannot or will not take preventive therapy may have periodic chest x-rays at the discretion of their primary care provider.

TB medication for TB infection may be provided at no cost to individuals without health insurance. See the section in this manual on 'Ordering Anti-tuberculosis Medication' for more detailed information.

Notify the TB Control Program of individuals with adverse reactions to medications taken for TB infection.

Other Resources

ATS/CDC/IDSA Treatment of Tuberculosis, 2003

ATS/CDC/IDSA Treatment of Drug-Susceptible Tuberculosis, 2016

Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection, (pg. 735)

Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection

Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium Tuberculosis Infection

Active TB Disease Initial Evaluation

A diagnosis of active tuberculosis disease (ATBD) may be considered for any individual who has an abnormal chest x-ray consistent with TB or for any individual who has a persistent cough lasting 3 weeks or more or other signs or symptoms compatible with TB including bloody sputum, chest pain, night sweats, fatigue, weight loss, loss of appetite or persistent fever. A qualified medical provider should make the diagnosis. The index of suspicion for TB should be very high in areas of high prevalence or among groups with a high prevalence of TB.

In Utah during 2016, 70% of TB cases were exclusively pulmonary, 25% of cases were extrapulmonary, and 5% were both pulmonary and extrapulmonary. The symptoms of TB depend on the site affected. TB of the spine may cause pain in the back; TB of the kidney may cause blood in the urine. Extrapulmonary TB should be considered in the differential diagnosis of ill persons who have systemic symptoms and who are at high-risk for TB. Pulmonary TB should always be ruled out when extrapulmonary TB is diagnosed.

Procedure

a. For individuals whom a diagnosis of TB is being considered a *complete medical and social history* should be documented. This should include questions pertaining to risk factors for TB exposure, infection or disease, symptoms of TB, underlying health conditions, risk factors for HIV infection or HIV antibody status (if unknown or not current, counseling and testing should be strongly recommended), and information about contacts (especially high-risk contacts, where immediate action may be necessary). If the individual received prior treatment for TB and the drug regimen was inadequate or if the individual did not adhere to therapy, TB may recur and may be drug resistant.

b. A *physical examination* is an essential part of the evaluation of any individual. It cannot be used to confirm or rule out TB, but it can provide valuable information about the individual's overall health and other factors that may affect how TB is treated.

c. If there is no documentation that a tuberculin skin test (TST) or Interferon Gamma Immune Assay (IGRA) [Quantiferon (QFT) or T-Spot] has been performed, it should be done.

d. Individuals who have a positive TST or IGRA result and/or symptoms suggestive of TB should be evaluated with a *chest x-ray*. Radiographic abnormalities that strongly suggest ATBD include upper-lobe infiltration, particularly if cavitation is seen, and patchy or nodular infiltrates in the apical or subapical posterior upper lobes or the superior segment of the lower lobe (but abnormalities may be present anywhere within the lungs or pleura). If abnormalities are noted, or the individual has symptoms suggestive of extrapulmonary TB, additional diagnostic tests should be conducted.

   Abnormalities on a chest x-ray may be suggestive of, but are never diagnostic of TB. Chest x-rays may be used, however, to rule out the possibility of TB in a person who has a positive reaction to a TST or QFT and no symptoms of disease.

The radiographic presentation of pulmonary TB in HIV-positive individuals may be unusual. Typical apical cavitary disease is less common among such individuals. They may have infiltrates in any lung zone, mediastinal and/or hilar adenopathy, pleural effusion, or they may have a normal chest radiograph, although this latter finding rarely occurs.

Old, healed TB can produce various radiographic findings such as pulmonary nodules, with or without fibrotic scars or visible calcifications. Nodules and fibrotic scars may contain slowly multiplying tubercle bacilli with the potential for future progression to ATBD.

Pregnant women who are highly at risk of having ATBD should undergo a chest x-ray without delay, even during the first trimester, using a lead shield.

Individuals suspected of having extrapulmonary TB disease should undergo a chest x-ray to rule out pulmonary TB disease.

Children (especially younger than 10 years old) commonly present with persistent opacities and/or hilar or subcarinal enlarged nodes. These findings may be difficult to see on a frontal view alone. Therefore a 2-view (anterior/posterior and lateral) film should be done. The child should, if possible, be referred to Primary Children's Hospital (PCH) for their chest x-ray, and the State Pediatric Consultant may be consulted. Referral forms must accompany the individual, and can be found at: http://health.utah.gov/epi/diseases/TB/forms/

The TB Control Program consults with expert pulmonologists to provide interpretations for suspected/known TB cases in both adults and children. Consult with the TB Control Program for information.

e. Bacteriologic tests are performed on specimens for TB diagnostic purposes:
   - Smear examination - the specimen is concentrated, placed on a slide, and stained with a solution that detects acid-fast bacilli (AFB). Many individuals with TB have negative AFB smears.
   - Culture of the specimen for AFB - the specimen is placed in a special media that allows mycobacterial growth. Further biochemical and DNA tests are used to identify the type of AFB if growth occurs. Positive cultures for Mycobacterium tuberculosis complex (MTB) confirm the diagnosis of TB. However, TB may also be diagnosed on the basis of signs and symptoms in the absence of a positive culture.
   - Direct tests for Mycobacterium tuberculosis complex (MTBC) - the first smear positive respiratory specimen should be tested directly for the presence of MTBC and Rifampin resistance by the detection of genetic material in the sample. Contact the Utah Public Health Laboratory for availability and instructions.
   - Susceptibility testing from cultures positive for MTB complex - the organism is tested for resistance to drugs commonly used to treat TB. Isoniazid, rifampin, ethambutol, and pyrazinamide are routinely tested. Under certain circumstances, an isolate may be sent to CDC for molecular detection of drug resistance (MDDR) in order to quickly determine the likelihood of multidrug-resistant TB (MDR-TB) and/or extensively drug-resistant TB (XDR-TB).

- DNA fingerprinting (genotyping) is used to identify specific strains of TB and is a tool to track TB transmission. Related isolates show the same pattern. It can also be used to identify lab contamination.

    - Sputum samples should be obtained for smear and culture examination when pulmonary, pleural, or laryngeal TB is suspected. Three samples should be collected 8-24 hours apart, with at least one being an early-morning specimen (alternatively see the following for a second acceptable procedure: NTCA/APHL Consensus statement on the use of the Cepheid Xpert MTB/RIF assay in making decisions to discontinue airborne infection isolation in healthcare settings) **before drugs are started** (see manual section: 'Utah Public Health Laboratory Specimen Collection and Transport' for more details). Because TB can also occur in almost any anatomical site, a variety of other clinical specimens (e.g. urine, cerebrospinal fluid, pleural fluid, pus, or biopsy specimens) should be submitted for examination when extrapulmonary TB disease is suspected. If a diagnosis of pulmonary TB disease cannot be established from sputum, other procedures may be necessary, including bronchoscopy and gastric aspiration.

If AFB Smear is:	and, If Culture is:	Interpretation and Actions
Positive	Pending	Treat as if ATBD if clinical history is suggestive of TB until proven otherwise (especially if GeneXpert+)
Positive	Positive for AFB	Assume MTB until proven otherwise (unless supporting history strongly suggests non-tuberculous mycobacteria (NTM)).
Negative	Positive for AFB	Await ID; if MTB (or high suspicion of), probably lowly infectious, but manage as ATBD.
Positive	Positive for MTB	Diagnosis of ATBD.
Negative	Positive for MTB	Same interpretation and actions as directly above.
Positive or Negative	Positive for NTM	Not infected with MTB, not considered contagious. Refer to primary care provider for treatment.
Positive or Negative	Negative for MTB and NTM	No bacteriologic evidence for MTB. If individual has clinical symptoms not explained by another diagnosis and the suspicion for MTB is high, may still have active infection with MTB. Consult with TB Control Program.
Positive or Negative	Mycobacterium still present	Once identified as MTB do not probe each specimen. If still present after 2 months re-probe and then every month after.

f. A culture result of MTB or *M. Tuberculosis* complex provides a diagnosis of TB. However, a false-positive culture should be considered when the results do not fit the individual's clinical status. Individuals having only one positive culture should be re-evaluated for the possibility that the culture may be a false positive.

Other mycobacteria (e.g. *M. Avium* complex [MAC], *M. kansasii*, *M. chelonae*) may cause pulmonary disease but are not contagious (although evidence suggests M. chelonae-abscessus may be communicable among cystic fibrosis patients). These organisms will be identified through various laboratory methods. Additionally, these organisms may also be present intermittently in small numbers and may not be pathogenic. Although uncommon, a person may be infected with more than one type of mycobacteria at any given time. See manual section: 'Utah Public Health Laboratory Specimen Collection and Transport' for more details.

Individuals who are suspected or diagnosed with ATBD must be reported to the TB Control Program within 24 hours. This would include, but is not limited to: any smear positive or culture AFB positive, and/or positive direct test, individuals with a chest x-ray highly suspicious for ATBD, and/or any individual started on multiple TB drug therapy.

Helpful checklists for organizing an initial interview with an individual can be found at:

http://health.utah.gov/epi/diseases/TB/resources/step_by_step_tb.pdf

http://health.utah.gov/epi/diseases/TB/resources/suggested_supplies.pdf

Other Resources

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children, 2016

ATS/CDC/IDSA Treatment of Tuberculosis, 2003

ATS/CDC/IDSA Treatment of Drug-Susceptible Tuberculosis, 2016

Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

NTCA/CDC Guide to the Application of Genotyping to Tuberculosis Prevention and Control

Basic Guidelines for Treating Active TB Disease

Individuals who have confirmed active TB disease (ATBD) (e.g. individuals with positive cultures for *Mycobacterium tuberculosis* complex (MTB) or a clinical diagnosis by a qualified health care provider) or individuals who are considered highly likely to have ATBD should be started on appropriate treatment immediately. It is not necessary to wait for laboratory confirmation of MTB before starting treatment.

Procedure

a. **The responsibility for successful treatment is clearly assigned to the public health provider or clinician and not to the individual. The clinician is carrying out a public health function with responsibility not only for prescribing an appropriate regimen but also for successful completion of therapy.**

b. Treatment regimens must contain multiple drugs (and correct dosages) to which the organism is susceptible. The administration of a single drug or the addition of a single drug to a failing regimen can lead to the development of a strain of TB resistant to that drug. The preferred regimen for treating ATBD consists of an initial two month phase of four drugs: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) followed by a 4 to 7 month continuation phase of INH and RIF. Ethambutol can be discontinued when drug susceptibility results show the infecting organism to be fully drug-susceptible, and PZA is generally stopped after 2 months. PZA is also not recommended for use in pregnancy (the absence of PZA will require an additional 3 months of treatment). See ATS/CDC/IDSA Treatment of Tuberculosis, 2003 and ATS/CDC/IDSA Treatment of Drug-Susceptible Tuberculosis, 2016 for more details on medications.

c. Extended treatment is recommended for individuals with drug-susceptible pulmonary TB who have cavitation noted on the initial chest film and who have positive sputum cultures at the time 2 months of treatment is completed. Treatment may also be extended when only one of the above is true if disease is extensive or immunosuppression significant. In addition, variations in drugs prescribed due to drug resistance, intolerance or malabsorption may warrant a longer duration of treatment (as will TB of the bone, joints or central nervous system). Repeat sensitivity testing and/or drug blood levels may be indicated if inadequate response to treatment is suspected.

d. Pyridoxine (Vitamin B-6) is recommended for some individuals receiving INH as part of their treatment regimen to prevent peripheral neuropathy. It should be used in persons at risk for neuropathy (nutritional deficiency, HIV-positive, renal failure, diabetes, and alcoholism), as well as pregnant and breast feeding women.

e. Research has shown that non-compliance with self-administered treatment for ATBD leads to high failure rates and development of drug resistance. **Therefore it is required by Utah law that all individuals be on directly observed therapy (DOT).** This includes both pulmonary and extrapulmonary TB. See Utah Administrative Code R388-804, Special Measures for the Control of Tuberculosis. It is strongly advised to use a

treatment contract which serves both as an education tool for the individual and documentation that may prove useful, should the individual become noncompliant.

Go to: http://health.utah.gov/epi/diseases/TB/forms/atbd/active_tb_agreement.pdf for an example of a treatment contract.

f. Clinical experience suggests that individuals being managed by DOT administered 5 days a week have a rate of successful therapy equivalent to those being treated 7 days a week. Thus, a daily DOT schedule is preferred and may be given on a 5 day a week or 7 day a week schedule. Intermittent therapy (thrice weekly) may be appropriate for some individuals with drug susceptible disease (exception: thrice weekly dosing acceptable with PZA monoresistance). In the intensive phase of treatment (typically first 2 months) intermittent dosing is not acceptable with HIV or cavitary disease or smear positive, or other concerns for increased risk of treatment failure, as discerned by the prescribing provider. In the continuation phase, thrice weekly dosing is acceptable for patients older than 15, at provider discretion. For children < 15, intermittent dosing is not acceptable with HIV infection, or extensive pulmonary or disseminated disease. In general, twice weekly dosing is no longer acceptable. See the2016 guidelines referenced in paragraph b or contact the TB Control Program for details.

g. TB medications should be administrated together as a single dose leading to higher and potentially more effective serum concentrations.

h. TB transmission prevention precautions **must** be followed for individuals who are known or suspected of having ATBD who are sputum smear positive for acid-fast bacilli. Individuals with negative sputum smears for acid-fast bacilli, but with positive cultures for *Mycobacterium tuberculosis* complex may still transmit TB, especially if coughing.

i. Individuals are not considered infectious if they meet all the following criteria:

- They are on adequate therapy for 2-3 weeks
- They have significant clinical response to therapy (i.e., reduction in cough, resolution of fever)
- They have three negative AFB sputum smears collected 24 hours apart, with at least one being an early morning specimen.

j. Individuals should be monitored bacteriologically every 1-2 weeks until smears convert to negative and at least monthly until two consecutive sets are culture negative. Susceptibilities should be done on the initial positive culture. Cultures reported as “mycobacterium still present” will be re-probed at 2 months and every month it is still positive. If the individual is not improving consider the development of resistance, poor absorption of drugs or that the individual may not be taking medications and consult with the TB Control Program.

k. Consult the TB Control Program for information regarding the treatment of individuals if they are: drug resistant, children, HIV-positive, and/or pregnant.

l. The basic principles that underlie the treatment of pulmonary TB also apply to extrapulmonary forms of the disease. Thus, a 6-month course of therapy is

recommended for treating TB involving any site with exception of 6-9 months for bone joint and 9-12 months for central nervous system.

m. RIF may decrease the effectiveness of oral contraceptives, as well as interact with multiple other medications. An alternative method of birth control should be used during RIF therapy. See 2016 guidelines pg 10, Table 8 for common drug interactions.

DRUG	ADVERSE REACTIONS	MONITORING	COMMENTS
Isoniazid (INH)	-Hepatic enzyme elevation -Hepatitis -Hypersensitivity reactions -Peripheral neuropathy -Mild effects on central nervous system -Lupus-like syndrome -Monoamine poisoning	-Baseline (and monthly, as needed) hepatic enzymes for adults -Repeat measurements if baseline is abnormal, if high risk for adverse reactions, if symptoms of adverse reactions	-Hepatitis risk increases with age and alcohol consumption -Pyridoxine can usually prevent peripheral neuropathy *See ATS/CDC/IDSA Treatment of Tuberculosis, section 7.2.2 for drug interactions.
Rifampin (RIF)	-GI upset -Orange discoloration of body fluids -Hepatitis -Immunologic reactions -Flu-like symptoms -Rash	-Baseline CBC, platelets, and hepatic enzymes for adults -Repeat if baseline abnormal or if symptoms of adverse reactions	-Significant interactions with methadone, birth control pills, and other drugs -Colors body fluids orange -May permanently discolor soft contact lenses *See ATS/CDC/IDSA Treatment of Tuberculosis, section 7.2.2 for drug interactions.
Pyrazinamide (PZA)	-Hepatitis -Rash -GI upset -Joint aches -Hyperuricemia -Gout	-Baseline uric acid and hepatic enzymes for adults -Repeat if baseline abnormal or if symptoms of adverse reactions	-Treat hyperuricemia only if individual has symptoms -Little information about the safety during pregnancy
Ethambutol (EMB)	-Optic neuritis -Permanent alterations in visual acuity or color perception -Cutaneous reactions	-Baseline and monthly tests of visual acuity and color vision	-Not recommended for children too young to be monitored for changes in vision unless TB is drug resistant

n. All individuals with ATBD should be offered HIV counseling and testing. In the presence of HIV infection, it is critically important to assess the clinical and bacteriological response. TB treatment regimens may need to be altered for HIV-positive individuals taking protease inhibitors. Because of the complexity of management of TB in an HIV-positive individual, it is strongly recommended that consultation with an expert in the management of both TB and HIV disease be considered. See CDC guidelines for Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis.

o. Careful attention should be given to measures that foster adherence to therapy (e.g., incentives and enablers). See section on 'Incentives and Enablers' in this manual or consult with the TB Control Program for assistance with incentives and enablers. Intermittent therapy regimens are available for select individuals. Consult the TB Control Program for more information.

p. A case manager should be assigned to ensure that individuals receive appropriate monitoring, complete treatment, and that contacts are examined. See manual section on 'Contact Investigation' for more details.

q. When therapy is interrupted see 2016 guidelines pg 8, Table 6 for recommendations.

r. A full course of therapy is determined more accurately by the total number of doses taken, not solely by the duration of therapy. (See 2016 guidelines pg 4, Table 2)

s. For pulmonary ATBD, a chest x-ray and sputum should be done at the completion of treatment.

Other Resources

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

UDOH Management of Common Side Effects of INH, RIF, PZA, and EMB

Contact Investigation

Contact investigation is the second most important strategy to prevent and control TB in the United States and is one of the best ways to find individuals who have active TB disease (ATBD). The purpose of the investigation is to find contacts who (1) have ATBD so that they can be given treatment and further transmission can be stopped, (2) have TB infection so they can be given treatment, and (3) are at high risk of developing ATBD and therefore require prophylactic treatment until TB infection can be excluded. Each local health department (LHD) is responsible for ensuring that a complete and timely contact investigation is conducted for all TB cases and for sputum acid- fast bacilli (AFB) smear positive individuals with a high index of suspicion for TB reported in its jurisdiction.

Who is a Contact?

Contacts are persons exposed to someone with confirmed TB disease or a sputum AFB-smear positive individual with a high index of suspicion for TB. Exposure to TB is time spent with or near such a person and is determined by the duration, proximity, and intensity of the shared time. Contacts generally include family members, roommates or housemates, close friends, coworkers, classmates, and others. Public health agency staff usually identify contacts by interviewing the person with ATBD and by visiting the places where that person spends time regularly.

When is a Contact Investigation Done?

A contact investigation is a systematic procedure for tracing, testing, and evaluating persons who have been exposed to someone with infectious TB. In general, a contact investigation should always be initiated within three working days of report to the LHD of a sputum AFB-smear positive case or an individual with a high index of suspicion for TB (e.g. symptoms and/or cavitary chest x-rays).

Infectiousness depends on a variety of factors, but is more likely when individuals have:

- Hoarseness or other symptoms of laryngeal TB
- Cough
- Positive sputum AFB smear or culture results for *Mycobacterium tuberculosis* (MTB) complex. Evidence suggests that transmission can occur in sputum AFB smear-negative cases as well.
- Cavity on chest x-ray
- Inadequate or no treatment

Young children with pulmonary TB disease are rarely infectious, so a contact investigation is generally not conducted for them. Instead a **source case investigation** (looking for the source of exposure) is done. However, young children with ATBD should be evaluated for infectiousness and a contact investigation may be warranted in some circumstances.

A source case investigation is usually done when:

- A child < 5 years old is found to have TB disease (required by the TB Control Program), and may be considered when a child < 2 is diagnosed with TB infection

- A severely immunocompromised person who does not have a known history of TB infection is found to have ATBD
- A cluster of TST conversions is found in a high-risk institution (e.g. health care or correctional facility).

A source case investigation is conducted to determine who transmitted TB to the child, index patient, or persons in the cluster of skin test conversions; whether this person is still infectious; whether this person was reported to the health department; or if others were infected by the same source patient.

Supervisory clinical and management staff should make decisions regarding prioritization of contact investigations. Setting priorities between two or more contact investigations is a decision that should be made based on the likelihood of infectiousness of the index case:

- Positive sputum AFB smear
- Pulmonary TB with positive culture
- Extra-pulmonary TB and/or clinical/provider-diagnosed cases

If program resources are limited, priority should be given to contacts that were exposed to the most infectious individuals with TB or to those who are at highest risk for progressing to disease, if infected. The TB Control Program **DOES NOT PAY** for testing or follow-up for non-contacts (persons who have not shared time or were not near a person with infectious TB).

Steps in a Contact Investigation

A successful contact investigation requires careful gathering and evaluation of detailed information, often involving many people. In general, contact investigations follow a process that includes the following basic steps:

1. Medical Record Review

Review the individual with TB's medical record and information from the clinician to determine whether the individual is infectious and, if so, for how long. Knowing when the person was infectious helps to determine which contacts are at risk. In general, count back 3 months prior to the time the individual reported symptoms or the first positive finding (i.e. abnormal chest x-ray or positive smear), whichever is longer. If the individual is asymptomatic and did not have positive AFB sputum smears or a cavitary chest x-ray, go back 1 month from the date of suspicion of TB disease.

Table 1. Guidelines for estimating the beginning of the period of infectiousness of persons with TB, by index case characteristic

Characteristic			
TB symptoms	AFB* sputum smear positive	Cavitary chest radiograph	Recommended minimum beginning of likely period of infectiousness
Yes	No	No	3 months before symptom onset or first positive finding (e.g., abnormal chest radiograph) consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first positive finding consistent with TB disease, whichever is longer
No	No	No	4 weeks before date of suspected diagnosis
No	Yes	Yes	3 months before first positive finding consistent with TB

SOURCE: CDC Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis.

2. Patient Interview (TB Case Interview)

The patient interview is one of the most critical parts of the contact investigation and should be done in person. If the interviewer does not communicate well enough with the patient to get accurate information about symptoms, places where the patient spent time, and contacts, people who need evaluation and treatment may be missed. The majority of TB patients in Utah are foreign-born individuals, and case managers should be prepared to arrange to have the interview conducted in the patient's primary language if necessary.

The interviewer should keep in mind that if the patient first learns of their new TB diagnosis during the initial interview, they may be overwhelmed. Thus, **follow-up interviews should be scheduled to educate patients and to complete a thorough contact investigation**. Good communication (asking open-ended questions), good listening skills, patient education, and establishing and maintaining a trusting relationship are essential during all interviews.

The initial interview should occur **no more than 1 working day** after the case is reported for sputum AFB smear positive cases or individuals with a high index of suspicion for TB and within 3 days for all other cases. During the interview, the individual identified with TB should be asked more about:

- Symptoms – type and onset; especially cough and sputum production
- Places where the individual spent time while he/she was infectious (e.g. household – including guests and visitors, work, school, leisure, recreation, transportation*[1], incarceration, travel, medical/dental or beauty appointments)
- Any contacts
- How often and how long the contacts were exposed
- Locating information for the contacts

Some individuals may be reluctant to identify some or all of the contacts. For example, an individual may not want to identify people who use illegal drugs with him/her or who are undocumented. The interviewer should be sensitive to the individual's fears, explain the importance of testing the contacts, and **assure the individual that all information will be kept confidential (including the individual's name).**

3. Field Investigation

A field investigation means visiting the individual's home or shelter, workplace[2], and other places where the patient said he/she spent time while infectious to identify contacts and evaluate the environmental characteristics of the places where exposure occurred. The public health worker should assess for:

- Room size

---

[1] If air travel may be involved, WHO guidelines (adopted by CDC) require 8 hours or more contact. Go to: http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.363_eng.pdf for further guidance. For additional assistance and/or to make a referral to CDC, contact the TB Control Program.

[2] See the Workplace Contact Investigation Protocols for detailed guidance

- Crowding
- Ventilation
- Contacts (especially children) and their locating information
- Evidence of other contacts who may not be present (e.g. pictures of others who may live in the dwelling, shoes left by others who may live in the house, maintenance/cleaning workers in the home, toys left by children).

Close contacts that are present should be educated about the purpose of the contact investigation; basic TB transmission; and the importance of completing medication evaluation and, if applicable, treatment for TB infection or ATBD.

4. Risk Assessment for MTB Transmission

The infectiousness of the i individual identified with TB is dependent upon the duration of time when the individual was infectious and estimated degree of infectiousness. The degree of infectiousness is estimated from information regarding the patient's symptoms, sputum smear results, and other conditions identified during the medical record review and patient interview. The greater the degree of infectiousness, the more likely transmission will occur.

The risk of transmission in a particular space depends on the concentration of infectious droplet nuclei in the air. Small room size, crowded conditions, poor ventilation and lack of air cleaning systems increase the risk of transmission of MTB.

The length and closeness of exposure between the individual identified with TB and a particular contact are key factors in assessing the contact's risk. Persons who frequently spend a lot of time with the individual or have been physically close to the patient are at higher risk of becoming infected.

Regardless of the length of exposure, it must be considered whether there are contacts who have a high risk of developing TB disease if infected: contacts <5 years of age, HIV-positive or other immunocompromised persons, and persons with certain medical conditions.

5. Prioritization of Contacts

Prioritization of each contact is done at the outset and guides how the contact will be evaluated. The assignment of high, medium, or low-priority status is dependent on the characteristics of the index patient, the vulnerability of the contact, and circumstances of exposure. To use time and resources wisely, the contact investigation should initially be focused on the high or medium-priority contacts. Low-priority contacts have had limited exposure to the index case and have a low probability of recent infection; therefore, a TST or IGRA at the end of the window period 8-10 weeks after (infectious) exposure is preferred for these contacts.

Based on the index case characteristics, refer to the following figures at the end of this chapter for guidance on prioritizing contacts:

- Figure 1: AFB sputum smear positive or cavitary
- Figure 2: AFB sputum smear-negative/culture positive
- Figure 3: Extrapulmonary or sputum smear/culture negative pulmonary TB

- Figure 4: Source case investigations in young children

In addition, the TB Control Program encourages contact investigations limited to household members for extrapulmonary, clinical, and provider-diagnosed cases.

6. Evaluation of Contacts

Evaluation of contacts includes at least a medical history, review of TB symptoms, and TST or IGRA. Contacts should also be offered HIV counseling and testing and be asked about: their current symptoms of TB, risk factors for developing TB disease, date of last exposure, history or treatment of previous TB infection or disease, documented previous TST or IGRA results, and previous exposure to TB.

a. TST/IGRA

An initial TST/IGRA must be given as soon as possible to high- and medium-priority contacts. **For TSTs, a reaction of 5mm or greater is considered positive for contacts; a positive IGRA result is positive in all circumstances.** Contacts with a positive reaction should be further evaluated for ATBD, including chest x-ray, and, if warranted, lab testing.

Because it takes 2-8 weeks after TB infection for the body's immune system to react to a TST or IGRA (window period), contacts who had a negative reaction on the initial test should be retested 8-10 weeks after the date of last exposure (DLE) to the individual identified with TB (index case). If the contact is still exposed to the index case, the DLE is determined as follows.

a) If the index case is sputum smear positive, the DLE is the date when the index case had at least 3 consecutive negative sputum smears, diminished symptoms, and has been on treatment for 2 weeks.
b) If the index case is sputum smear negative/sputum culture positive, enter the date when the index case has been on treatment for at least 2 weeks and is stable and/or improving.
c) For all other cases, enter the index case's treatment start date.

Infants: Infants under 6 months of age may have a false-negative TST reaction because their immune systems are not yet able to react to tuberculin. It is not known whether IGRA testing is valid in young children. Thus, infants need careful clinical evaluation. The Pediatric Consultant should be involved in the decision-making process.

Special Groups: Contacts who have TB symptoms, are HIV-positive, have other immunosuppressive conditions, or are < 5 years of age – and who are exposed to sputum smear positive or sputum smear negative/culture positive cases - should have a chest x-ray at the same time as the initial skin test or IGRA (regardless of the result) to evaluate for TB disease. This is because of their high risk of quickly developing TB disease. In addition, contacts <5 years and immunocompromised contacts should be considered for treatment of TB infection (once ATBD is ruled out) even if the initial skin test reaction or IGRA is negative during the window period. Treatment may be discontinued if the 8-week follow-up skin test or IGRA is still negative and the contact is not at continued risk for exposure to infectious TB. (See Figures 5 and 6 on pages 36 and 37).

Contacts with previously-positive TST/IGRA results: Contacts who have **documentation** of a previous positive TST or IGRA should not receive another test but should be evaluated for TB disease, including a review of symptoms and obtaining a chest x-ray (if indicated) (see Figure 9 on page 39). Contacts without documentation should be evaluated according to the standard algorithm.

b. CXR/TB symptoms

Contacts who have an abnormal chest x-ray or symptoms of TB disease should have 3 sputum specimens collected at least 8 hours apart (with one being an early morning sample), for smear and culture examination, regardless of his/her TST or IGRA reaction.

It is recommended that case managers refer to the following figures at the end of this chapter, which are from the CDC's Contact Investigation Guidelines for guidance on evaluating contacts:

- Figure 5: Contacts aged <5 years
- Figure 6: Immunocompromised Contacts
- Figure 7: High/medium priority Immunocompetent Adult and Children ≥5 years
- Figure 8: Low-priority contacts
- Figure 9: Contacts with Documented Previous Positive TST/IGRA

c. Documenting Contact Investigations

Results of all contact investigations should be documented on the UDOH CI Record and sent to the TB Control Program at 30 days, 120 days, and at completion of treatment for contacts with newly-diagnosed TB infection. Data regarding contacts should also be entered into UT-NEDSS. If data entry assistance is needed, LHDs should contact the TB Control Program.

Any out-of-jurisdiction contacts require an Interjurisdictional Referral to be submitted to the TB Control Program. The referral will be forwarded, and follow-up will be assumed by the TB Control Program as needed. (See section on Interjurisdictional Referrals in this manual.)

7. Treatment and Follow-Up for Contacts

Contacts who have a positive sputum smear or chest x-ray result suggestive of current TB disease should begin treatment for ATBD.

The following contacts should be offered treatment for TB infection:

- Contacts with a positive TST or IGRA and no evidence of TB disease
- High-risk contacts who have a negative TB skin test reaction, or negative IGRA, who may develop TB disease quickly after infection. This includes: children under 5 years of age (see Figure 5 on page 36), people who are HIV-positive, and other immunocompromised contacts (see Figure 6 on page 37).

Contacts recently infected with TB are high-priority for treatment of TB infection because they are at high risk of developing ATBD; the highest risk of developing ATBD

is in the first 2 years after infection. Contacts who are HIV-positive or other immunosuppressed contacts may be given a full course of treatment for TB infection, regardless of their TB screening result because of the possibility of a false-negative test result (see Figure 6 on page 37).

Contacts who start treatment for TB infection or ATBD should be monitored to ensure compliance and completion of treatment. Contacts with TB infection who have a high-risk for progressing to ATBD or who are at risk for non-adherence should be considered for directly observed preventive therapy (DOPT) when possible (e.g., people who are: HIV-positive or immunosuppressed, experiencing homelessness, abuse substances). Children < age 5 **must** receive DOPT.

8. Decision About Whether to Expand Testing

When determining whether to expand a contact investigation, consideration of the following factors is recommended:

- achievement of program objectives with high- and medium-priority contacts; and extent of recent transmission, as evidenced by:
  - unexpectedly high rate of infection[3] or TB disease in high-priority contacts (e.g., 10% or at least twice the rate of a similar population without recent exposure, whichever is greater),
  - evidence of secondary transmission (i.e., from individuals with TB who were infected after exposure to the source patient),
  - infection of contacts aged <5 years,
  - contacts with change in TST or IGRA status from negative to positive between their first and second test, and
  - TB disease in any contacts who had been assigned a low priority.

In the absence of evidence of recent transmission, a contact investigation should not be expanded to lower priority contacts. When program evaluation objectives are not being achieved, a contact investigation should be expanded only in exceptional circumstances, generally those involving people who are highly infectious with high rates of infection among contacts or evidence for secondary cases and secondary transmission. Expanded investigation must be accompanied by efforts to ensure completion of therapy.

The decision about expanding a contact investigation to the next group of contacts should be made by clinical and supervisory staff, based on an assessment of all available information. This should be done as soon as it becomes clear that transmission may have occurred.

9. Evaluation of Contact Investigation Activities

---

[3] To calculate the infection rate among a given group of contacts:

A. Determine the number of contacts with newly-identified positive TST/IGRA.
B. Determine the total number of contacts without a documented previous positive skin test: subtract the number of contacts with a documented previous positive skin test from the total number of contacts.
C. Determine the infection rate: divide A by B and multiply by 100; the resulting percentage is the infection rate for the group of contacts.

An evaluation of the contact investigation activities should be conducted with or by a supervisor to determine such things as:

- Were an appropriate number of contacts identified?
- Were the highest-priority contacts located and tested?
- Was the contact investigation performed in all settings: household or residence, work or school, and leisure or recreational environments?
- Was the contact investigation expanded appropriately? Were contacts completely evaluated (including second skin test if needed) and given appropriate therapy if they had TB infection or disease?
- How many infected contacts completed a regimen of treatment for TB infection?
- Did all identified cases complete an adequate treatment regimen?
- Did children under age 5 receive DOPT?
- Were HIV+ contacts strongly considered for DOPT?

The answer to these questions will help determine how successful the contact investigation has been.

Results of all TB contact investigation activities should be documented on the CI Record and submitted to the TB Control Program upon completion (including names and locating information for any out-of-state contacts identified), and data regarding contact should be entered into UT-NEDSS. Contacts residing outside of Utah require an Interjurisdictional Referral form be completed by the originating jurisdiction, and forwarded to the TB Control Program (see manual section on Interjurisdictional Referrals). Intrastate referral procedure will depend on the electronic capabilities of both the sending and receiving jurisdiction, but the TB Control Program must still be notified. The information will be compiled and evaluated by TB Control Program management staff as part of ongoing program evaluation activities.

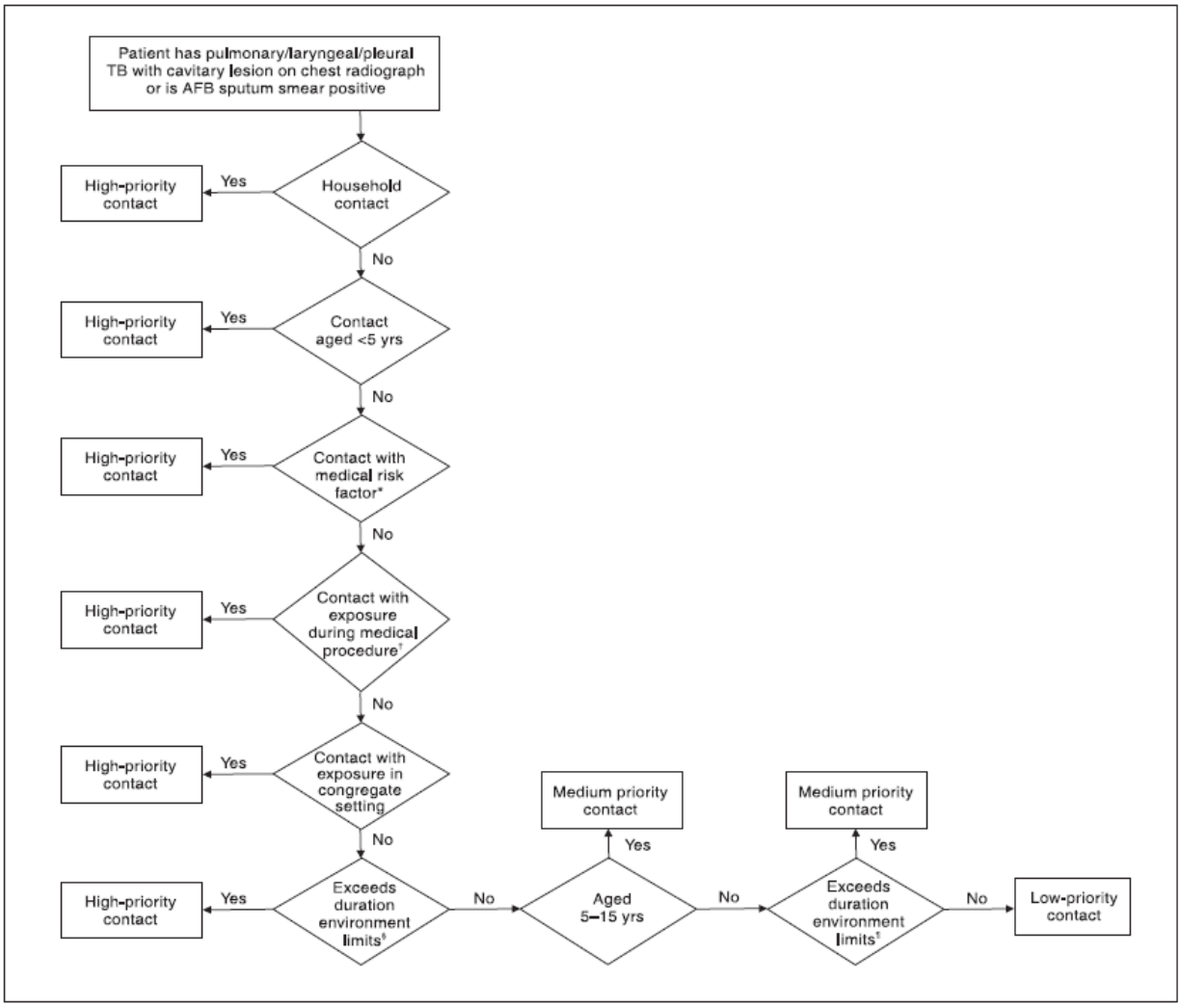
Other Resources

Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection --- United States, 2010. *Recommendations and Reports.* June 25, 2010 / 59(RR05);1-25

CONTACT PRIORITIZATION AND EVALUATION ALGORITHMS

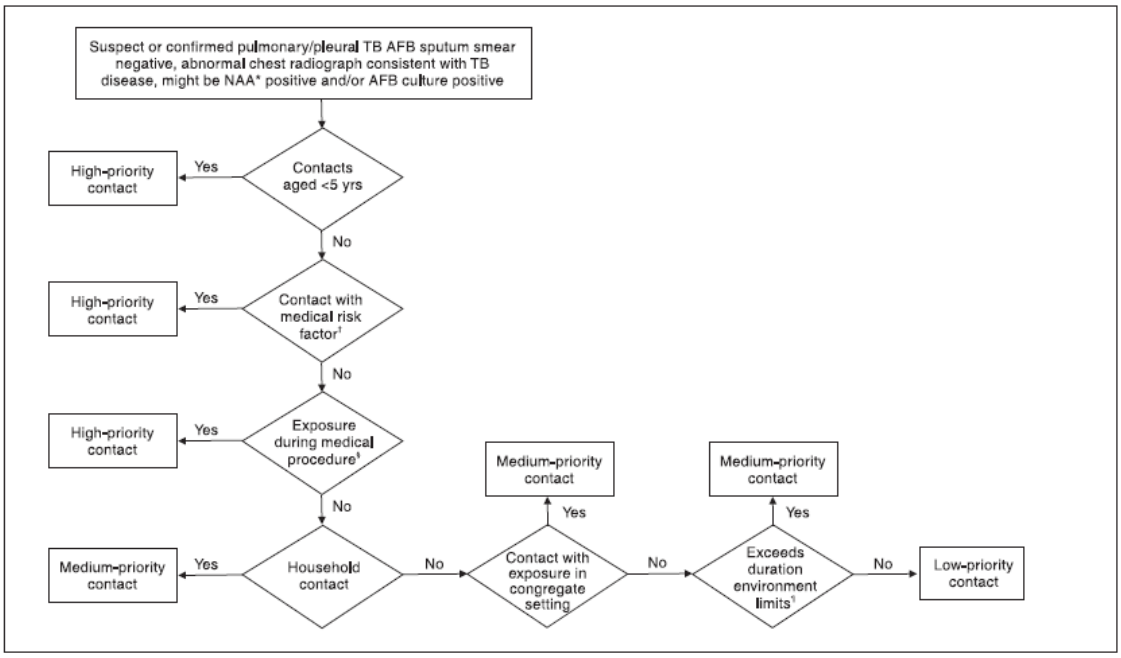
A. CONTACT PRIORITIZATION - BY INDEX CASE CHARACTERISTICS

Figure 1. Prioritizing Contacts: Where index case has AFB sputum smear-positive or cavitary TB.



* Human immunodeficiency virus or other medical risk factor.
† Bronchoscopy, sputum induction, or autopsy.
§ Exposure exceeds duration/environment limits per unit time established by the health department for high-priority contacts.
¶ Exposure exceeds duration/environment limits per unit time established by the health department for medium-priority contacts.

Figure 2. Prioritizing Contacts: Where index case is AFB sputum smear-negative, CXR abnormal for TB, and NAAT and/or presumed/confirmed culture positive.



* Nucleic acid assay.
† Human immunodeficiency virus or other medical risk factor.
§ Bronchoscopy, sputum induction, or autopsy.
¶ Exposure exceeds duration/environment limits per unit time established by local TB control program for medium-priority contacts.

Figure 3. Prioritizing Contacts: Where index case has extrapulmonary or sputum smear/culture negative pulmonary TB.

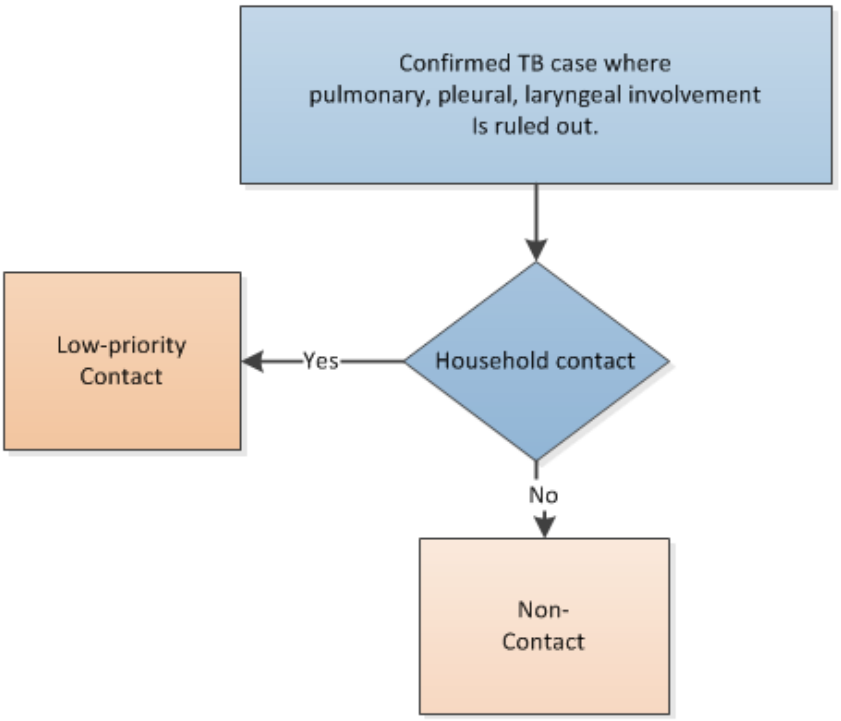
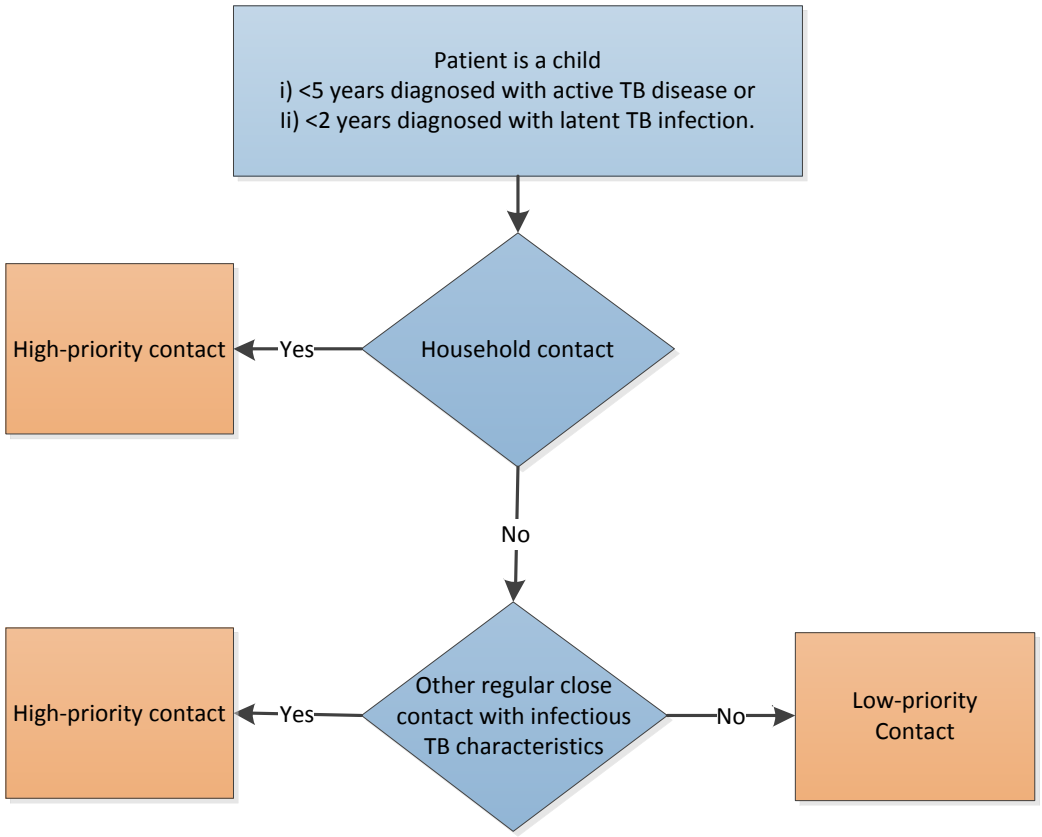
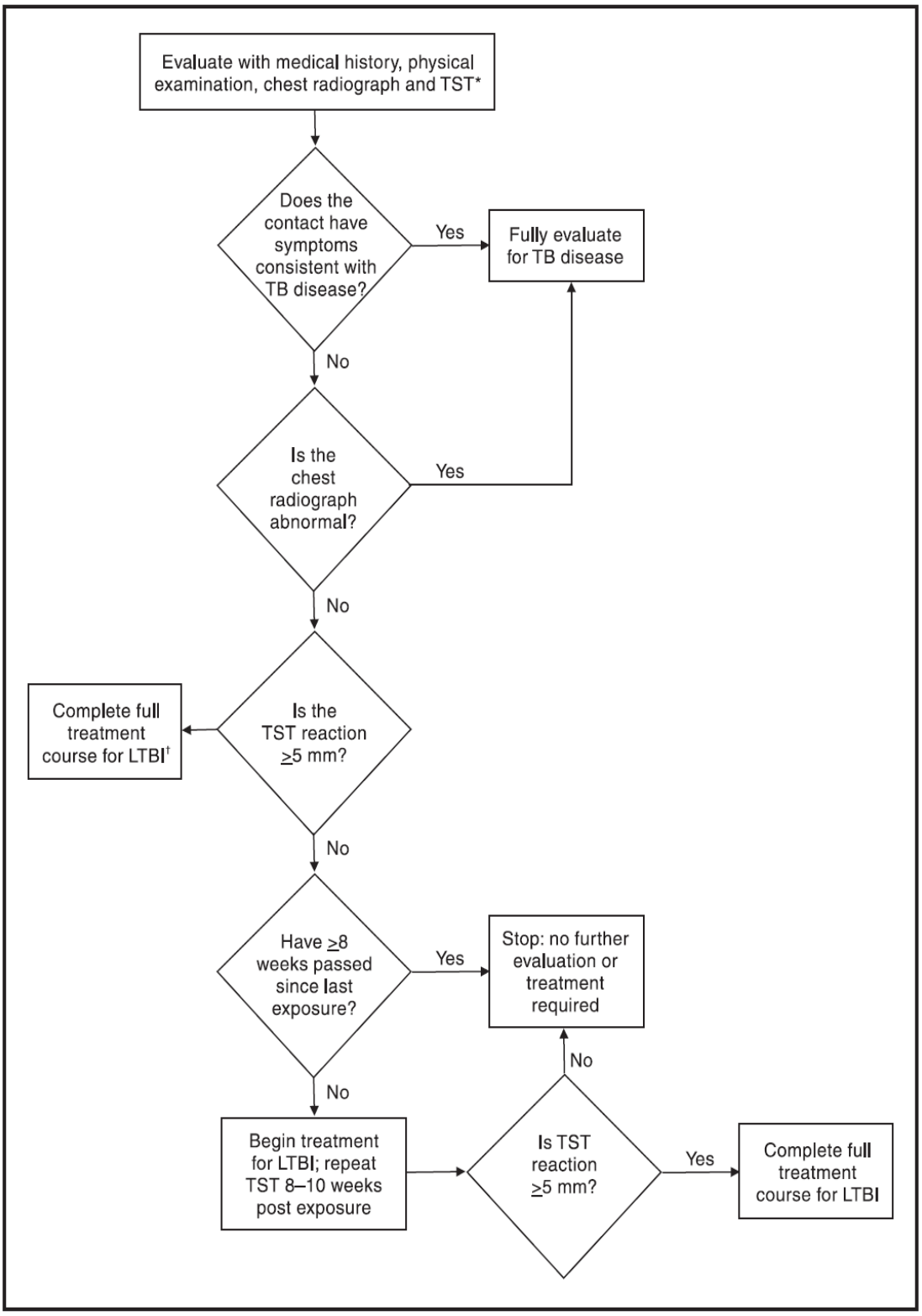


Figure 4. Prioritizing Contacts: For source case investigations in young children.



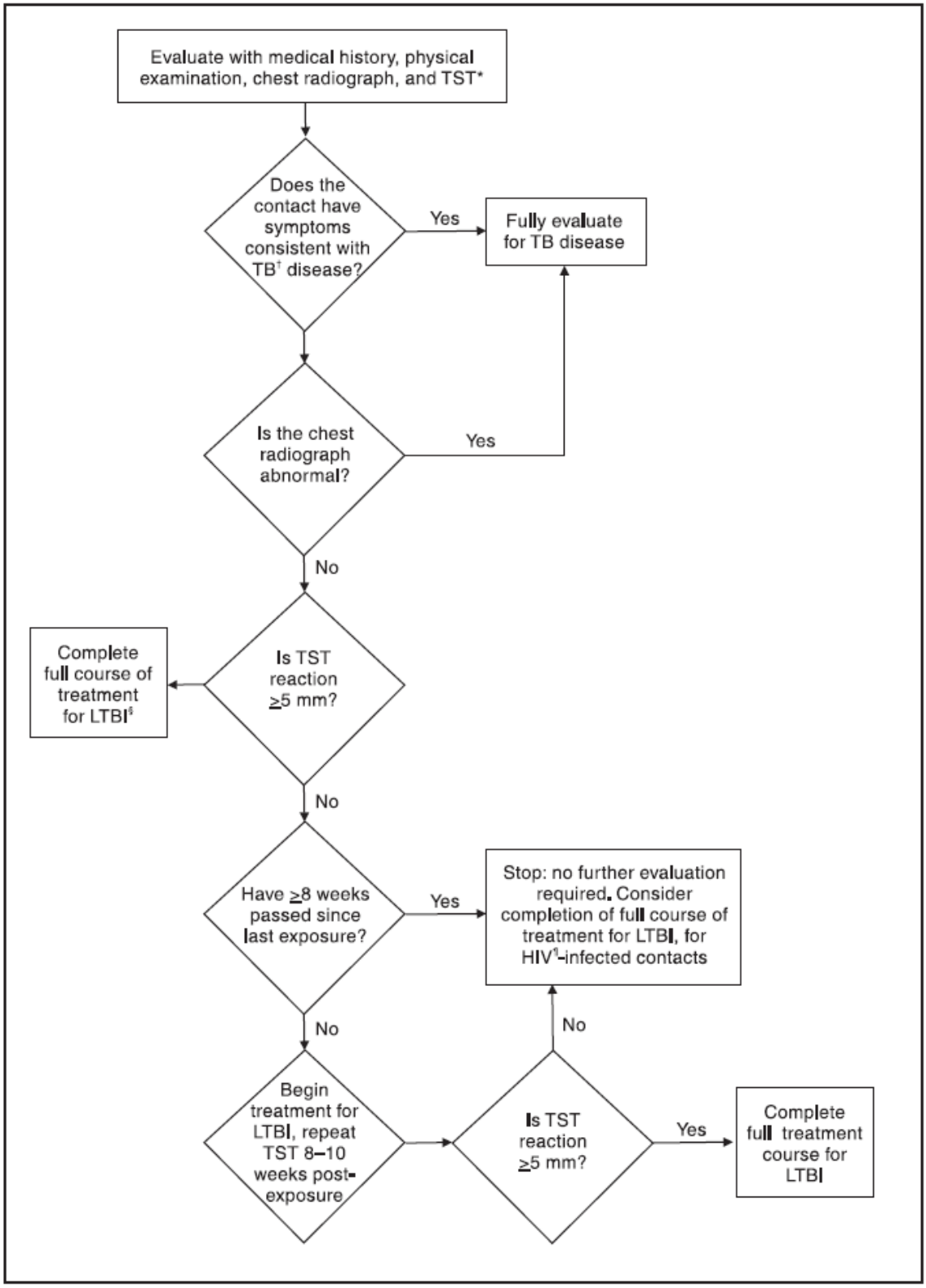
B. CONTACT FOLLOW-UP – BY CONTACT CHARACTERISTICS

Figure 5. Contacts <5 years: Evaluation, treatment, and follow-up



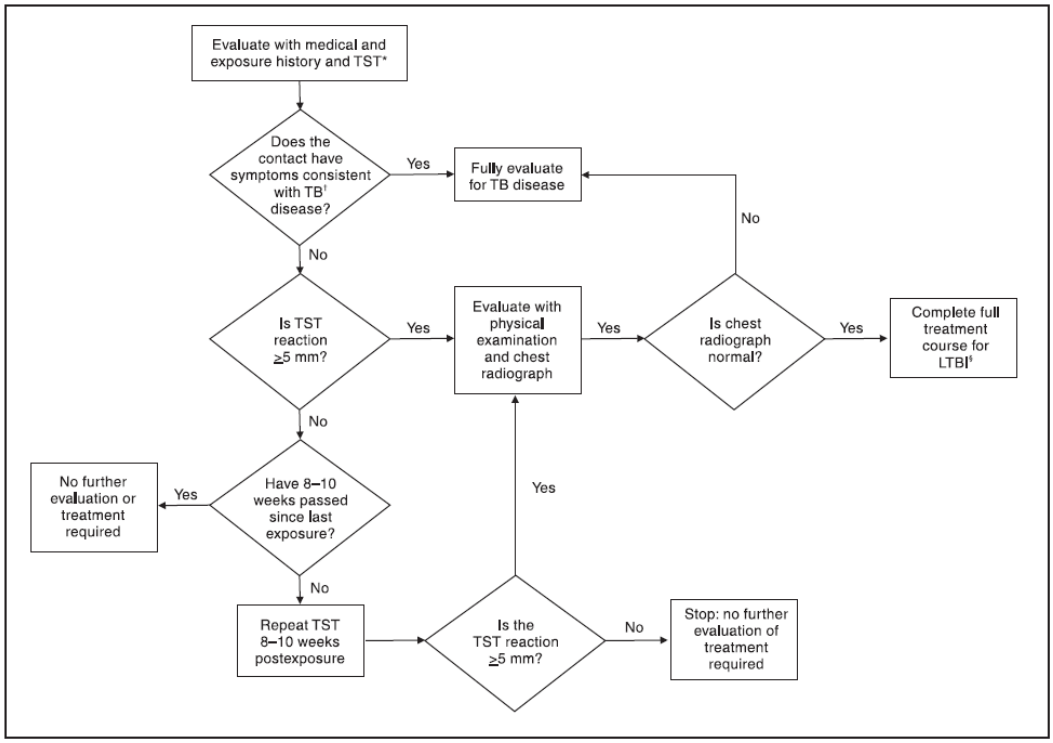
* Tuberculin skin test.
† Latent TB infection.

Figure 6. Immunocompromised Contacts: Evaluation, treatment, and follow-up



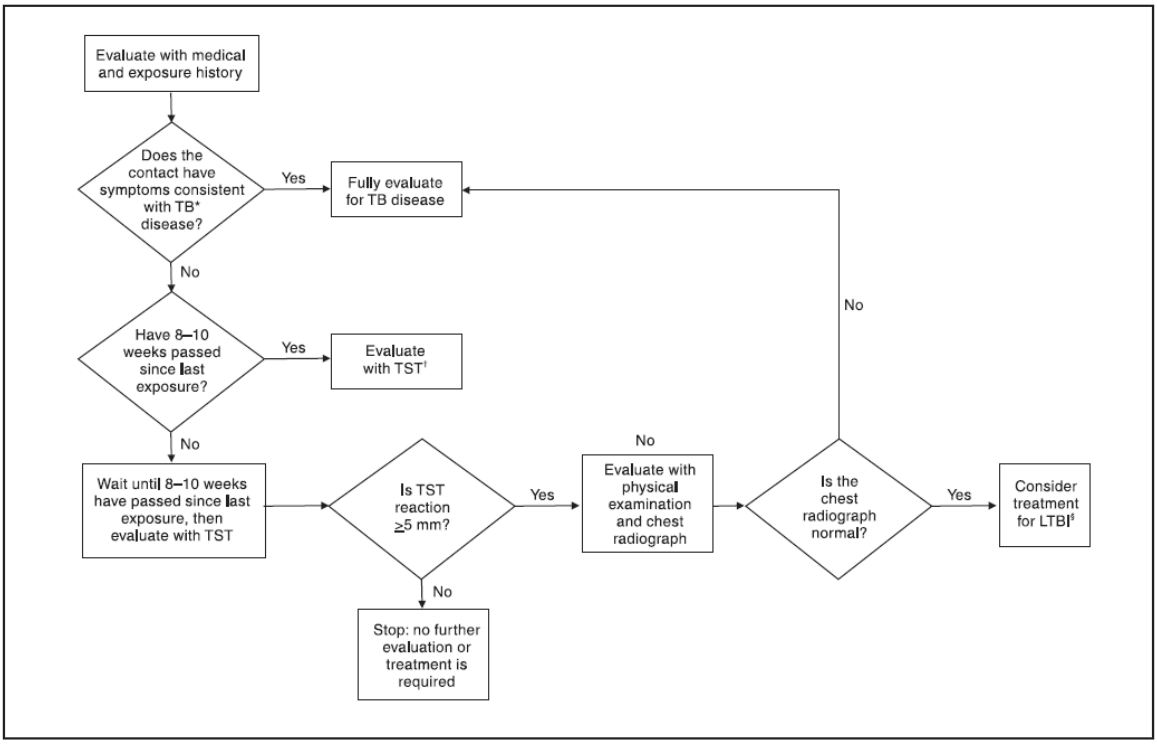
* Tuberculin skin test.
† Tuberculosis.
§ Latent TB infection.
¶ Human immunodeficiency virus.

Figure 7. High- and medium-priority contacts who are immunocompetent adults or children 5 years or older: evaluation, treatment, and follow-up



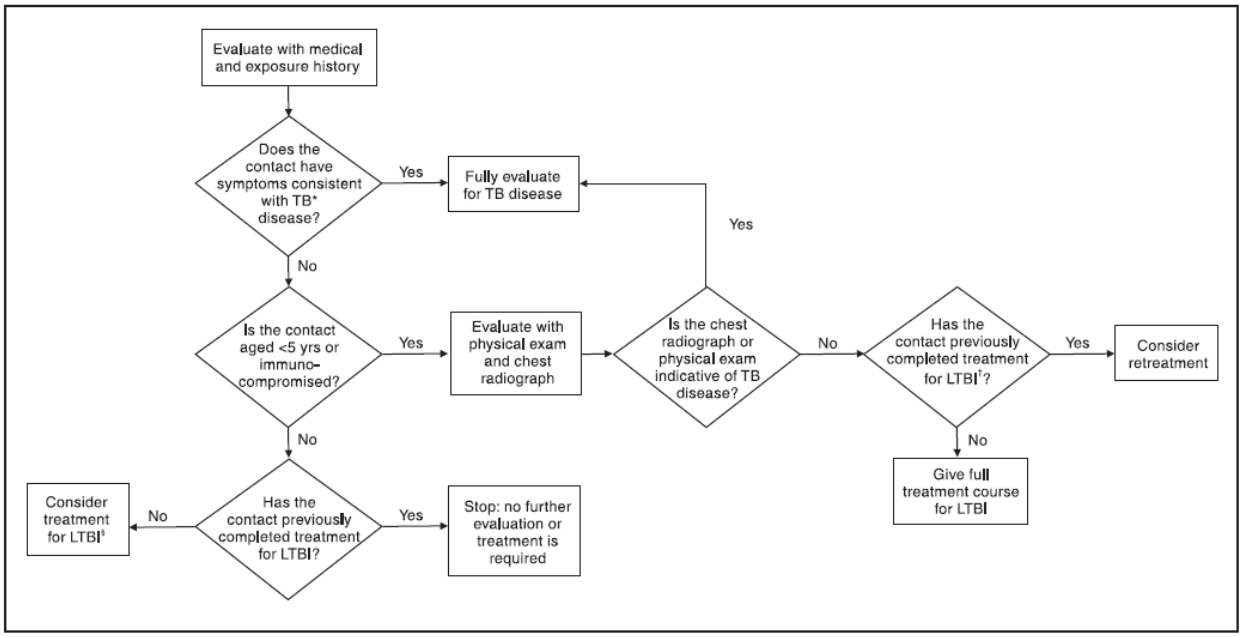
* Tuberculin skin test.
† Tuberculosis.
§ Latent TB infection.

Figure 8. Low-priority contacts



* Tuberculosis.
† Tuberculin skin test.
§ Latent TB infection.

Figure 9. Contacts with documented previous positive TST or IGRA



*Tuberculosis.
†Latent TB infection.
§Before initiation of treatment, contacts should be evaluated fully for TB disease.

Source for all figures: CDC Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis

Interjurisdictional Referrals

When an individual is moving out of the jurisdiction originating the case, or is discovered to be living in another jurisdiction, the originating department should ensure that the necessary steps are taken to transfer the case to the receiving jurisdiction, as outlined below. The Utah Department of Health (UDOH) TB Nurse Consultant (when appropriate or requested) will ensure proper routing and follow-up, and report back to the originating department upon request.

Procedure

Individuals moving out of Utah: *All* need to be closed by the local health department (LHD) with an Administrative LHD case status of "Out of State", and the Interjurisdictional Referral form completed and forwarded to the Nurse Consultant, who will then forward to the appropriate state (or national) health department. Include pertinent paperwork as needed or requested (e.g. labs, radiology reports, prescriptions, monthly medication pick-up/patient assessment or DOT log, summary note). The Nurse Consultant will follow up with the receiving jurisdiction, and report back to the sending jurisdiction, as requested or required.

Individuals moving into Utah: All Interjurisdictional Referrals coming into Utah must be routed through the TB Control Program. The Nurse Consultant will open a file in UT-NEDSS and attach paperwork received from the sending jurisdiction. The Nurse Consultant will also notify the receiving jurisdiction by phone, email or through the Task function in UT-NEDSS; and will communicate with the referral jurisdiction as necessary. For those Utah districts not using UT-NEDSS for non-Class B or non-contact TB Infection, the Nurse Consultant will route the paperwork via fax or email.

Individuals moving within Utah: Since the state needs to track individuals with possible TB, contacts, active cases, and Class Bs, cases for individuals moving within Utah should be rerouted in UT-NEDSS and the Nurse Consultant and receiving jurisdiction advised by phone, email, or through the UT-NEDSS Task function. The Nurse Consultant can assist as needed. Non-Class B and non-contact TB infections, *may bypass the state, however be aware that not all LHDs are using UT-NEDSS for TB infection.* (Check with the Nurse Consultant for the most up-to-date list.) *Use the Interjurisdictional Referral and Follow-Up form for intrastate transfers if the receiving or originating LHD will not use the UT-NEDSS file.* In all cases, include pertinent paperwork as needed or requested (e.g. labs, radiology reports, prescriptions, monthly medication pick-up/patient assessment or DOT log, summary note).

Isolation Considerations

An individual with active TB disease (ATBD) will be considered infectious, and therefore capable of transmitting TB to others, when they have disease in the lungs, airways or larynx and have positive acid fast bacilli (AFB) sputum smears. Other factors that correlate with the contagiousness of an active case are the presence of cough, cavitation on chest radiograph, inappropriate or short duration of treatment, or poor clinical response to treatment. Transmission, although less likely, does occur with smear negative, culture positive individuals. A facility (hospital, jail, or other congregate setting) housing a potentially infectious individual must consult with public health (the local or state health department) before discharging the person into the public (Utah Code R388-804).

Procedure

a. An individual who is considered infectious should be given a surgical mask to wear, instructed to remain at home, or evaluated for the need for hospitalization. The environment should be evaluated for high-risk contacts (e.g. people who are immunosuppressed, children <5 years, pregnant women) who may be at risk for developing disease.

b. Individuals are to remain in isolation until they meet the following criteria:
   - They are on adequate therapy for 2-3 weeks;
   - They have significant **clinical response to therapy** (i.e., reduction in cough, resolution of fever); and,
   - They have **three** negative AFB sputum smear results collected 24 hours apart, with at least one being an early morning specimen.

c. Individuals with extrapulmonary TB are not infectious, unless they have pulmonary or laryngeal TB in addition to their extrapulmonary disease, or have an abscess or open lesion requiring treatment that may lead to aerosolization of wound drainage (has been documented, but is a rare occurrence). Wound care requires the use of an N-95 respirator, and the individual should be in airborne and contact isolation if the wound is weeping. Always keep a weeping wound covered.

d. In general, children who have pulmonary TB are less likely to spread TB than adults because children do not usually develop a cough strong enough to aerosolize TB organisms. However, transmission from children can occur in certain situations, especially if they are diagnosed with upper-lobe, cavitary disease. Therefore, children with TB should be evaluated for infectiousness using the same factors as above for adults.

e. If an individual fails to adhere to isolation and is considered a public health risk, consult the TB Control Program, and refer to manual section 'Isolation of Non-adherent Individuals with Tuberculosis.'

f. If there is a concern of an infectious person travelling on an airplane, the CDC can add them to their 'Do Not Board' list. This will need to be done through the TB Control Program, and the final determination on adding or deleting someone from

this list will be the sole responsibility of the CDC. The CDC can also establish a 'border lookout' if there is a concern of an infectious person entering the U.S. by means other than air transportation. See the manual section, 'Travel Restrictions', for more details.

Other Resources

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

CDC Federal Air Travel Restrictions for Public Health Purposes

Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings

WHO Tuberculosis and Air Travel. Guidelines for Prevention and Control

UDOH Court-Ordered Treatment and Involuntary- Isolation Guidelines for the Control of Tuberculosis

Transmission Prevention & Infection Control Planning

In accordance with federal and state law, an effective TB infection control program must be implemented by all health care facilities, ambulatory-care settings, emergency departments, and other health care settings, and reviewed annually. The extent of the TB infection control program should be based on a risk assessment for transmission of *M. tuberculosis* and appropriate control measures to minimize that risk in a given setting. The infection control program includes all paid and unpaid persons working in healthcare settings who have the potential for exposure to infectious *M. tuberculosis*.

Procedure

a. Personnel should be assigned to perform an assessment of the risk for transmission of TB in a particular setting, area or occupational group based on:
   - The profile of TB in the community
   - The number of individuals with TB admitted to the area or ward, or the estimated number of individuals with TB to whom health care workers (HCWs) in an occupational group may be exposed
   - The results of analysis of HCW skin test or interferon-gamma release assays (IGRA) conversions (where applicable) and possible person-to-person transmission of MTB

b. **Administrative controls** to reduce the risk of exposure to persons with infectious TB should include:
   - Developing and implementing effective written policies and work practices to ensure the rapid identification, isolation, diagnostic evaluation, and treatment of persons likely to have ATBD
   - Implementing effective work practices among health care workers in the health care facility

c. Written TB infection control protocols must be developed to include the following:
   - Triage to promptly identify individuals who may have TB
   - Promptly evaluate individuals who have TB symptoms
   - Place individuals in a separate area apart from others and not in open waiting areas (ideally in a room or enclosure with special ventilation maintained under negative pressure)
   - Give individual a surgical mask to wear until he/she can be transported to an appropriate isolation room or facility, or until he/she leaves the building
   - If a mask is not available, give the individual a tissue and instruct them to cover their mouth and nose when coughing or sneezing
   - Schedule appointments to avoid exposing others, especially HIV-positive or immunocompromised persons
   - Avoid performing a cough-inducing procedure (e.g., sputum inductions) on individuals who may be infectious unless the procedure is absolutely necessary and performed using local exhaust ventilation devices such as booths or special enclosures or in a room that meets ventilation requirements for TB isolation

- Allow enough time to pass for at least 99% of airborne contaminants to be removed before placing another individual in a room or area previously occupied by an infectious individual (Consult the manufacturers operating instructions or a qualified engineer to define the length of time needed to remove at least 99% of airborne contaminants.) A general guide can be found at the following link: Guidelines for Environmental Infection Control in Health-Care Facilities. CDC 2003.
- If the individual is placed in TB isolation and is not wearing a mask, all persons[4] entering the room should be fit-tested for and must wear respiratory protection that meets minimum requirements for TB transmission prevention (at least an N-95) TB transmission prevention precautions can be discontinued if the diagnosis of TB is ruled out or if contagiousness is ruled out.

d. Personnel must be educated and trained, as appropriate for their work responsibilities and duties, regarding TB. Training should occur before initial assignment, and the need for additional training re-evaluated periodically. Education should include: clinical information, epidemiology of TB, infection control practices to prevent and detect TB transmission in health-care settings, TB and immunocompromising conditions, and TB and public health. For a complete list, see page 14 of CDC's Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings.

e. Personnel must be counseled and screened for TB and TB infection; therefore, employers must develop a TB screening program, which includes using tuberculin skin testing or IGRA, for persons in the facility with the potential for exposure to TB. HCWs, including home health nurses, clinic workers and emergency medical technicians, should be included in a TB screening program if the risk assessment indicates that they are at risk for exposure. This means TST upon employment **using the two-step method, (if IGRA is used, two-step testing is not necessary or recommended)** and at repeated intervals determined by their risk of exposure thereafter. Any worker who develops symptoms of TB disease or whose TB screening test result converts to positive should be evaluated promptly and reported to the TB Control Program.

f. **Engineering controls** to prevent the spread and reduce the concentration of infectious droplet nuclei in the air, include:
   - Ventilation systems to maintain negative pressure and exhaust air properly in TB isolation rooms
   - HEPA filtration and ultraviolet irradiation in high-risk areas

g. A respiratory protection program for personnel must include: the selection of **National Institute for Occupational Safety and Health (NIOSH)-approved particulate respiratory protection** which meets the minimum requirements for TB

---

[4] Visitors should be limited to close contacts who have already been exposed during the infectious period. They may be offered respiratory protection (i.e., N95) and instructed by health care workers on the use of the respirator before entering an airborne infection isolation room. In addition, before allowing non-fit-tested visitors to enter the room, the individual should don a surgical mask and enough time should elapse enabling at least 99% of contaminants to be removed from the air. The individual should continue to wear the mask throughout the visit. It is recommended that children < 5 and immunosuppressed individuals not be allowed to visit a potentially infectious case.

transmission prevention, medical evaluation and fit testing, training in the use and maintenance of respirators, and program evaluation.

h. Facilities that admit individuals with ATBD must initiate isolation in a private isolation room with special ventilation maintained under negative pressure relative to other parts of the facility. The room must be monitored daily while in use to assure that appropriate ventilation is maintained, the door must remain closed, and the individual should only leave the room for medically essential purposes. For the safety of all workers and visitors, the isolation room must be clearly identified as housing a potentially infectious person. When the individual must leave the room, the person should wear a surgical mask that covers the nose and mouth at all times. Individuals who are placed in isolation rooms should be educated about the transmission of TB, the reasons for isolation, and the importance of staying in their rooms. The individual should also be instructed to cover their nose and mouth when coughing or sneezing.

   The number of persons entering the room should be limited and those entering the room must wear appropriate personal respiratory protective devices. These devices must adequately fit the worker or visitor and be “user seal” checked before use. **Individuals evaluated or admitted to an inpatient facility and determined to have sputum smear positive suspected or known active TB disease (ATBD) cannot be released until the state or local health agency has made arrangements for appropriate post discharge management.** The individual is considered noninfectious when all of the following criteria are met:
   - On adequate therapy for 2-3 weeks;
   - Have significant **clinical response to therapy** (i.e., reduction in cough, resolution of fever); and,
   - Have **three** negative AFB sputum smear results collected 24 hours apart, with at least one being an early morning specimen.

   Proper isolation procedures must be maintained while at the facility. Isolation should only be discontinued when it is determined that the individual is no longer contagious. Settings/facilities unable to adequately evaluate individuals who have, or are suspected to have, infectious TB should develop a triage system to identify, manage and refer these individuals to another facility for diagnostic evaluation and treatment.

i. Some individuals with likely or known ATBD may be evaluated or treated in an outpatient setting under the supervision of, or directly provided by the local public health agency.

j. Contact the TB Control Program for consultation regarding the appropriateness of home placement for individuals. Persons who are placed at home should be instructed to cover their nose and mouth when coughing or sneezing and be instructed on the importance of taking prescribed therapy and directly observed therapy (DOT). Health care workers must wear appropriate respiratory protection when visiting individuals with confirmed or suspect infectious TB. Avoid performing cough-inducing procedures on individuals who are infectious or use appropriate respiratory protection and perform in a well-ventilated area. Visitors must be cleared by public health.

References

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

Improving Adherence with Therapy

Adherence to medication regimens for TB is a priority and can be accomplished through the use of Directly Observed Therapy (DOT), and the use of incentives and enablers. DOT is considered the standard of care for individuals with active TB disease (ATBD), is required by the Utah Administrative Code Communicable Disease Rule (R388-804), and is recommended for use with high-risk individuals with TB infection. The responsibility for successful treatment is clearly assigned to the public health program or private provider, not to the individual.

Procedure

a. DOT is the standard method of providing treatment to all persons with ATBD. Many health care providers believe they can predict whether a particular individual will take medication as prescribed. However, data indicate that providers, on average, are correct only 50% of the time. In addition, DOT allows for the immediate detection of non-compliance so that actions can be taken to avoid treatment failure.

b. Health care providers must recognize that even with DOT, additional strategies and efforts are necessary for treatment success. It is important to use any tool available in order to promote adherence to therapy.

c. Consider entering into a "contract" with the individual that clearly states their responsibilities in regards to treatment.

d. Learn as much as possible about the individual's health history, beliefs and attitudes about TB, sources of social support, and potential barriers to treatment prior to starting treatment.

e. Work with a medical interpreter or a person of the same cultural background and gender as the individual, if possible.

f. Designate a person to administer DOT who does not have strong emotional ties with the person receiving treatment. Suitable designees might include school nurse/staff, employee health, public health, or visiting nurse, clergy, or other responsible person. Family members are not the appropriate choice to assist because of power struggles and family dynamics.

g. Mutually agree on a time and location for DOT; be creative and flexible.

h. Be aware of individuals who may require techniques to assess for complete ingestion of medication (e.g., hiding pills in mouth, vomiting after pills swallowed).

i. Use incentives and enablers to assist in improving adherence. The TB Control Program can assist with rent, food coupons, payment of limited bills, and rewards for specific milestones in treatment. Housing is available in some communities. Specific incentives are available to assist young children and contacts to cases of ATBD to complete treatment for TB infection. Contact the TB Control Program for more information on the use of incentives and enablers.

j. Look for early warning signs of future adherence problems (e.g., individual feels medicine is no longer needed because they are feeling well, difficulty in accessing health care, transportation issues, worksite concerns, etc.). See 'Procedure for Managing Persons at Risk to Be Lost to Treatment' in the document COURT-ORDERED TREATMENT AND INVOLUNTARY – ISOLATION GUIDELINES FOR THE CONTROL OF TUBERCULOSIS.

k. Provide effective education to individuals and key people in their environment.

l. Provide individual with needed health or social services or make referral to other health or social service agencies.

m. Use a team of personnel whose members work together to assist each individual in completing treatment.

n. Establish an efficient, client-friendly clinic system for scheduling appointments, keeping records, and monitoring adherence.

o. If, despite your best efforts, the individual does not adhere to DOT voluntarily, Utah State statutes allow court-ordered isolation/quarantine. See next manual section on 'Isolation of Non-Adherent Individuals with ATBD' or COURT-ORDERED TREATMENT AND INVOLUNTARY – ISOLATION GUIDELINES FOR THE CONTROL OF TUBERCULOSIS). Contact TB Control Program for more information and assistance.

Other Resources

ATS/CDC/IDSA Treatment of Tuberculosis

CDC Self Study Module on TB, Module 9 Patient Adherence to TB Treatment

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

Isolation of Non-Adherent Individuals with ATBD

In partnership with the local health departments (LHDs) and health care providers, the Utah Department of Health is responsible for implementation of the Utah Communicable Disease Act and Communicable Disease-Treatment, Isolation and Quarantine Procedures (Utah Health Code 26-6B). This statute delineates the process for ordering involuntary treatment, isolation, and quarantine of persons with public-endangering communicable diseases who are unable or unwilling to fully participate in their prescribed treatment.

Procedure

a. Within the context of tuberculosis disease, the first priority of public health is to prevent further transmission of TB in the community by an infectious individual. This is accomplished by identifying all persons with highly suspect or confirmed active TB disease (ATBD), and ensuring appropriately prescribed treatment is completed. **In order to safeguard appropriate use of scarce resources and comply with the civil liberty rights of the individual, it is recommended that the less restrictive levels of care be pursued aggressively before progressing to more restrictive levels.**

   The levels of care are:
   - **Level of Care 1**: Prescribed outpatient treatment, including directly observed therapy (DOT), provided by a health care provider, clinic, or LHD for those individuals both willing and able to fully participate in the treatment of their ATBD.
   - **Level of Care 2**: Enhanced provision of outpatient treatment with use of incentives, enablers, DOT, electronic surveillance, etc., for individuals who indicate an unwillingness or inability to undergo prescribed medical treatment, or have demonstrated poor adherence to treatment that has been previously initiated. Implementation of these additional measures ensures completion of treatment.
   - **Level of Care 3:** Secure/locked housing such as long-term care settings, for those persons who have not responded to Level 2 strategies and are non-infectious. Adequate measures are provided that minimize/eliminate the flight risk of these individuals (this measure is currently not available in Utah).
   - **Level of Care 4**: Secure/locked hospital unit or facility offering negative pressure isolation and staff trained in TB control for accommodating individuals with ATBD who have failed adherence to treatment at less restrictive levels of care (this measure is available in Utah).

b. The Advisory Council for the Elimination of Tuberculosis defines non-adherent behavior as the inability or unwillingness to follow a prescribed treatment regimen. This may be demonstrated by refusing medication, taking medication inconsistently, missing healthcare provider appointments, failing to report for DOT, disregarding masking requirements, or disregarding travel restrictions.

c. Although many health care providers believe they can predict a client's adherence to treatment, research indicates their predictions are correct only about 50% of the

time. **The strongest predictor of adherence to treatment is the individual's history of adherence. The strongest predictor of future adherence problems is a history of non-adherence to treatment, particularly with TB medications.** If there is documentation of non-adherence with previous TB treatment or therapy for TB infection, the likelihood that the individual will be successful in adhering to the current treatment regimen is questionable.

d. Other indicators for high-risk of non-adherence include: history of other medical treatment non-adherence; substance abuse; mental, emotional, or certain physical impairments that interfere with the ability to self-administer medications; children and adolescents. It is recommended that health care providers formally evaluate each individual's potential non-adherence at the time TB medication is prescribed. It is also recommended that a treatment plan is used as a contractual agreement. See the following link for an example: http://health.utah.gov/epi/diseases/TB/forms/atbd/active_tb_agreement.pdf

e. If non-adherence with prescribed TB medications is a concern, contact the TB Control Program to discuss, prior to initiating any isolation procedures. Documentation of non-adherence is essential to success with this process.

References

UDOH Court-Ordered Treatment and Involuntary- Isolation Guidelines for the Control of Tuberculosis

Travel Restrictions

The state and/or local health department will assume the responsibility of identifying the steps necessary to curb transmission of TB, of informing the individual of their responsibilities, and of enforcing the treatment plan as documented (see manual sections on treatment of active disease, and isolation). As it may sometimes become necessary to administratively enforce travel restrictions, procedures are in place to assist in the authority of such restrictions.

Procedure

a. Ensure that the individual has been thoroughly informed of their responsibility to follow the treatment plan, and of the health department's ability to involuntarily restrict their movement and behavior.

b. If the individual expresses a desire to leave the jurisdiction of the local health department providing case management, establish a plan of action that will not compromise the public's health. This includes maintaining a verifiable continuation of directly observed therapy, and restrictions related to infectiousness.

c. If the individual is planning to use any form of mass transit, determine the feasibility of such travel and counsel the person accordingly. This includes transportation by bus, train, ship, or plane. Individual infectiousness and need for voluntary isolation is discussed in the manual section, 'Isolation Considerations'; the health department's ability to restrict movement and behavior is discussed in the manual section, 'Isolation of Non-Adherent Clients with ATBD.'

d. If said travel will involve something other than simply local travel, the Centers for Disease Control and Prevention (CDC) maintains a 'Do Not Board' procedure to prevent travel from occurring. Utilization of CDC's 'Do Not Board' procedure requires that specific steps are followed and case information provided to assist in the decision to include the patient on a 'Do Not Board' list. Only CDC can add a name to/remove a name from this list, under the advice of the jurisdiction managing the case.

Protocol for Air Travel 'Do Not Board List'

In the event that an individual with suspected or confirmed infectious ATBD intends to attempt to board an airplane (or other mode of transportation, e.g. ship, long-distance train or bus), the CDC maintains a 'Do Not Board List' in order to prevent such an individual from doing so. CDC has the final authority as to who to include on this list and when to remove them. Inclusion on this list also places the individual on a 'Border Watch List' in order to restrict such a person's movement across the Mexican or Canadian borders, and isolate them as appropriate.

If an individual is to be considered for this action, the following procedure is required:

- The local health department, or other provider, should contact the TB Control Program as soon as an individual's intent is known. The minimum amount of information needed is the individual's name, sex and date of birth. Additional

information such as immigration status and citizenship, as well as specific travel plans is helpful. Contact the Utah State TB Controller at 801-538-9906 or cell # 385-321-2064. The TB Controller will be able to speak with CDC 24/7, and will be able to take action within 2 hours or less. **CDC and UDOH request that initial communication be facilitated through the TB Control Program. Local health departments are asked not to call CDC directly.**

- A representative from the state and/or local health department needs to be available for a conference call to review the case. Be ready to discuss clinical status (including infectiousness, length of time on adequate regimen, drug resistance), compliance issues, whether (and when) or not the individual has been instructed not to travel, and actions taken to prevent travel.

- If the individual does attempt travel, the local health officer should initiate a temporary administrative order for involuntary isolation, and proceed accordingly. See UDOH Court-Ordered Treatment and Involuntary- Isolation Guidelines for the Control of Tuberculosis for further details.

- CDC will determine whether the individual warrants inclusion on the list. The TB Control Program will contact CDC when it is determined that the individual no longer requires travel restrictions.

Other Resources

CDC Federal Air Travel Restrictions for Public Health Purposes

WHO Tuberculosis and Air Travel. Guidelines for Prevention and Control.

DNB Questionnaire for Local Health Departments

Demographic Information:

1) Patient's name (last, middle, first):_____
2) Aliases:_____
3) Gender: [ ] Female [ ] Male [ ] Unknown
4) Date of Birth:_____
5) Race:_____
6) Ethnicity:_____
7) Nationality:_____
8) Aliases' Date of Birth:_____
9) Identifying features (photo if available):

_____

_____

10) What is the patient's legal status in the United States?
a. U.S. Citizen
b. Legal permanent resident
c. Asylee
d. Parolee
e. Refugee
f. Visa Waiver
g. B1/B2 Tourist/Business
h. F1/F2 Student Status/Family of
i. H1/H2 Working Group/Family of
j. J1/J2 Exchange Visitor/Family of
k. Unknown
l. Other:_____

11) Documents used to establish patient's identity:
a. Birth certificate
b. Social Security card and number:_____
c. Passport
d. Driver's license (state, number and expiration date):_____
e. Class B papers
f. Other:_____

12) Passport Country (can list more then one if patient has more then one passport):

_____

_____

13) Passport Number(s):

_____

_____

14) Is the patient currently in the U.S.? If yes, location:

_____

_____

If no, location:

_____

_____

15) Family/Emergency Contact Information:
a. Relationship:_____
b. Name:_____

c. Address (street, city, state, country):_____
_____
d. Phone(s):_____
e. Relationship:_____
f. Name:_____
g. Address (street, city, state, country):_____
_____
h. Phone(s):_____
i. Relationship:_____
j. Name:_____
k. Address (street, city, state, country):_____
_____
l. Phone(s):_____

Travel Plans:
1) Pending travel dates:_____
2) Reservation details (destination, carrier(s), time(s), ticket number(s)):
_____
_____
_____
_____

Clinical Information:
1) Is the patient's disease confirmed? [ ] Yes, confirmed [ ] No, suspect
2) What was the date (mm/dd/yy) of the confirmed or suspect diagnosis?_____
3) Please note clinical signs, symptoms and any other additional information that supports suspected/confirmed diagnosis, and whether they are current:
_____
_____
_____
_____
4) Has the patient improved since starting drug therapy? [ ] Yes [ ] No
Explain:_____
_____
_____
5) What treatment is the patient currently receiving? List all drugs, dosages, administration routes and frequency:_____
_____
_____
_____
_____
_____
6) Is patient on DOT by a health care worker? [ ] Yes [ ] No [ ] Unknown
7) How many days a week is DOT?_____
_____
8) Treatment start date:_____
_____
9) Is patient compliant with treatment? [ ] Compliant [ ] Non-compliant [ ] Unknown

10) Does patient have a prior history of TB? [ ] Yes [ ] No [ ] Unknown
a. If yes - date of previous TB diagnosis:_____
b. If yes - prior TB treatment (please list medications if known):_____
_____
_____
_____
_____
c. If yes: was patient compliant with prior TB treatment? [ ] Yes [ ] No [ ] Unknown
11) What is current TB site? Circle all that apply:
a. Pulmonary
b. Extra-pulmonary
c. Laryngeal
d. Unknown
12) Date and results of CXR:_____
_____
_____
[ ] Cavity [ ] Miliary
13) Date and results of CT scan:_____
_____
_____
[ ] Cavity [ ] Miliary
14) Was sputum collected? If yes, how?
a. Induced
b. Spontaneous
c. Unknown
d. Bronchial washings (bronchoscopy)
15) Was sputum collected in the U.S.? [ ] U.S. [ ] Other country:_____
16) **Sputum Results Table:**

Sputum Collection Date	**AFB Smear***	**Culture****	**MTD*****

*Options for AFB Smear are 1+, 2+, 3+, 4+, Rare, Few, Numerous
** Options for Culture are MTB Complex, Atyp, Negative, Pending
***Options for MTD are positive (RIF sensitive or resistant), negative, pending

17) Culture sensitivities done? If yes:
a. Pan-sensitive or resistance to no more than one of the first line agents
b. MDR
c. XDR
d. Other: _____
e. Pending
18) If drug sensitivities are pending, is patient a contact to a drug-resistant case? [ ] Yes [ ] No
[ ] Unknown - If yes, what is the index case's resistance pattern?_____

Utah Public Health Laboratory / Mycobacteriology Laboratory

The Utah Public Health Laboratory (UPHL) tests for the presence of acid-fast bacilli (AFB) in clinical specimens submitted by private health care providers and public agencies. The laboratory also determines the identification of AFB species and performs susceptibility testing on *Mycobacterium tuberculosis* complex. Private laboratories also refer isolates to the laboratory for identification and susceptibility testing. With the exception of blood cultures for AFB, these services are provided at no charge for local and state health departments. A charge is incurred by private providers.

Policy

Submitting Specimens

Specimens should be delivered to the *Utah Public Health Laboratory* at 4431 South 2700 West, Taylorsville, Utah either by courier or U.S. mail as soon as possible after collection. See 'Specimen Collection and Transport' section in this manual for detailed instructions.

Testing Schedule

Specimens are processed once a day, Monday through Friday for AFB culture. Specimens that are received in the laboratory by 11:00 A.M. are included in that day's "run".

AFB smears from specimens processed Monday through Friday are generally read by 5:00 P.M. on the same day.

Identification of *M. tuberculosis* complex is performed as required and completion of testing in some cases can take several weeks.

After identification of the first specimen to grow AFB positive cultures, the local and state health departments then send subsequent cultures looking for the patient to have a conversion to negative culture results. Identification of subsequent positive cultures that match colony morphology is only completed for two months. At the end of the two months (calculated from date of collection, not date tested) the lab will re-identify if the culture is still AFB positive. If there is a significant change in colony morphology the lab will also identify the new colony morphology to ensure that identification is still correct.

Procedure

Testing Methods

AFB smears are stained using the Auramine O method and examined using fluorescent microscopy.

Specimens that are likely contaminated with other bacteria are processed using the NALC-NaOH method and inoculated to 7H11 solid medium and to BACTEC MGIT broth medium.

Specimens from sterile sites are inoculated directly to 7H11 solid medium and to BACTEC MGIT broth medium. Though they are not tested at the UPHL and are in turn sent out to (Colorado Department of Public Health and Environment (CDPHE) for reference testing; blood and bone marrow specimens are inoculated to BACTEC Myco/F-Lytic broth.

Identification is determined by Accuprobe DNA probe.

Reporting Schedule

AFB reports are made to the requesting provider by the method they have specified. This can be by phone, fax, or E-mail.

AFB smear results are generally reported within 24 hours after UPHL received the sample.

Positive cultures are reported as they are found and identification results are reported as the testing is completed.

Negative cultures are held for a minimum of seven weeks. Final “no growth” cultures are reported once a week.

DNA Genotyping of *Mycobacterium tuberculosis*

DNA genotyping of *M. tuberculosis* is a useful epidemiological tool that can be used to detect possible outbreaks, track the transmission of *M. tuberculosis* in the population or obtain evidence that cross contamination has occurred in the laboratory. The CDC has contracted with several Public Health laboratories to provide this service to the states.

The initial isolate from each new Utah patient found to have *M. tuberculosis* complex in specimens submitted to the UHPL will be sent to a CDC contract laboratory for DNA genotyping. Other laboratories performing AFB testing on Utah residents are requested to send isolates of *M. tuberculosis* to the UPHL, which will then submit them for genotyping.

There are cases where additional isolates may be submitted. Patients whose isolates have become resistant and patients who have become negative on culture and then have reverted to positive will have the second isolate submitted to determine if the patient has become infected with a new strain. The TB Program may also request additional submission of isolates when they feel it is appropriate.

GeneXpert, a direct method of detecting MTB RNA from raw samples. First-time positive smear sputum samples (as well as any specific samples requested by the TB Control Program). The lab is not validated to test for tissue or other specimen sources. Molecular Detection of Drug Resistance is a new method of rapid sensitivity testing that

can be ordered if specific criteria are met. These are not performed at the UPHL. For further information, contact the TB Control Program.

Other Resources

Guide to the Application of Genotyping to Tuberculosis Prevention and Control. CDC.

Murray et al. 2003. Manual of Clinical Microbiology, 8th ed. American Society of Microbiology, Washington DC.

Public Health Mycobacteriology, A Guide for the Level III Laboratory, Centers for Disease Control. 1985.

Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis *MMWR* 2009; 58 (01); 7-10

***Utah Public Health Laboratory* Contacts**

The following contacts can all be reached through the main laboratory phone number: **(801) 965-2400**.

Alessandro Rossi, PhD, Infectious Disease Laboratory Chief Scientist
Lori Smith, BS, Infectious Disease Technical Supervisor
Musarrat Jahan, PhD, Microbiologist

Utah Public Health Laboratory
Specimen Collection and Transport

The Utah Department of Health (UDOH) Public Health Laboratory (UPHL) tests a variety of specimens for mycobacterial culture. With the exception of blood cultures for AFB, these services are provided at no charge for local and state health departments. A charge is incurred by private providers. The quality of the specimens collected and proper transport of those specimens to the laboratory are critical to the successful isolation of AFB (acid-fast bacilli).

Procedure

Specimens should be collected and submitted in sterile, leak proof, disposable, appropriately labeled, laboratory-approved containers. **Label sputa collection container before giving to the client or collecting specimen.** All specimens can be collected in the sterile collection tubes supplied by the UHPL. Do not use waxed containers, as they may provide false-positive smear results.

Initial specimens should ideally be collected prior to the initiation of anti-mycobacterial chemotherapy. Specimens should be collected aseptically, or the collection method should bypass areas of contamination as much as possible in order to minimize contamination with indigenous flora. Avoid contamination with tap water or other fluids that may contain either viable or nonviable environmental mycobacteria, since saprophytic mycobacteria may produce false-positive culture and/or smear results.

Sputum: Sputum, both expectorated and induced, is the principal specimen obtained for the diagnosis of pulmonary tuberculosis. Collect 3 specimens, preferably 5-10 ml, from a deep, productive cough at least 8-24 hours apart, with at least one being an early-morning specimen. It is recommended that dentures, if present, be removed before collection of sputum specimens. If the specimen is not an early morning sample, or if the client has eaten or used tobacco, rinse mouth with water.

- For expectorated sputum, clients should be instructed to cough deeply to produce specimens distinct from saliva, or nasopharyngeal discharge. The client should be instructed to press the rim of the container under the lower lip at the time of expectoration to minimize the chance of contaminating the outside of the container.
- For induced sputum, use sterile hypertonic saline, and avoid sputum contamination with nebulizer reservoir water to avoid possible false-positive culture or smear results due to saprophytic mycobacteria. Indicate on the requisition whether the specimen is induced or expectorated to ensure proper handling, as induced sputa appear watery and much like saliva. Pooled sputum specimens are unacceptable specimens for mycobacterial culture because of increased risk of contamination.***** *(See end of this section for a tip on sputum collection with patients having difficulty with spontaneous production.)*

Bronchoalveolar Lavage Fluids and Bronchial Washing: Bronchial washings, bronchoalveolar lavage fluid, transbronchial biopsy specimens, and brush biopsy specimens may all be collected during bronchoscopy. Collect at least 5 ml of bronchial washing or bronchoalveolar lavage fluid in a sterile container. Avoid contaminating the

bronchoscope with tap water. Frequently, bronchoscopy causes the client to produce sputum spontaneously for several days after the procedure, and specimens collected a day or two after bronchoscopy enhance detection of mycobacteria.

Gastric Lavage Fluids: Aspiration of swallowed sputum from the stomach by gastric lavage may be necessary for infants, young children and the obtunded. On each of 3 consecutive days, collect 5-10 ml of fluid in a sterile container without a preservative. Fasting, early-morning specimens are recommended in order to obtain sputum swallowed during sleep. Gastric contents are initially collected with a sterile suction syringe connected to a tube inserted in the stomach. Sterile saline (20-30 ml) may then be induced into the stomach and aspirated as lavage fluid. The gastric contents and lavage fluid may be pooled in a sterile container. These specimens should be processed within 4 hours. If the specimens cannot be processed within 4 hours, adjust fluid to neutral pH with 100mg of sodium carbonate immediately following collection. Unneutralized specimens are not acceptable, as acid is detrimental to the mycobacteria.

Blood: Cultures for the isolation of mycobacteria from blood are usually reserved for the immunocompromised clients. The BACTEC Myco/F-Lytic bottle is specifically designed for the recovery of mycobacteria from blood. The Myco/F-Lytic medium can be directly inoculated with 5ml of blood. If blood needs to be transported before inoculation of BACTEC medium, use sodium polyanetholsulfonate (SPS) or heparin as an anticoagulant. Blood collected in EDTA (purple top tube) or blood that is coagulated is not acceptable. Blood samples are not tested at the Public Health Lab, but are sent to the Colorado Department of health and Environment (CDPHE) for reference testing.

Urine: Collect the first morning specimens, either by catherization or midstream clean catch, into a sterile container on 3 consecutive days. Appropriate cleaning of genitalia should precede collection. Organisms accumulate in the bladder overnight, and the first morning void provides best results. Specimens collected at other times are dilute and thus not optimal. A minimum of 40 ml is usually required for culture. Pooled specimens and small volume specimens are not acceptable for testing.

Stools: Generally cultures from feces for mycobacteria are not an encouraged source, except for patients with AIDS. Stool specimens (>1g) should be collected in sterile, wax-free, disposable clean containers or transferred from a bedpan or from plastic wrap stretched over the toilet bowl and sent directly to the laboratory.

Body Fluids: Body fluids (cerebrospinal (CSF), pleural, peritoneal, pericardial, etc.) are aseptically collected by aspiration or surgical procedures. Collect as much as possible (10-15ml minimum) in a sterile container or syringe with a luer tip cap. CSF culture requires at least 5 ml. Bloody specimens may be anticoagulated with sodium polyanethol sulfonate (SPS).

Tissues (Lymph Node, Skin, Other Biopsy Material): Aseptically collect at least 1g of tissue, if possible, into a sterile container without fixative or preservative. Do not immerse in saline or other fluid or wrap in gauze. For cutaneous ulcers, collect biopsy material from the periphery of the lesion. Specimens submitted in formalin are unacceptable.

Specimen Transport: All specimens should be refrigerated (except blood) prior to transport to the laboratory. When shipping specimens:

- Make sure that the specimen is in the appropriate sterile specimen collection container
- Seal the container and label appropriately: with patient name, date of birth, and date and time the specimen was collected
- Place the sealed specimen container into a second shipping container. A test requisition form must accompany each specimen and is also placed with the second container

The test requisition forms can be obtained from the laboratory Technical Services group at: (801) 965-2400 or on the internet at: https://health.utah.gov/lab, click on "Infectious Disease" tab and then select the "Client Services Manual" under Bureau of Microbiology.

If a test request form is obtained from the internet it is essential that the proper provider code be entered in the appropriate field. This code determines where test results are sent. If you do not know your provider code, call the Technical Services group or the AFB laboratory at (801) 965-2400.

Specimen Containers suitable for mailing clinical specimens in the U.S. mail can be obtained from the Technical Services group by calling (801) 965-2400. These containers are designed primarily for sputum specimens and have prepaid postage and are only available for local and state health departments.

Send specimens to:

Utah Public Health Laboratory
4431 South 2700 West
Taylorsville, UT 84119-8600
Map & Directions

Other Resources

CDC. Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005. MMWR 2005; 54:RR-17.

Jorgensen, Pfaller, Carroll, Funke, Landry, Richter, Warnock. Manual of Clinical Microbiology, 11th ed. 2015. ASM Press. Washington, DC.

U.S. Department of Health and Human Services 1985: Public Health Mycobacteria: Guide for Level 3 Laboratory.

*****Patients who have difficulty producing sputum may find it helpful to deep-breath steam. One method might be to inhale the vapors from a freshly boiled pot of water, in order to loosen deep secretions.

QuantiFERON®-TB Gold In-Tube: FAQ's

Test Principle

The QuantiFERON®-TB Gold In-Tube assay (QFT) is an in vitro diagnostic laboratory test that aids in the detection of infection with *Mycobacterium tuberculosis*. It uses human whole blood, with patented assay technology based on the measurement of Interferon-gamma (IFN-γ) secreted from stimulated T-cells previously exposed to *Mycobacterium tuberculosis*. The QFT is a straightforward laboratory test that involves simple steps. There are several options available for your facility depending on your resources and preferences. Most facilities choose to simply draw blood and send it to the UPHL within 15 hours, but if distance or schedule do not allow for arrival at the public health lab within the 15-hour limit, samples may be incubated and centrifuged at your facility. The following steps outline the procedures for the three different options:

Option 1 (*preferred)*: On-Site Collection (15 hour time constraint)

1. Collect 1 mL blood into each of the three Blood Collection Tubes (Gray, Red, and Purple).
2. After blood collection, mix the tubes thoroughly, by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).
3. Transport tubes at room temperature. Tubes need to arrive at the laboratory within 15 hours of collection, and by 4:00 P.M. Mon-Fri.

Option 2 (*not recommended*): On-Site Collection and Incubation (70 hour time constraint, upright transport)

1. Collect 1 mL blood into the three Blood Collection Tubes (Gray, Red, and Purple).
2. After blood collection, mix the tubes thoroughly, by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).
3. As soon as possible, and within 16 hours of collection, incubate tubes upright at 37°C for 16-24 hours. Be certain to document date and time for each step.
4. Tubes need to arrive at the laboratory within 72 hours of incubation completion, and by 4:00 P.M. Mon-Fri.

Option 3 (*discouraged)*: On-Site Collection, Incubation, and Centrifugation (refrigerated transport)

1. Collect 1 mL blood into the three Blood Collection Tubes (Gray, Red, and Purple).
2. After blood collection, mix the tubes thoroughly, by shaking vigorously for at least 5 seconds (please remember that simply inverting the tubes is not sufficient).
3. As soon as possible, and within 16 hours of collection, incubate tubes upright at 37°C for 16-24 hours. Be certain to document date and time for each step.
4. As soon as possible, and within 72 hours of incubation, centrifuge tubes at 2000-3000 g (RCF) for 15 minutes. Be certain to document date and time for each step.
5. After centrifugation, tubes must maintain a temperature of 2-8°C.

6. Tubes need to arrive at the laboratory within a week of centrifugation, and by 4:00 P.M. Mon-Fri. Tubes must be maintained at a temperature of 2-8°C during transport.

Some of the Frequently Asked Questions relating to the assay are listed below. The answers provided act as a guide only.

Blood Collection

The blood hasn't reached the black mark on the side of the Blood Collection Tube. Is this important?

The mark on the side of the tubes indicates the 1 mL fill volume. QFT Blood Collection Tubes have been validated for volumes ranging from 0.8 to 1.2 mL. If the level of blood in any tube is not close to the indicator mark, it is recommended to obtain another blood sample.

How important is the tube mixing process?

The antigen mixing process ensures even distribution of stimulating antigens to allow white blood cells to ingest and process antigen for presentation to T-cells, thus leading to IFN-secretion. It is a very important step in the QFT and poor mixing will lead to low and incorrect results. Mix the tubes by vigorously shaking the tubes vigorously for at least 5 seconds, ensuring that the entire surface of the tube has been coated with blood. Thorough mixing is required to ensure complete mixing of the blood with the tube's contents. Causing the blood to froth will not adversely affect the performance of the test. Universal blood handling precautions should be used. A demonstration video can be viewed on the Cellestis website at: www.cellestis.com

Can the blood collection tubes be transported lying down?

Yes and No.

(Option 1)-- Tubes can be transported lying down only after the tube-mixing step has been done and prior to incubation.

(Option 2)-- If tubes are transported after incubation, but prior to centrifugation, care should be taken to ensure that *tubes remain upright during transport*.

(Option 3)-- Tubes transported after centrifugation, may be transported lying down if necessary.

At what temperature can the blood be transported to another site, or held prior to incubation at 37°C?

(Option 1, Option 2)-- Blood should be held and transported at Room Temperature (17°C to 27°C). Do not refrigerate the blood or place on ice.

(Option 3)-- Blood should be held and transported at (2°C to 8°C), refrigerated or placed on ice.

Blood Incubation and Centrifugation

What if 37°C incubation starts more than 16 hours after the time of blood collection?
The Package Insert specifies that the 37°C blood incubation must commence within 16 hours of collection. Blood samples incubated more than 16 hours after collection are likely to exhibit a decreased IFN-γ response due to cellular breakdown (death), leading to loss of sensitivity and inaccurate results.

Can I incubate the blood collection tubes lying down?

QFT Blood Collection Tubes must be kept upright during incubation at 37°C.

Do I have to centrifuge the tubes immediately after removal from incubator?

QFT Blood Collection Tubes may be held between 2°C and 27°C for up to 3 days before centrifugation or harvesting.

The gel plug hasn't moved during centrifugation. What should I do?

After incubation of tubes at 37°C, the plasma is separated from the cells by centrifuging for 15 minutes at 2000 - 3000 RCF (g). The gel plug should move to separate the cells from the plasma. If this does not occur, the tubes should be re centrifuged at a higher speed.

The plasma doesn't appear the color it normally does. Is this OK?

Plasma from the QFT Blood Collection Tubes can appear more red than usual but this is normal. It should be noted that the color of plasma, even those without any red blood cell contamination, can vary from almost colorless to shades of yellow/pale brown; some plasma samples even have an opaque character. These qualities have not been found to affect QFT results.

*<u>**The UDOH will typically not pay for Quantiferon testing**</u>.

Check with the UPHLfor pricing and availability. QFT is approved for use in any situation where a PPD would be used, but its' accuracy in children under age 5 and immunosuppressed individuals is currently unclear. QFT may be used instead of, but not in addition to PPD testing, as the meaning of conflicting results is also unclear.

Confidentiality in TB Control

The TB Control Program recognizes **confidentiality** is an essential issue in many different aspects of TB control. All information pertaining to individual clients shall be maintained in strict confidentiality according to this written policy.

Health care workers need to be aware of their agency policies on confidentiality, as well as those that are relevant to client health care worker encounters. The collection, management, and sharing of data gathered on TB clients must be held in the strictest confidence.

The CDC Self Study Modules on Tuberculosis, Confidentiality in Tuberculosis Control provides in depth information, which is recommended for all health care workers in TB Control. (http://www.cdc.gov/tb/education/ssmodules/pdfs/module7.pdf)

Reasonable safeguards and policies should be in place to protect an individual's privacy, such as: staff orientation to HIPAA laws and signing of a confidentiality agreement, locked files (preferably behind a locked door), password protection of electronic information, shredding of paper containing sensitive data.

Criteria for Hospitalization in Secure TB Unit at UUMC

To provide a secured facility for court ordered, non-adherent individuals with TB; uninsured individuals requiring hospitalization for active TB disease (ATBD); possible infectious or infectious individuals experiencing homelessness, and those who pose a public health threat to contacts in their living environment.

Policy and Procedure

Individuals requesting admission to the University of Utah Hospitals and Clinics' (UUH&C) Secured TB Unit (STBU) must follow the STBU Protocol. Prior approval **MUST** be received from the TB Control Program Manager or Nurse Consultant as well as the designated pulmonary physician at UUH&C before attempting to transport an individual.

Rule-out TB and TB clients must have funding for their UUH&C admission authorized by the TB Control Program. The TB Control Program will pay for admissions as the payer of last resort.

Non-adherent individuals with TB must be admitted to the STBU under court order. For details on the isolation process refer to the UDOH Court-Ordered Treatment and Involuntary- Isolation Guidelines for the Control of Tuberculosis.

Individuals should not be sent to the emergency department or admitted through the emergency department, unless prior arrangements have been made.

TB Evaluation for Class B Refugees/Immigrants

The Department of Homeland Security (DHS) and Citizenship and Immigration Services (USCIS) requires an overseas examination of all immigrants and refugees (per CDC Immigration Requirements: Technical Instructions for Tuberculosis Screening and Treatment . A Tuberculin Skin Test (TST), or Quantiferon (QFT) may be done. A chest x-ray (CXR) is done to screen for active infectious tuberculosis disease (ATBD). Refugees/immigrants with abnormal chest x-rays suggestive of clinically active TB have sputum smear examinations to determine if they have ATBD. Refugees/immigrants identified with ATBD are treated prior to departure for the United States. Once the refugee/immigrant is no longer infectious, and has completed treatment, U.S. resettlement can occur. If disease is extrapulmonary only, travel is not restricted. (See the 2007 TI for exceptions pertaining to children under age 10.) Class B conditions indicate the need for the refugee/immigrant to follow-up in the United States. The TB Control Program considers Class B conditions that include an abnormal chest x-ray as possible ATBD until the evaluation is complete. Local health departments have 30 days to locate and initiate clinical evaluation, and 90 days to complete.

Procedure

- CDC sends a report to the TB Control Program and the UDOH Refugee Health Program as well, via their secure electronic system (EDN). If the report is not available on EDN, the refugee resettlement agency will forward the Class B documents to the TB Control Program.
- TB Control Program forwards this Class B report to the local health department (LHD) in whose district the refugee/immigrant will reside. The Refugee Health Program will assist in locating refugees and arranging for interpreting services if needed.
- LHD completes evaluation for TB. If refugee/immigrant has ATBD, the TB Control Program will be notified and appropriate treatment begun.
- The Class B evaluation Worksheet (included with original CDC documents) is completed, signed by the physician, and sent back to the TB Control Program.
- The TB Control Program forwards the completed report electronically to the Division of Quarantine, Centers for Disease Control and Prevention.

Protocol for Class B TB[β]

(Class B status per 2007 CDC Technical Instructions, amended 10/1/09; all previous 2007 Technical Instructions versions have been superseded)

1) No TB class[Ψ]

No Class B follow up

If arrival subsequently has a +PPD or QFT[ΨΨ] at their refugee health screening, proceed accordingly, *but do not submit any Class B paperwork.*

2) Class B1 Pulmonary TB

Obtain history, do PPD or QFT* if no record (from either Class B paperwork or refugee health screening). Bring to clinic** (or the provider your LHD uses for Class B follow up), repeat CXR. If there is suspicion of active disease, the arrival is HIV+, or if the repeat film in the U.S. is abnormal, collect sputums. Sputums may also be ordered at provider discretion.

3) Class B1 Extrapulmonary TB

Obtain history, do PPD or QFT* if no record, and bring to clinic**. Obtain CXR (if pre-departure CXR exists, repeat if respiratory s/s, if CXR >3 months old, or at provider discretion). Collect sputums if indicated.

4) Class B2 (LTBI)

Obtain history, repeat CXR prn or if film from country of origin is >6 months old. If treatment will be offered, CXR must be no more than 3 months old. ***May have physican sign after a chart check, if appropriate.****

5) Class B3

Evaluate for Contact prophylaxis.

Proceed as with any contact. If pre-departure TST is < 5mm, or QFT negative, repeat if it cannot be verified as being done > 8 weeks after exposure. If CXR was done before departure, repeat prn or if film is > 6 months old. If treatment will be offered, CXR must be no more than 3 months old. ***May have physician sign after a chart check, if appropriate.****

Submit Worksheet signed/dated by provider. If the patient is pending starting LTBI treatment, please submit the Worksheet as soon as the provider has signed off; we can update the record after treatment has begun.

**If Class B papers indicate history of infection or disease, do PPD or QFT at provider discretion.*

**with pre-departure documentation and film(s), if available.

***It is always preferable to repeat the CXR and have the applicant examined by a physician, but this is subject to physician discretion with B2 and B3. **(If the CXR is >6 months old, repetition is mandatory.)**

Ψ *Some arrivals may appear to be misclassified.* ***The Class assigned on the paperwork cannot be changed, but appropriate clinical follow up should be done regardless.***

β Occasionally, an arrival (especially an immigrant from a lower incidence country) may still be classified under the 1991 Technical Instructions. If their designation is 'B2', but their pre-departure CXR was diagnosed as a TB-related abnormality, work them up as a B1.

ΨΨ ***UDOH may pay for QFT for B1 immigrants, if funding is available.***

Testing for TB infection in Schools

Universal tuberculin skin testing (TST), or IGRA, of all students in school settings **is not recommended.** Only children at increased risk of TB exposure should be considered for testing. In Utah, high-risk children include contacts of persons with active TB disease (ATBD), newly arrived foreign-born children from high prevalence areas, children of migrant farm workers, children with socio-economic risk factors such as homelessness, living in a shelter, or caretaker with risks such as intravenous drug use.

Procedure

- Decisions regarding implementation of a school-based testing program should be made jointly by local public health professionals in collaboration with school nurses and school administrators. The TB Control Program is available for consultation.

- A decision to conduct a TB screening program is a decision to treat TB infection, if identified and resources are available. Targeted testing of children at high-risk for TB infection must be accompanied by a plan for providing necessary follow up. This plan must include resources for providing a chest x-ray, medical evaluation and treatment for TB infection, which includes medication and nursing case management time.

- It is recommended that new students be assessed for risk factors upon entrance to school. Go to the World Health Organization [WHO] Global Atlas for Infectious Diseases (click on "view more indicators, and select Incidence for most current year) for the WHO's most up-to-date listing of international TB incidence.

- If a TB screening program is implemented, students with identified risk factors should then be screened at ages 4-6 and 14-16.

- Evaluation of the data on the number of tests administered, results of the test, number identified with TB infection or ATBD, and number who complete treatment should be reviewed with local health departments. If a low incidence of ATBD or TB infection is identified, decisions to continue the screening program should be re-evaluated.

Other Resources

Minnesota Department of Health Guidelines for Decisions Regarding TB Screening of Elementary and Secondary Students.

Rutgers Global Tuberculosis Institute Tuberculosis Handbook For School Nurses

Utah Department of Health, TB Rule R388-804-4, Screening priorities and Procedures.

Testing for TB Infection in Post Secondary Schools

Universal testing of all students in school settings is **not recommended**. Targeted testing is recommended for all international students originating from high incidence countries. (Refer to the World Health Organization [WHO] Global Atlas for Infectious Diseases for the most up-to-date listing of international TB incidence.) Students whose studies or obligations involve **extensive** international travel to high incidence countries are also candidates for testing prior to travel and 8-10 weeks following their return to the United States. Risk in addition to being foreign born should be considered in determining who to screen (see ACHA Guidelines: Tuberculosis Screening and Targeted Testing of College and University Students and the Heartland National TB Center's document 'Model Tuberculosis Prevention Program for College Campuses for more information). Screening of students in health care professions is addressed in the manual section 'Screening for TB in Health Care and other 'Congregate Settings.'

Procedure

- Decisions regarding implementation of a school-based screening program should be made jointly by local public health professionals in collaboration with school nurses and school administrators. The TB Control Program is available for consultation.

- A decision to conduct a TB screening program is a decision to treat TB infection if identified and resources are available. Targeted testing of students at high risk for TB infection or active TB disease (ATBD) must be accompanied by a plan for providing necessary follow up. This plan must include resources for providing a chest x-ray, medical evaluation, and treatment for TB infection, which includes medication and nursing case management.

- Evaluation of the data on the number of tests administered, results of the test, number identified with TB infection or ATBD, and number who complete treatment should be reviewed with the local health department(s). If a low incidence of ATBD or TB infection is identified, decision to continue the screening program should be re-evaluated.

Other Resources

Utah Department of Health, Bureau of Epidemiology, TB Rule, R388-804 Screening priorities and Procedures.

Testing for TB infection in Dialysis Centers

Routine tuberculin skin testing (TST) or Quantiferon (QFT) of hemodialysis clients is recommended.

Rationale: The incidence of TB in individuals with end stage renal disease (ESRD) is estimated to be 10-15 times higher than in the general population. ESRD is associated with immunosuppression, and individuals are more likely to be elderly or belong to certain minority groups in which TB rates are higher. Individuals with ESRD are more likely than the general population to have diabetes. Those with TB infection may be more likely to progress to active TB disease (ATBD).

ATBD may be difficult to diagnose with symptoms often attributed to underlying chronic renal disease. Individuals receiving hemodialysis spend prolonged periods of time together in health care facilities, thereby increasing the potential for TB transmission if a person has active disease.

Procedure

- Each new individual initiating dialysis should be assessed for symptoms of TB and risk factors for TB.

- The 2-step method should be used when evaluating the individual (see chapter on 'Testing for TB Infection'). QFT may be used in place of a TST, and is preferred for individuals with a history of the Bacillus Calmette-Guerin (BCG) vaccine. .

- If the TST is negative, a second test should be placed in 1-3 weeks (unless there is documentation of a negative test within the previous 365 days). If the second test is negative, the patient may be considered to be not infected. A negative QFT does not require a second confirmatory test.

- Each new individual with an identified risk factor for, or symptoms of TB should also have a chest x-ray regardless of TST or QFT results.

- ATBD should be considered with abnormal x-ray results if:
    - the individual is from an area of high incidence of TB
    - the skin test result is >5 mm
    - there is known exposure to someone with ATBD
    - the individual is experiencing symptoms of ATBD

- Any individual with a positive TST or QFT, or a documented history of a previous positive TST or QFT should be evaluated for treatment and started on appropriate prophylaxis (see chapter on 'Treatment of TB Infection'), unless there is documentation of previous adequate treatment

- Annual testing should be performed on individuals with negative results.

- Any individual placed on treatment for TB infection should be considered for directly observed therapy (DOT).

- Questions regarding dosing and timing of medications with dialysis should be directed to the TB Control Program at (801) 538-6191 or the local health department.

Other Resources

CDC Core Curriculum on Tuberculosis, What the Clinician Should Know

Tuberculosis Transmission in a Renal Dialysis Center

UDOH Tuberculosis Provider Guide - Testing for TB Infection & Guidelines for Post-Test Referral

Screening for TB in Health Care & other High-Risk Congregate Settings

A high-risk congregate setting includes: health-care facilities (both in and outpatient), long-term care facilities (e.g. nursing homes), correctional facilities, homeless shelters, and substance abuse treatment programs. Employees and volunteers should be screened for TB in all high-risk congregate settings, according to Centers for Disease Control and Prevention (CDC) guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, CDC guidelines for the Prevention and Control of Tuberculosis in Correctional and Detention Facilities, and rules established by the Occupational Safety and Health Administration (OSHA). Individuals in these facilities should be screened using the same guidelines as for employees, except that acute care, in and outpatient health care facilities (e.g. hospitals, medical clinics) should not routinely screen individuals except for cause (e.g. symptoms indicating possible TB, individual is at high risk for TB).

Procedure

All facilities: Baseline screening, of all new employees and volunteers with a potential for exposure to *M. tuberculosis* through air space shared with persons with infectious TB disease, should be initiated before they are permitted to work. This would include skin testing (2-step for those without a documented negative skin test within the past year), or Quantiferon (QFT) blood testing (do not 2-step), and/or a chest x-ray for those with (or a documented history of) a positive test. Documentation of a previous chest x-ray may suffice unless the applicant has symptoms that could be indicative of TB. (See chapter on 'Testing for TB Infection' for clarification.) **Do not skin test an individual with a documented history of a previous positive TST**. **Do not use QFT as a confirmatory test to a positive TST without first seeking expert consultation.** A history of the Bacillus Calmette-Guerin (BCG) vaccine **is not** a valid reason to not be tested. Pregnancy **is not** a contraindication to being tested. A new employee with an abnormal chest x-ray and/or symptoms indicative of possible TB may not work until cleared by the local health department, or a private provider. Screening should also be done after any significant exposure to active TB. Consult with the local and/or state health department for assistance.

Health-care and long-term care facilities: CDC guidelines permit a facility to establish a schedule for periodic testing of employees based on their assessed risk. An annual risk assessment is necessary to determine the procedure to follow. A facility classified as *low risk* is not required to do periodic testing; *medium risk* would require annual testing, and facilities classified as having *potential ongoing transmission* might need to test employees every 8 – 10 weeks, until lapses in infection control have been corrected. See the CDC guidelines for definitions and procedures for each risk class, as well as a risk assessment tool.

Correctional facilities: CDC guidelines classify facilities as *minimal* or *non-minimal risk* (see the guidelines for definitions). Most facilities should screen employees at least annually. Employees of minimal risk facilities may not need to be screened periodically, and employees of non-minimal risk facilities may need to be screened more frequently.

Testing intervals should be based on an annual risk assessment, and with consultation from the local and/or state health department.

Homeless shelters: Employees should be screened at least annually and more frequently if warranted. Residents should be screened (at least for cough, and then chest x-ray as deemed appropriate by medical staff) at admission. Consult with the local and/or state health department for further guidance.

Substance abuse treatment programs: While probably not essential, it would be prudent to consider annual screening of employees; and screening of residents (and their children if they are being housed with them) at admission. This recommendation is based on the fact that substance users, especially intravenous drug users, are at higher than average risk for exposure to TB (although statistics in Utah don't currently reflect this statement). Contact the Utah Division of Substance Abuse and Mental Health, 801-538-3939 for further guidance.

Disease Reporting

The following is a summary of reportable conditions related to tuberculosis in the state of Utah:

Condition / Test Result	Reportable by Whom
Confirmed or suspected cases of active tuberculosis disease, regardless of whether confirmed by laboratory test	Health care providers, hospitals, other similar private or public institutions, or any other person providing treatment to the confirmed or suspected case **must report within 24 hours to the TB Control Program or Local Health Department.** A report of test results by a laboratory does not relieve the attending physician/ health care worker of his/her reporting obligation.
Smears or cultures positive for acid-fast bacilli (AFB), cultures positive for *Mycobacterium tuberculosis* (MTB), and other positive laboratory tests indicative of MTB infection.	All laboratories that perform TB testing and in-state laboratories that send specimens for out-of-state testing **must report within 24 hours to the TB Control Program or Local Health Department.** A report by the physician/health care worker does not relieve the laboratory of its reporting obligation.
Any active TB disease client on directly observed therapy that has missed three consecutive daily doses, or two consecutive intermittent doses.	Medical providers and health care organizations **must report within 7 days to the TB Control Program or Local Health Department.**

Procedure

The TB Control Program will need the following information regarding a reported confirmed/suspect TB case:

- Name
- Date of birth
- Address
- Sex
- Race/ethnic origin
- Marital status
- Site of disease
- Symptoms/onset dates
- Hospital admission information
- Bacteriology results, date(s), and name of laboratory performing test(s)
- X-ray results (if applicable)
- HIV testing information
- TB skin test results (in mm), or Quantiferon test results and date of test
- Drug therapy (medications used, dates given)
- Type of isolation/quarantine arrangements
- Other pertinent medical & epidemiological information
- Provider's names/addresses/telephone numbers

Whom to Notify Regarding Active/Suspect TB:

All cases, suspect cases and positive laboratory results must be reported within 24 hours to the local health department or the TB Control Program.

Telephone report to the Utah Department of Health, TB Control Program at (801) 538-6191. After hours 1-888-EPI-UTAH (374-8824). Fax reports to (801) 538-9913.

References

Special Measures for the Control of Tuberculosis, Rule R388-804.

Managing a TB Outbreak

Definitions for TB outbreak are relative to the local context. Outbreak cases can be distinguished from other cases only when certain associations in time, location, patient characteristics, or *Mycobacterium tuberculosis* attributes (e.g., drug resistance or genotype) become apparent. In low-incidence jurisdictions, any temporal cluster of cases is suspicious for an outbreak. (http://health.utah.gov/epi/diseases/TB/plan.pdf)

A working definition for a potential "TB outbreak" is helpful for planning and response and may include any of the following six criteria:

Criteria based on surveillance and epidemiology:

- An increase has occurred above the expected number of TB cases;
- During a contact investigation (CI), two or more contacts are identified as having TB disease, regardless of their assigned priority, (i.e., high-, medium-, or low-priority);
- Any two or more cases occurring within one year of each other are discovered to be linked, and the linkage is established outside of a CI (i.e., two patients who received a diagnosis of TB disease outside of a CI are found to work in the same office and only one or neither of the persons was listed as a contact to the other); and
- A genotyping cluster leads to discovery of one or more verified transmission links which were missed during a CI within the prior two years.

Criteria based on program resources:

- Transmission continues despite adequate control efforts by the TB control program and
- CI associated with increased cases requires additional outside help.

Program Resources

One of the purposes of the TB Control Program is to provide enhanced TB treatment and public health follow-up for those diagnosed with TB infection or active TB disease (ATBD). All newly diagnosed cases of ATBD will receive the appropriate evaluation, treatment, follow-up and incentives/enablers necessary to complete treatment within 12 months of diagnosis (> 12 months if resistant to at least Rifampin, TB meningitis, pediatric miliary TB or bacteremia). Screening activities (to include evaluation of symptoms, tuberculin skin test or QFT, and chest x-ray) will be provided for contacts of cases and migrant school children and their families.

The TB Control Program reimbursing the costs for TB medications, pharmacy dispensing fees and administrative costs for the treatment of TB disease and infection through local health departments.

As resources permit, the TB Control Program will provide incentives to encourage individuals to complete a prescribed course of TB treatment. Appropriate incentives include food coupons, limited housing expenses, time limited utility expenses or others that are deemed appropriate by the nurse consultant and case manager and receive prior approval by the program manager. (See manual section on 'Incentives and Enablers')

Medical and pharmaceutical consultants who specialize in the diagnosis and treatment of TB infection and disease are available to provide technical advice.

Direct reimbursement for pre-authorized services and/or food coupons and/or other incentives can be requested by following the guidelines set forth in the 'Incentives and Enablers' section of this manual.

Medical consultants may either be contacted by local health department staff or through the TB Control Program TB Nurse Consultant. Billing for consulting services is done directly between the consultant and the Utah Department of Health. Pharmaceutical questions should be referred through the TB Control Program TB Nurse Consultant.

Quantiferon Testing and Chest X-Rays

In some case the TB Control Program may assist in paying for Quantiferon (QFT) testing and CXRs.

Class B1 Immigrants and Refugees
The TB Control Program has limited funding allocated for QFT testing for B1 immigrants (costs for B1 refugees should be covered by Medicaid). The public health nurse must submit a request, via email, to the TB Control Program's manager; the request should include the individual's full name, date of birth, and indicate if refugee or immigrant.

Contacts to ATBD
The TB Control Program may assist with costs associated with QFT for contacts to individuals with ATBD. The following criteria will be used to guide the determination process of whether or not the TB Control Program will assist with costs:

- Availability of funding
- Contact investigation to pulmonary case is **large**, resulting in a financial burden on the local health department
- Contact investigation to pulmonary case is large **and** contacts have a history of BCG
    - Contact investigation to an extrapulmonary case meeting the above criteria may be considered; however pulmonary cases are the TB Control Program's priority.

The public health nurse must submit a request, via email, to the TB Control Program's manager; the request should include the individual's full name, date of birth and case name. Recognizing that each situation is unique, the TB Control Program will review each request on a case by case basis. **Please note that the criteria listed above do not guarantee that the TB Control Program will provide assistance with QFT costs**.

Chest X-rays
The TB Control Program may also assist with CXR costs for contacts individuals with ATBD using the same criteria listed above. This assistance is also dependent on available funding.

Ordering Anti-tuberculosis Medication

The TB Control Program will reimburse local health departments (LHDs) for approved anti-tuberculosis medication, PPD and pharmaceutical copays. The program funds medication for individuals who lack medical coverage for these medications and meet the criteria for an active case, a contact to an active case, a suspect case, or for the treatment of TB infection in high risk populations.

For individuals who have medical coverage and have active or suspect TB, are contacts to an active case, or are considered high risk for infection, the program may elect to reimburse the cost of medications or pharmaceutical copays based upon which is most cost effective for the program.

Procedure

- LHDs establish a relationship with a local pharmacy to provide dispensing services.
- When initiating an individual on 4-drug therapy, the public health nurse must complete and submit the "TB Patient Medication Insurance Verification."
- Regarding preventative treatment, UDOH will reimburse the cost of INH for high-risk patients as defined by CDC as being PPD+ in the 5 or 10 mm categories. UDOH may consider RIF as an alternative, but only after a reasonable attempt to use INH fails (or is contraindicated) and a provider orders it. Due to cost difference between INH and RIF, UDOH may elect to either reimburse RIF or copay where applicable.
- The reimbursement of anti-tuberculosis medication and copay reimbursement is based upon the funds available to support program objectives and requirements. Services may be reduced or eliminated if funding becomes impacted or in anticipation of expected changes to funding. The TB Control Program reserves the right to make final decisions on individual eligibility. Eligibility decisions are based on current medical practice, funding availability, and recommendations from the most current treatment guidelines endorsed by the American Thoracic Society and the Centers for Disease Control and Prevention.

TB Control Program:
Use of State PPD

Use of PPD purchased with Program funds is restricted to the following:

Reasons for Skin Test	UDOH Supply	
	Yes	No
Condition of Employment (e.g. corrections, nursing home, etc.)		X
Condition of School		X
Condition of Volunteer Work		X
Correction/Detention Facility Inmate	X	
Refugee	X	
Immigrant	X	
Persons Experiencing Homelessness	X	
Persons with Substance Abuse Challenges	X	
Immunocompromised Persons	X	
Migrant Worker	X	
Migrant Headstart Enrollment	X	
Pre-Missionary		X
Post-Missionary	X	
Nursing Home or Senior Day Care Patient		X
TB Cases	X	
TB Suspect	X	
TB Contacts	X	

INCENTIVES AND ENABLERS

Assistance is determined on a case by case basis; priority is given to individuals with ATBD requiring isolation or individuals infectious suspects. Types of assistance may include rent, car insurance, utilities, food coupons, and toys for pediatric cases and/or contacts. The "TB Incentive/Enabler Request Form" should be used when requesting assistance.

The TB Control Program may also provide assistance with medical costs for underinsured or uninsured individuals with ATBD; these costs **must be related to TB**. Assistance is determined on a case by case basis and is not guaranteed.

- Request for assistance should be submitted via email to the TB Control Program Mgr., cc: Nurse Consultant and include rationale for service/procedure along with facility's contact information.
    - **Uninsured patients must provide verification of Medicaid denial.**
- The TB Control Program will either deny the request or provide provisional approval.
- If provisional approval is given, the TB Control Program will negotiate rates and amount of assistance directly with the provider.
- Once negotiations are finalized, the TB Control Program will provide the local health department with written confirmation of approval which will include the approved assistance amount.

The TB Control Program is the payer for last resort. Every effort should be made to identify and secure other payment sources. **Emergency room and urgent care visits will not be covered.**

Required Reports and Forms

The TB Control Program requires the following reports local health departments (LHDs) being reimbursed for PPD or anti-TB medications from the Program: 1) QuarterlyTB Skin Test Report; and/or 2) Monthly TB Activity Report. LHDs can choose to enter the Activity Report information into EpiTrax in lieu of submitting the reports. The TB Control Program requires information for the following reports from LHDs: 1) Report of Verified Case of Tuberculosis (RVCT) and 2) Aggregate Reports for Tuberculosis Program Evaluation (ARPE) Follow-up and Treatment for Contacts to TB Cases. While forms generated at the LHD level may be of assistance in documentation of TB evaluation, treatment for TB infection or active TB disease (ATBD), they are not required to be sent to the TB Control Program.

Procedure

The Quarterly TB Skin Test Report is required for agencies being reimbursed for PPD from the TB Control Program and should only include data on testing conducted using state-reimbursed PPD. The Monthly TB Activity Report is required for LHDs using TB Control Program anti-TB medications to treat patients for LTBI. LHDs can choose to enter this data into EpiTrax in the Investigation/Disposition (Required) tab. The completed reports are due by the 15th of each month for the previous quarter or month. Report(s) can be e-mailed to tbreports@utah.gov

The Report of Verified Case of Tuberculosis (RVCT) is completed on new cases of ATBD. The TB Nurse Consultant completes this with the case manager by telephone when the case is confirmed.

A CI Record (Contact Investigation) form, documenting follow up testing and treatment of contacts to ATBD contains the information needed for the ARPE report. The contents of the form are in EpiTrax for each contact event and should be completed by the case manager on each ATBD contact. Information should be entered into EpiTrax after the first round of testing, the second round of testing (where applicable), and when all contacts have completed treatment for LTBI. LHDs can contact the UDOH TB Control Program for assistance with data entry on large CIs.

Sample forms recommended to assist the case manager in accurate record keeping are available on the TB Control Program website.

Site Visits

Tuberculosis services are provided in a variety of settings. The official agency, the Utah Department of Health TB Control Program, is charged by law with the responsibility of coordinating the control of TB. Public health's oversight role has been expanded even further beyond mandatory reporting of cases and ensuring completion of treatment. Health department TB control programs are reviewing the quality of the diagnostic, treatment, and prevention services given to individuals. The quality of care and effectiveness of the TB Control Program is reviewed and evaluated in the following ways: telephone consultation, reports, site visits, and cohort review.

Procedure

The TB Control Program will contact the local health department (LHD) nursing director and TB nurse to schedule a site visit.

The TB Clinic Structure and Management Form will be used to evaluate the LHD TB Program and services provided. See Site Visit Tool on the TB Control Program's website.

A report of findings of the site visit will be sent to the health officer, nursing director and TB nurse.

The site visit will be utilized for the TB Control Program staff to meet with TB nurses in their environment, to provide consultation and education as indicated, and to strengthen the partnership of the agencies.

Other Resources

Tuberculosis Nursing: A Comprehensive Guide to Patient Care, Standards of Care. The National Tuberculosis Controllers Association, Second edition 2011.

Medical Interpreters/Translators

Title VI of the Civil Rights Act of 1964 prohibits discrimination on the basis of race, color, or national origin by any entity that receives federal financial assistance. Under Title VI of the law, hospitals, Health Care Maintenance Organizations, social services and other entities that receive Federal financial assistance from the Department of Health and Human Services (HHS) are required to take the steps necessary to ensure that individuals with limited English proficiency (LEP) can meaningfully access the programs and services. The requirements apply to state-administered, as well as private and non-profit facilities and programs that benefit from HHS assistance. The Office for Civil Rights is responsible for compliance with the law as it applies to HHS assisted programs.

Medicaid providers are required to provide foreign language interpreters for Medicaid clients who have limited English proficiency. Clients are entitled to an interpreter to assist in making appointments for qualified procedures and during visits. Providers must notify clients that interpretive services are available at no cost.

Interpretive services for Medicaid, PCN and CHIP clients are free. Please contact your healthcare provider to request the interpretative services for your health, dental and mental health appointments. If you need an interpreter, call the Medicaid Information Line at 801-538-6155 or 1-800-346-4128. https://medicaid.utah.gov/interpreter-services

It is strongly recommended that providers encourage clients to use professional services rather than relying on a family member or friend, though the final choice is theirs.

State Consultants

The following state consultants may be contacted by public health and health care practitioners only:

Barbara Cahill, MD
Pulmonology
University of Utah Health Care
801-585-3135
Barbara.Cahill@hsc.utah.edu

Krow Ampofo, MD
Pediatric Infectious Disease
University of Utah Health Care
Primary Children's Hospital
801-581-6791
Krow.Ampofo@hsc.utah.edu

Classification System for TB

Class	Type	Description
0	No TB exposure Not infected	No history of exposure Negative tuberculin skin test (TST) or IGRA (QFT, T-Spot)
1	TB exposure No evidence of infection	History of TB exposure Negative TST or IGRA (done at least 8 – 10 weeks post exposure)
2	TB infection No TB disease	Positive TST or IGRA Negative bacteriological studies (if done) No clinical or radiographic evidence of active TB
3	TB, clinically active	*M. tuberculosis* cultured (if done) Positive TST or IGRA and clinical, bacteriological, or radiographic evidence of current active TB disease
4	TB Not clinically active	History of episode(s) of TB **or** Abnormal but stable radiographic findings Positive TST or IGRA Negative bacteriologic studies (if done) **and** No clinical or radiographic evidence of current disease
5	TB suspected	Signs and symptoms of TB disease; diagnosis pending

Reference

CDC Self-Study Modules on Tuberculosis, Module 1 (pg.23; Table 1.2)

TB Medicaid Program

States can choose to provide Medicaid financing for coverage of tuberculosis-related services to low-income individuals who are infected with TB. This eligibility group serves individuals who are not otherwise eligible for Medicaid based on the traditional eligibility categories.

Services available to people who are eligible under the optional TB group include the following TB-related services:

- Prescribed drugs;
- Physician's services (including outpatient hospital services, rural health clinic services, and federally qualified health center services);
- Laboratory and X-ray services (including those to confirm the presence of infection);
- Clinic services and federally qualified health center services;
- Case management services; and
- Services (other than room and board) designed to encourage completion of regimens of prescribed drugs by outpatients, including services to directly observe the intake of prescribed drugs.

To be covered these services must be related to the treatment of TB.

Utah TB Medicaid Program-TB Positive Group:

Patients apply for Medicaid through the regular application process; however also need to indicate that they are being treated for ATBD. Utah's policy for the TB Positive Group is as follows:

Medical Condition

- Clients must be infected with tuberculosis or be suspected of being infected with tuberculosis.

Medicaid Requirements

- The general eligibility requirements apply. Clients must:
  - File an application;
  - Give worker required verification for eligibility;
  - Be a state resident;
  - Be a US citizen or eligible alien

Scope of Services

- Same TB-related services as listed above

http://health.utah.gov/chip/Medicaidpolicy/300/392_TB_Positive_Group.htm

UTAH DEPARTMENT OF
HEALTH

Tuberculosis Control
Physical Address: 288 North 1460 West Salt Lake City, Utah 84116
Mailing Address: Box 142104 Salt Lake City, UT 84114-2104
Phone: (801) 538-6191
Fax: (801) 538-9913
Website: http://health.utah.gov/epi/diseases/TB