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DEPARTMENT OF HEALTH

Tuberculosis Manual

For County and Municipal Health Departments

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Chapter 1: Introduction to the Pennsylvania Tuberculosis (TB) Manual

PURPOSE

This manual is designed to present the key steps and crucial information needed to perform TB control tasks in Pennsylvania. Where additional or more detailed information is available, references and/or hyperlinks to CDC guidelines and other resources are provided.

AUDIENCE

The audience for this manual includes community health nurses (CHNs)[1], outreach workers, TB clinicians, public health officers, regional consultants, and state TB program staff.

State Health Centers and State Contracted Clinics will be referred to as "SHCs" or "State Clinics." Licensed physicians who evaluate and treat patients with tuberculosis (TB) disease and latent tuberculosis infection (LTBI) in State Clinics are referred to as "TB clinicians."

PURPOSE OF TB CONTROL

The goal of TB control in the United States is to reduce TB morbidity and mortality by:

- Preventing transmission of *Mycobacterium TB (M.TB)* from persons with contagious forms of the disease to uninfected persons
- Preventing progression to active TB disease among persons with LTBI

The four fundamental strategies to reduce TB morbidity and mortality include:

- Early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment
- Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen
- Identification of other persons with LTBI at risk for progression to TB disease, and treatment of those persons with an effective drug regimen
- Identification of settings in which a high risk exists for the transmission of *M.TB* and the implementation of effective infection control measures

To protect the health of all citizens, TB control is the responsibility of both the private and public health sectors of medicine. All new suspected and confirmed cases of TB must be reported to the Pennsylvania Department of Health (DOH) via Pennsylvania's version of the National

[1] Throughout this manual, the job title of community health nurse (CHN) is used to refer to nurses who provide patient care in a public health setting regardless of whether they work in a state health center or a county or municipal health department.

Electronic Disease Surveillance System (PA-NEDSS). Patients may be treated by private clinicians or by TB clinicians. DOH will assist and advise private clinicians and other agencies that treat TB patients or conduct TB control activities. By regulation, the department has a responsibility to see that persons with TB in the infectious stage accept medical supervision for their disease so that they become non-infectious.

LAWS PERTAINING TO TB CONTROL

Pennsylvania laws on TB can be found in the Administrative Code of 1929 and the Disease Prevention and Control Law of 1955, 35 P.S. Sec. 521.1

Under the provisions of the Pennsylvania Administrative Code of 1929 and the Disease Prevention and Control Law of 1955, DOH has the authority to "protect the health of the people of this Commonwealth, and to determine and employ the most efficient and practical means for the prevention and suppression of disease."

28 Pa Code § 27.21a (b)(2) requires that tuberculosis, suspected or confirmed active disease (all sites) must be reported within five work days after being identified by symptoms, appearance or diagnosis. Reports may be submitted electronically via PA-NEDSS or by calling the local SHC or county/municipal health department (CMHD).

The Pennsylvania Public School Code of 1949, Section 1402(a)(4), requires that students be tested for TB. However, since 1997 School Districts may request approval from the Secretary of Health for a modified health plan to not test students for TB in accordance with current recommendations of the American Thoracic Society, the CDC and the American Academy of Pediatrics. School Districts that receive approval are not required to submit the form for students but must continue to submit information as required for staff employees and volunteers. For more information, see the School Health TB webpage.

The United States Code contains sections that provide authority to 1) contract with the states for research on the causes, prevention and treatment of disease, 2) cooperate with states to prevent the spread of communicable diseases, and 3) provide grants to states for preventive health programs.

QUALITY OF CARE

For TB programs, quality of care is evaluated based on the achievement of objectives and adherence to standards.

Objectives reflect outcomes and program targets and are based largely on the national objectives established by the Centers for Disease Control and Prevention (CDC).

Standards are an accepted set of conditions or behaviors that define what is expected and acceptable regarding job duties, performance, and provision of services. Pennsylvania TB Program standards are established based on applicable laws as well as national guidelines.

NATIONAL AND STATE PROGRAM OBJECTIVES

The National Tuberculosis Indicators Project (NTIP) was developed to facilitate the use of existing data from the Electronic Disease Notification (EDN) and National Electronic Disease Surveillance System (NEDSS) to help U.S. TB control programs evaluate their program effectiveness and prioritize their activities.

The NTIP objectives are categorized in eight major groups:

1. Goals for Reducing TB Incidence
2. Objectives on Case Management and Treatment
3. Objectives on Laboratory Reporting
4. Objectives on Contact Investigations
5. Objectives on Examination of Immigrants and Refugees
6. Objectives on Data Reporting
7. Objectives on Program Evaluation
8. Objectives on Human Resources Development

The current NTIP objectives can be found on the CDC website at: https://www.cdc.gov/tb/programs/evaluation/indicators/default.htm. To monitor progress towards achievement of the NTIP objectives, the Pennsylvania TB Program has established a state goal for each NTIP objective based on epidemiology data and recent program performance. Call the TB Program at 717-787-6267 for more information about the state goals.

NATIONAL TB GUIDELINES

United States guidelines for the diagnosis, treatment and case management of persons with LTBI or TB disease have been developed, and updated as appropriate, by nationally accepted authorities including the American Thoracic Society (ATS), the Infectious Diseases Society of America (IDSA), and the CDC, and generalized recognized experts in TB control, including the National TB CHN Coalition (NTNC) and the National TB Controllers Association (NTCA). These guidelines constitute standards of care for the medical treatment and control of TB and should be available for reference by each TB staff member.

A complete list of current TB guidelines by topic or date of issuance can be found on the CDC website at https://www.cdc.gov/tb/publications/guidelines/default.htm.

GENERAL ROLES, RESPONSIBILITIES AND CONTACT INFORMATION

Pennsylvania TB Program Staff

- Ensures compliance with applicable public health laws and regulations related to TB reporting and control
- Conducts statewide TB surveillance, data evaluation, and development of policies and guidelines for the control and/or elimination of TB in the state

- Coordinates between local and other state jurisdictions and consults on all aspects of TB prevention and control, including case management, contact investigation, and outbreak investigation
- Provides training and education and supports programs for the treatment of TB cases, suspects, and those with LTBI
- Reviews requests for Reimold Funds of $300 or more to provide patients in need with basics like food, shelter and transportation.

The contact numbers for the TB Program staff are:

Phone: 717-787-6267

Fax: 717-772-4309

Medical Consultations

Medical consultations for cases of LTBI or TB disease are provided by either 1) the physicians who serve as state medical consultants or 2) clinicians at the Global TB Institute at the New Jersey Medical School at Rutgers.

State Consultants

The state has two medical consultants, one for all cases and the other specializing in pediatric cases. Individually they:

- Review medical records for active TB cases as part of the annual Cohort Review process
- Provide consultation to TB clinicians and clinic staff as needed

To request a consultation by one of the state consultants, call the Pennsylvania TB Program at 717-787-6267.

Global TB Institute (GTBI)

The GTBI is a CDC-funded TB Center of Excellence (COE) that provides medical consultation to health care providers via a toll-free number. To request a consultation, call 1-800-4 TB DOCS (1-800-482-3627).

State Health Centers (SHCs) and County/Municipal Health Departments (CMHDs)

- Receive reports of suspected or confirmed cases of TB within their jurisdictions and report them to the Pennsylvania TB Program
- As required by Pennsylvania regulations, ensure that TB cases within their jurisdictions are appropriately isolated (if infectious) and complete treatment
- Perform contact investigations for suspected and confirmed cases of infectious TB
- Record case management findings and contact investigation results on a timely basis in PA-NEDSS for review by the Pennsylvania TB Program
- Conduct targeted testing and treatment of high-risk populations and individuals
- Provide clinical services for patients with LTBI, patients suspected of having TB, TB cases, and contacts of TB cases.

Current contact information for SHCs and CMHDs is provided under the “Quick Links” heading on the Pennsylvania TB Program web page.

Private Medical Providers

- As required by Pennsylvania regulations, report suspected or confirmed TB cases to their local public health department or DOH
- Coordinate the care and treatment of patients with the local SHC or CMHD to ensure that TB cases are appropriately managed
- Provide all information related to the diagnosis and treatment of TB to the local SHC or CMHD
- In conjunction with the local SHC or CMHD, assume responsibility for the successful completion of therapy of each TB patient that they manage

PA DOH Bureau of Laboratories (BOL)

- Provides full diagnostic TB services, including AFB smear; culture isolation, identification, and susceptibility testing; and TB direct detection by nucleic acid probe
- Provides consultation, training, and referral services to other laboratories performing TB diagnostic services such as CDC’s laboratory and PA’s assigned genotyping lab at the Michigan Public Health Laboratory.

The contact numbers for the BOL are:

Phone: 610-280-3464

Fax: 610-450-1932

Private Laboratories

- Private laboratories that provide diagnostic TB services must report positive AFB smears, cultures and drug susceptibility tests via PA-NEDSS.

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Until further notice, refer to the CDC website for current guidance about COVID-19 mRNA vaccines and TB testing.

Chapter 5: Diagnosis of Latent TB Infection (LTBI) and TB Disease

INTRODUCTION

PURPOSE

Use this chapter to understand the procedures for:

- Diagnosing TB disease
- Diagnosing LTBI
- Prioritizing treatment for patients with LTBI who are at high risk for progression to TB disease

POLICY

The following individuals should be evaluated for TB disease:

- Persons who show or report signs and symptoms of TB
- Persons who test positive for *M. tuberculosis* and:
  - are a contact to an infectious case of TB;
  - have at least one risk factor for TB exposure; or
  - are at increased risk of progression from LTBI to TB disease.

Only after a diagnosis of TB disease has been eliminated can LTBI be diagnosed. Individuals at high risk for progression from LTBI to TB disease should be prioritized for LTBI treatment. Refer to Chapter 6, Treatment of LTBI, for more information.

Anyone who tests positive for TB or is suspected of having TB disease is eligible to receive medical evaluation and treatment services at a state health center (SHC) or county or municipal health department (CMHD).

The interferon gamma-release assay (IGRA) test is considered the standard of care when testing patients 2 years of age or older for *M. tuberculosis* infection.

BACKGROUND

Individuals exposed to infectious TB have typically been categorized as having either LTBI or TB disease. Today, it is more widely accepted that TB is a continuum that starts with exposure and escalates to infection, subclinical (asymptomatic) disease, and non-severe to severe

(symptomatic) disease. Where a patient falls on the continuum correlates with bacterial burden i.e., the higher the burden of *M. tuberculosis*, the more likely the patient is to have symptomatic TB disease. Movement along the continuum is also influenced by other factors including the health of the patient's immune system, the virulence of the TB strain, and the impact of various environmental factors on the intensity of exposure.

QUICK START CHECK LIST

A Quick Start Checklist is included in Appendix A to this chapter. It was designed as a tool for public health nurses when evaluating a patient for LTBI or TB disease. The tasks should be performed by licensed nursing, medical, and laboratory staff as appropriate.

HIGH-RISK GROUPS

As shown in **Table 1: Persons at High Risk for LTBI and Progression to TB Disease,** certain factors identify persons at high risk for LTBI and/or progression to TB disease.

Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country who has tested positive for the human immunodeficiency virus (HIV) is at a much higher risk of having active TB than a US-born individual with HIV infection.

TABLE 1: PERSONS AT HIGH RISK FOR LTBI AND PROGRESSION TO TB DISEASE

For LTBI:	For Progression to TB Disease:
• High-priority contacts such as housemates, coworkers or contacts of persons who have smear-positive pulmonary or laryngeal TB • Infants, children, and adolescents exposed to adults in high-risk categories • Immigrants from countries with a high incidence of TB (Asian, African, Latin American, and Eastern European countries have TB rates 5–30 times higher than U.S. rates, and an increasing percentage of TB cases here are occurring among immigrants from those countries) • Recent immigrants from Mexico • Migrant workers • Persons who have recently spent over 3 months in high-incidence countries (such as missionaries) • Native Americans	• Persons with HIV infection • Infants and children 5 years of age and younger • Persons infected with *M. tuberculosis* within the previous 2 years • Persons with a history of untreated or inadequately treated TB disease • Persons with radiographic findings consistent with previous TB disease • Persons who, within the past year, misused injectable or non-injectable drugs, or consumed excessive amounts of alcohol

For LTBI:	For Progression to TB Disease:
• Persons with high rates of TB transmission: – Homeless persons – Injection drug users – Persons with HIV infection – Persons living or working in institutions with individuals at risk for TB such as: ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities	• Persons with any of the following clinical conditions or other immunocompromising conditions: – Silicosis – Diabetes mellitus – End-stage renal disease (ESRD)/chronic renal failure, hemodialysis – Some hematologic disorders (e.g., leukemias and lymphomas) – Other malignancies (e.g., carcinoma of head, neck, or lung) – Body weight more than or equal to 10% below idea body weight – Prolonged corticosteroid use – Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF- α] antagonists) – Organ transplantation – Gastrectomy – Chronic malabsorption syndromes – Jejunoileal bypass

Sources: CDC. Guidelines for preventing the transmission of *Mycobacterium TB* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5. Available at: https://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf
CDC. Targeted tuberculin testing and treatment of latent TB infection. *MMWR* 2000;49(No. RR-6):7–9. Available at: https://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

TB TESTING FOR M. TUBERCULOSIS INFECTION

There are two types of screening tests available for the detection of *M. tuberculosis* infection in the United States:

1. Interferon gamma-release assay (IGRA) blood test
2. Mantoux tuberculin skin test (TST)

Current clinical practice guidelines for the diagnosis of tuberculosis in adults and children favor the use of an IGRA over the TST. The key advantages of an IGRA are that it requires just one visit by the patient, results are typically available in 24-36 hours, and there is no risk of a false positive result due to prior inoculation with the Bacille Calmette-Guérin (BCG) vaccine.

The American Academy of Pediatrics (AAP) recommends either an IGRA or TST for children 2 years of age or older, however the IGRA is preferred for children previously vaccinated with BCG or who are unlikely to return for a TST to be read. For children less than 2 years of age, the TST remains the preferred test.

Patients who test positive for *M. tuberculosis* or exhibit the signs and symptoms of TB should undergo a medical evaluation for TB disease including a chest radiograph, medical history,

serology for HIV, physical examination and – if appropriate – bacteriologic examination of clinical specimens. Only after eliminating a diagnosis of TB disease can LTBI be diagnosed.

INTERFERON GAMMA RELEASE ASSAY

An IGRA is a blood test for *M. Tuberculosis* infection. It is the preferred test for children 2 years of age and older, persons previously vaccinated with BCG, and for immunocompromised patients – including those who are HIV positive or have AIDS. The key advantages of an IGRA test are that it requires just one visit by the patient, results are typically available in 24-36 hours, and there is no risk of a false positive result due to prior inoculation with the BCG vaccine.

Persons with a positive TB test result, regardless of whether they are asymptomatic, should be evaluated for TB disease before LTBI is diagnosed. At minimum, a chest radiograph should be examined for abnormalities consistent with TB disease.

A negative IGRA result does not exclude *M. tuberculosis* infection in persons with signs or symptoms suggestive of TB disease. Medical evaluation of such persons should include a history and physical examination, chest radiograph, bacteriologic studies, serology for HIV, and, when indicated, other tests or studies.

IGRA results are reported as positive, negative or indeterminant. An indeterminant result indicates there is no measurable immune system response to *M. tuberculosis*, suggesting an error in performing the test or immunosuppression due to a medical condition such as HIV or immunosuppressive medication such as TNF-alpha inhibitors.

TUBERCULIN SKIN TEST

The TST has limitations detecting infection with *M. tuberculosis*. A valid TST requires proper administration of tuberculin-purified protein derivative (PPD) via an intradermal injection into the volar surface of the forearm. In addition, patients must return within 48-72 hours to have the test read by a trained health care provider and the reading of the test result can be subjective. False-positive TST results can be caused by either infection with non-tuberculosis mycobacteria or prior inoculation with the BCG vaccine. If there is a question about the validity of a previously documented positive TST due to prior BCG vaccination or reservations about the administration or reading of the TST, the patient can be re-tested with an IGRA.

See Chapter 11: Targeted Testing for more specific information about the administration, reading and interpretation of the TST.

SPECIAL SITUATIONS

Pregnancy

Both the IGRA and the TST can safely be used to test pregnant women for TB, but pregnancy can affect the test results. A "low positive" IGRA result in a pregnant woman may be a false positive and she should be retested no sooner than 3 months postpartum.

Pregnant women with any of the following conditions are at increased risk for LTBI or TB disease and should be tested:

- Symptoms suggestive of TB disease;
- HIV infection;
- Behavioral risk factors for HIV;
- Medical conditions other than HIV infection that increase the risk for TB disease;
- Close contact with a person who has pulmonary or laryngeal TB disease; or
- Immigration from an area of the world where the incidence of TB is high.

Bacille Calmette-Guérin (BCG) Vaccine

BCG vaccines are live vaccines derived from a strain of *M. bovis.* Infants and children in countries with a high incidence of TB are commonly vaccinated with BCG to prevent meningeal TB. However, because the effectiveness of BCG vaccines in preventing infectious forms of TB has never been demonstrated in the United States, they are not recommended in this country as a TB control strategy, except under rare circumstances.

Due to the high incidence of false-positive TSTs in BCG-vaccinated individuals, an IGRA should be used instead of a TST to test anyone **2 years of age and older with a history of BCG vaccination**. For children less than 2 years of age, the TST is still the preferred test.

In those instances where BCG-vaccinated individuals are tested with the TST, proceed as follows:

- Consider diagnosis and treatment of LTBI in BCG-vaccinated persons with a TST reaction of equal to or greater than 10 mm induration who:
    - are frequently exposed to populations with a high prevalence of TB (e.g., some healthcare workers, employees and volunteers at homeless shelters, and workers at correctional facilities or drug treatment centers);
    - were born or have lived in a country with a high prevalence of TB; and/or
    - were ever exposed to a case of infectious TB, particularly if that case transmitted TB to others.
- These patients should also be evaluated for symptoms of TB disease and have a CXR. If the patient is coughing sputum specimens should be obtained for acid-fast bacilli (AFB) smear and culture testing. Refer to Appendix B of this chapter, Sputum Collection During TB Treatment.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with the TST for HIV-infected persons in the U.S.

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that cause an impaired cellular immune system include HIV

infection, severe or febrile illness, measles or other viral infections, Hodgkin's disease, sarcoidosis, live virus vaccination, and corticosteroid or immunosuppressive therapy. Persons with conditions such as these may have suppressed reactions to a TST even if infected with TB. However, there are no simple skin-testing protocols that can reliably identify persons as either anergic or non-anergic and that have been proven to be feasible for application in public health TB screening programs.

Documented Prior Positive TB Test (IGRA or TST)

Persons who previously tested positive for TB with either an IGRA or a TST will continue to test positive and should not have another TB test. If there is a question of the TST being a false positive, then an IGRA can be done. A low-risk individual who has a positive TST and a negative IGRA is *not* considered to be TB infected. However, a positive TST in a high-risk individual should be considered infected even if the IGRA is negative. However, if both the TST and the IGRA are positive then the individual is infected with *M. tuberculosis*. Such patients should then undergo a medical evaluation including chest radiography and a physical examination to rule out a diagnosis of TB disease.

Live-Virus Vaccines

The TST can be administered in conjunction with all vaccines. However, the measles (MMR) vaccine—and possibly mumps, rubella, varicella, and live attenuated influenza vaccines—may transiently suppress the response to PPD. Therefore, if a vaccine containing live virus (e.g., measles, smallpox) has already been given, the TST should be deferred until (or repeated) at least four weeks after the vaccine was administered.

When giving the TST and the MMR, one of the following three sequences should be used:

- Apply the TST at same visit as the MMR
- Delay the TST at least four weeks if the MMR is given first
- Apply the TST first and then give the MMR when the TST is measured.

The last option is the least favored because it delays the administration of the measles vaccine.

The CDC 2011 General Recommendations on Immunization: Recommendations of the ACIP state that "the same timing guidelines that apply to the interval between a live vaccine and TST apply to IGRA (i.e., 28 days between the live vaccine and IGRA if they do not occur on the same day), because IGRA (like TST) might be suppressed through immunologic mechanisms".

Chest Radiography (CXR)

All individuals who either test positive with an IGRA or a TST or exhibit signs and symptoms of TB should have a CXR to rule out pulmonary TB disease (see **Table 2: When a Chest Radiograph is Required and How to Follow up on Radiography Results**).

A posterior-anterior radiograph (x-ray source is positioned so the x-ray beam enters through the patient's back and exits via the chest) is the standard view used for the detection and

description of chest abnormalities in adults. In some instances, other views (e.g., anterior-posterior, lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.

For children, two-view chest radiography is the standard of care.

TABLE 2: TARGETED TESTING FOR LTBI: WHEN CHEST RADIOGRAPHS ARE REQUIRED AND HOW TO FOLLOW UP ON RADIOGRAPHY RESULTS

Signs or Symptoms of TB?	IGRA or TST Result?	Recent Exposure to an Infectious Case?	Chest Radiograph Result	Follow-up Action
No	Negative	No	CXR not recommended unless the patient has HIV infection or other forms of immunosuppression are present	
No	Positive	No	Normal	Consider treatment for LTBI
			Abnormal: Noncalcified fibrotic lesions suggestive of old, healed TB; comparison film available and stable	Consider evaluating for TB disease
			Abnormal: Consistent with TB disease; no comparison film available	Evaluate for TB disease
Yes	Positive or negative	Yes or no	Normal or abnormal	Evaluate for TB disease

IDENTIFYING SUSPECTED TB CASES

Be alert for cases of TB among persons who are contacts to an infectious case of TB and to persons with newly diagnosed *M. tuberculosis* infection – especially those at increased risk of progression to TB disease (see Table 1: Persons at High Risk for LTBI and Progression to TB Disease). Individuals who present with one or more of the common signs and symptoms of TB disease – fever, chills, a persistent cough for two to three weeks or longer, hemoptysis (coughing up blood), weight loss, loss of appetite, and fatigue – should be evaluated for TB disease. All persons who have a chronic cough for two to three weeks or more should be masked and placed in an airborne infection isolation room (AII) until confirmed noninfectious. Hemoptysis is a serious symptom and patients who cough up blood should be evaluated for TB disease as soon as possible.

The clinical presentation of TB varies considerably based on the extent of the disease and the patient's response. Suspect pulmonary TB and start a medical evaluation of the patient when the health history, clinical signs, symptoms, and radiographic findings listed in Table 3 occur among adults (see **Table 3:** When to Suspect Pulmonary TB in Adults). TB should be suspected in any patient who has a persistent cough for more than two to three weeks, or other signs and symptoms of TB.

A diagnosis of TB should also be considered in asymptomatic patients who have risk factors for TB and a CXR compatible with TB.

If a patient has a positive TST or IGRA, consider signs and symptoms of extra-pulmonary TB.

TABLE 3: WHEN TO SUSPECT PULMONARY TB IN ADULTS

Patient History	• Exposure to a person with infectious TB during lifetime • Positive test result for *Mycobacterium TB* infection • Presence of risk factors, such as immigration from a high-prevalence area, HIV infection, homelessness, or previous incarceration • Diagnosis of community-acquired pneumonia that has not improved after 7 days of treatment†
Common Signs and Symptoms of TB	• Prolonged coughing (i.e., for 2-3 weeks or longer) with or without production of sputum that might be bloody (hemoptysis)§, • Chest pain • Chills • Fever • Night sweats • Loss of appetite • Weight loss • Weakness or easy fatigability • Malaise (a feeling of general discomfort or illness)
CXR: Immunocompetent patients	Classic findings of TB are upper-lobe opacities, frequently with evidence of contraction fibrosis and cavitation
CXR: Patients with advanced HIV infection	Lower-lobe and multilobe opacities, hilar adenopathy, or interstitial opacities might indicate TB

† Patients treated with levofloxacin or moxifloxacin may have a clinical response when TB is the cause of the pneumonia.
§ Sputum produced by coughing does **not** need to be bloody to be a symptom of TB.
¶ These features are not specific for TB, and, for every person in whom pulmonary TB is diagnosed, an estimated 10–100 persons are suspected based on clinical criteria and must be evaluated.

Source: Adapted from: ATS, CDC, IDSA. Controlling TB in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

EXTRA-PULMONARY TB

M. tuberculosis bacteria can spread to other parts of the body via the bloodstream or lymph nodes. If a patient has a positive IGRA or TST but no evidence of pulmonary involvement, consider extra-pulmonary TB. Signs and symptoms of extra-pulmonary TB vary by disease site. Some of the more common forms of extra-pulmonary are listed in **Table 4:** Extra-Pulmonary TB Types, Sites, Patient Characteristics and Symptoms.

Patients diagnosed with extra-pulmonary TB disease should also be evaluated for pulmonary TB disease.

TABLE 4: EXTRA-PULMONARY TB TYPES, SITES, PATIENT CHARACTERISTICS AND SYMPTOMS
NOTE: THIS LIST IS NOT ALL-INCLUSIVE

Type of Extra-Pulmonary TB	Disease Site	Most Common Among:	Symptoms
Miliary or disseminated TB	Lungs, bone marrow	Children less than 4 years of age Immunocompromised patients The elderly	Fever, chills, weakness, malaise. With bone marrow involvement, symptoms may include anemia, thrombocytopenia or a leukemoid reaction
Genitourinary	Kidneys or bladder, uterus or ovaries in women, the prostate in men	Men or women	With kidney involvement, fever, back pain, or pyuria -without the typical urinary pathogens For female genital TB – infertility, pelvic or abdominal pain, menstrual disorders For male genital TB – lesions in the prostate, penis or testicles; male infertility
TB Meningitis	Central nervous system	Children less than 5 years of age Immunocompromised patients The elderly	Low-grade fever, headache, nausea and drowsiness that may progress to coma
TB Lymphadenitis	Lymph nodes in the posterior cervical and supraclavicular chains		Progressive swelling of the affected nodes, leading to inflammation and tenderness A draining fistula may also develop
Cutaneous TB	Skin		Skin ulcers – typically above an underlying TB site such as a lymph node or infected bone
TB of Bones and Joints	Usually weight-bearing joints (e.g., hips or knees), but can occur in hands, wrists or elbows – especially after injury. TB of the spinal vertebra is known as Pott's Disease		Progressive or constant pain in affected joints In Pott's Disease, narrowing of the joint space between vertebra may cause neurologic symptoms
Gastrointestinal (GI) TB	Esophagus, stomach, small intestine, or colon	Persons who ingest milk products infected with *M. bovis* Immunocompromised patients	Symptoms may be vague and nonspecific, or may mimic those of other GI conditions (e.g., esophageal ulcers or cancer, ulcerated gastric masses, Crohn's disease, sarcomas and appendicitis)
Ocular TB/ TB Uveitis	Ocular TB can involve the lid, conjunctiva, cornea and sclera. Ocular TB is a "diagnosis of exclusion" reached by a process of eliminating other possible diagnoses.		Ocular redness, discomfort, discharge, lid edema Foreign-body sensation, redness, tearing Granulomas

Sources: Merck Manual Professional Version. Accessed on Nov. 7, 2018 at https://www.merckmanuals.com/professional/infectious-diseases/mycobacteria/extrapulmonary-tuberculosis-tb
Schlossberg, David(ed). 2011. Tuberculosis and Nontuberculous Mycobacterial Infections, Sixth Edition

DIAGNOSIS OF TB DISEASE

Cultures or other laboratory tests that are positive for *M. tuberculosis* support a diagnosis of TB disease. However, TB may also be diagnosed based on clinical signs and symptoms in the absence of positive culture or other laboratory results.

An individual who is suspected of having TB disease requires a complete medical evaluation including the following:

- Medical history – including symptoms, exposure at any time to an infectious case of TB, previous diagnosis and treatment for LTBI or TB disease, and risk factors
- HIV screening
- Physical examination
- TB testing with an IGRA or TST
- CXR
- Bacteriologic examination

When a suspected case of pulmonary TB is identified, refer to Table 5 for guidance on the evaluation of patients in five clinical scenarios encountered by primary healthcare providers, including those serving in medical emergency departments.

TABLE 5: GUIDELINES FOR THE EVALUATION OF PULMONARY TB IN ADULTS IN FIVE CLINICAL SCENARIOS

Patient and Setting	Recommended Evaluation
Any patient with a cough lasting 2–3 weeks or longer	IGRA or TST and CXR: If the CXR is suggestive of TB*, collect 3 sputum specimens for AFB smear microscopy, culture, and a nucleic acid amplification test (NAAT)
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms lasting 2–3 weeks or longer†	IGRA or TST and CXR: If suggestive of TB, collect 3 sputum specimens for AFB smear microscopy, culture, and NAAT
Any HIV patient with unexplained cough or fever	IGRA or TST, CXR and collect 3 sputum specimens for AFB smear microscopy, culture, and NAAT
Any patient at high risk for TB with a diagnosis of community-acquired pneumonia who has not improved after 7 days of treatment†	IGRA or TST, CXR and collect 3 sputum specimens for AFB smear microscopy, culture, and NAAT
Any patient at high risk for TB with incidental findings on CXR suggestive of TB even if symptoms are minimal or absent†§	IGRA or TST, review previous CXR (if available), and collect 3 sputum specimens for AFB smear microscopy, culture, and NAAT

***** Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.
† See **Table 1**: Persons at High Risk for LTBI and Progression to TB Disease.
§ CXR performed for any reason, including targeted testing for LTBI and screening for TB disease.

Source: Adapted from: ATS, CDC, IDSA. Controlling TB in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

MEDICAL HISTORY

When completing a medical history, the clinician should ask the patient about:

- Symptoms of TB disease (Table 2 and Table 4)
- Exposure at any time during their lifetime to someone with infectious TB
- Previous diagnosis of LTBI or disease (Table 1)
- Risk factors (Table 1)
- Demographic factors (e.g., country of origin, age, ethnicity, occupation)
- Underlying medical conditions, especially HIV or diabetes, that may increase the patient's risk of progression from LTBI to TB disease
- Recent medical encounters (e.g., going to the emergency department for pneumonia)
- Previous antibiotic therapy and the condition treated

HIV SCREENING

The CDC recommends that the following patients be screened for HIV:

- All suspected or confirmed cases of TB disease
- Persons diagnosed with LTBI
- Contacts to suspected or confirmed cases of infectious TB disease

HIV infection is the most important known risk factor for progression from LTBI to TB disease. Because both conditions weaken the immune system, the progression from LTBI to TB disease can proceed quickly and, if untreated, be deadly. Emphasize to the patient that the HIV test is part of the baseline work-up for TB disease and that HIV status can affect the treatment of TB disease.

PHYSICAL EXAMINATION

A physical examination is an essential part of the medical evaluation of any patient suspected of having TB. It cannot be used to confirm or rule out TB disease, but it can provide valuable information about the patient's overall condition, inform the method of diagnosis, and reveal other factors – such as HIV status – that may affect TB disease treatment, if diagnosed.

CHEST X-RAY

For adults, a posterior-anterior radiograph of the chest is the standard view used for the detection and description of chest abnormalities. In some instances, other views (e.g., lateral or lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary and can be ordered by the TB clinician.

For children, two-view chest radiography is the standard of care. Many young children aren't tall enough for the posterior-anterior view.

Certain abnormalities on CXR are suggestive, but not diagnostic, of TB disease. In pulmonary TB, radiographic abnormalities are often seen in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. Lesions may appear anywhere in the lungs and may differ in size, shape, density, and presence or absence of cavitation, especially in HIV-infected and other immunosuppressed persons.

In HIV-infected persons, pulmonary TB may present atypically on the CXR. For example, TB may cause opacities without cavities in any lung zone, or it may cause mediastinal or hilar lymphadenopathy with or without accompanying opacities and/or cavities. In HIV-infected persons, almost any abnormality on a CXR may indicate TB. On the other hand, the CXR of an HIV-infected person with TB disease may appear entirely normal.

BACTERIOLOGIC EXAMINATION

See Table 6 to determine the types of specimens needed to assist in the diagnosis of TB.

TABLE 6: SPECIMENS FOR EXAMINATION

Suspected Diagnosis	Specimen Needed
Pulmonary or laryngeal TB	• Sputum (phlegm from deep in the lungs) samples for smear and culture examination. If the patient can't produce sputum, other procedures to obtain respiratory fluids may be necessary, including bronchoscopy or, for children, gastric aspiration. • If pulmonary TB is suspected but the smear is AFB negative, submit the sample for culture and request a nucleic acid amplification test (NAAT).
Extrapulmonary TB	Depending on the anatomical site, other clinical specimens are necessary, such as: • Urine • Cerebrospinal fluid • Pleural fluid • Pus or other aspirated fluid • Biopsy specimens

Refer to Table 7 for information on the bacteriology tests used to diagnose TB.

TABLE 7: BACTERIOLOGY TESTS USED IN DIAGNOSING TB DISEASE

Test	Description	Laboratory Turnaround Times
Acid-Fast Bacilli (AFB) Smear	• Provides strong inferential evidence for a diagnosis of TB. It's usually the first bacteriologic evidence of the presence of mycobacteria in a clinical specimen. • If positive, gives a semi-quantitative estimate of the number of bacilli being excreted (a measure of bacterial load and the patient's infectiousness).	• On-site test: within 24 hours from specimen collection. • Off-site test: within 24 hours from laboratory receipt of specimen (time from specimen collection to laboratory receipt should be 24 hours or less).
Nucleic Acid Amplification Test (NAAT)	• A test done on clinical specimens for the rapid identification of the *M. tuberculosis* complex. • NAATs performed by GeneXpert used will also provide a molecular rifampin resistance result • A NAAT does not replace the need for routine AFB smear and culture testing.	• Within 48 hours from specimen collection
Culture*	• Usually necessary for species identification of all clinical specimens suspected of containing mycobacteria. • Required for drug susceptibility testing and genotyping.	• Mycobacterial growth detection: within 14 days from specimen collection • Identification of mycobacteria: within 21 days from specimen collection • Cultures are reported out as negative after 7 weeks that produce no growth
Drug Susceptibility Testing◊	• For first-line drugs: Is performed on initial isolates of all patients to identify an effective anti-TB regimen. • For both first-line and second-line drugs: Is repeated on interim isolates when a patient remains culture-positive after 3 months of treatment.	• First-line drugs: within 30 days from specimen collection • Second-line drugs: within 4 weeks from date of request
MDDR (Molecular Detection of Drug Resistance) (CDC)	• MDDR testing is done for patients who present with a high suspicion of drug resistance to quickly identify drug resistance so that an effective anti-TB regimen can be started as soon as possible. • MDDR testing is done by the CDC's TB Reference Laboratory in Michigan. • Only samples in which *M. tuberculosis* complex has been detected should be submitted for MDDR testing, and such samples must be submitted by the state Bureau of Laboratories (BOL).	• Results re: first-line anti-TB drugs are typically available within 48 hours upon receipt at the CDC reference Laboratory. • If the MDDR confirms resistance to any first-line drugs, additional testing can be done to identify resistance to any second-line anti-TB drugs.

* One of the National TB Indicators Project (NTIP) objectives for 2025 is to increase the proportion of patients with suspected pleural or respiratory TB disease that have a sputum culture result reported.

◊ Another one of the NTIP objectives for 2025 is to increase the proportion of patients with positive culture results who have initial drug-susceptibility results reported.

Sources: ATS, CDC, IDSA. Controlling TB in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of TB: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
CDC fact sheet "Specimen submission guidelines for pathologic evaluation of possible mycobacterial infections", accessed on November 8, 2018 at https://www.cdc.gov/ncezid/dhcpp/idpb/pdf/mycobacterium-specimen-submission-guidelines-H.pdf
CDC training module "Whole-genome sequencing for investigation of TB transmission in the United States: current uses and future plans", accessed on November 8, 2018 at https://www.cdc.gov/tb/programs/genotyping/Tuberculosis_WGS_Training_Module.pdf

Because the majority of laboratories use tests that do not routinely distinguish *Mycobacterium tuberculosis* from closely related species, these laboratories report culture results as being positive or negative for "*Mycobacterium tuberculosis* complex." In almost all cases of human disease, isolates in the *M. tuberculosis* complex are, in fact, *M. tuberculosis*, but other species are possible. Other species in the *M. tuberculosis* complex include *M. bovis*, *M. africanum*, *M. microti*, *M. canettii*, *M. caprae*, *M. pinnipedii*, and *M. mungi*; of these seven species, six can cause clinical disease or be transmissible from person to person –*M. bovis*, *M. africanum*, *M. microti*, *M. canettii*, *M. pinnipedii*, and *M. mungi*. Therefore, disease caused by any of those six organisms should be reported as TB. The only exception is the bacillus Calmette-Guérin (BCG) strain of *M. bovis*, which can be isolated from persons who have received the vaccine for protection against TB or as cancer immunotherapy; disease caused by the BCG strain of *M. bovis* should not be reported as TB.

DIAGNOSIS OF LTBI

Patients who test positive for TB, but whose medical evaluation ruled-out a diagnosis of TB disease, should be diagnosed with LTBI.

Treatment of LTBI is essential to controlling and eliminating TB in the United States because it substantially reduces the risk that LTBI will progress to TB disease.

Individuals at high risk for progression from LTBI to TB disease (refer to Table 1 on pages 2 and 3 of this chapter) should be prioritized for LTBI treatment.

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CHAPTER 5, APPENDIX A: QUICK START CHECK LIST

The following Quick Start Checklist was designed as a tool for public health nurses when evaluating a patient for LTBI or TB disease. The tasks should be performed by licensed nursing, medical, and laboratory staff as appropriate.

Step	Date Completed
☐ Use the appropriate Pennsylvania Risk Assessment Form (Adult or Pediatric; see Chapter 11, Targeted Testing) to determine who is at increased risk of exposure to *M. tuberculosis* and should be tested.	
☐ Test using an interferon gamma-release assay (IGRA) blood test (preferred for patients 2 years of age or older) or a tuberculin skin test (TST; preferred for children younger than 2 years of age).	
☐ Do not test patients who have had a previous positive IGRA or TST result. Instead, screen the patient for the signs and symptoms of TB. If the patient is symptomatic, complete a medical evaluation for TB disease.	
☐ For patients who exhibit the signs and symptoms of TB, take infection control precautions immediately: • Have the patient wear a mask or cover their mouth • Advise staff to take personal respiratory precautions if necessary • Isolate patients who have positive acid-fast bacilli (AFB) sputum smear results or whose CXR reveals signs of cavitary disease • Advise the patient to restrict activities to their home while considered infectious	☐ ☐ ☐ ☐
☐ Patients who exhibit the signs and symptoms of TB or have a newly positive test for *M. tuberculosis* should undergo a medical evaluation for TB disease including a chest radiograph (CXR), medical history, serology for HIV, physical examination and – if appropriate – bacteriologic examination of clinical specimens.	

Step	Date Completed
☐ Patients with an abnormal CXR should be evaluated for current TB disease	
☐ For patients diagnosed with TB disease: • If not available, obtain baseline biochemistry tests for toxicity monitoring • Considering any special circumstances (e.g. HIV status, kidney insufficiency, liver disease, patient age, pregnancy), select and immediately start the patient on an appropriate treatment regimen • See Chapter 7 – Treatment of TB Disease	
☐ A diagnosis of LTBI can only be made once a diagnosis of TB disease has been ruled out.	
☐ If LTBI is diagnosed, recommend the shortest treatment regimen appropriate for the patient.	

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CHAPTER 5, APPENDIX B: SPUTUM COLLECTION DURING TUBERCULOSIS (TB) TREATMENT

BACKGROUND

Sputum smear and culture testing are essential in the laboratory diagnosis of pulmonary TB. Once the patient is on anti-TB treatment, sputum smear and culture results are used to evaluate the patient's infectiousness and response to treatment.

SPUTUM SPECIMEN COLLECTION

For diagnostic purposes, all persons suspected of having TB disease at any site should have sputum specimens collected for an acid-fast bacilli (AFB) smear and culture, even those without respiratory symptoms. If possible, specimens should be obtained in an airborne infection isolation (AII) room or other isolated, well-ventilated area (e.g., outdoors).

There are four collection methods for respiratory specimens – coughing, induced sputum, bronchoscopy and gastric aspiration. For descriptions of each method, refer to the CDC Core Curriculum, Chapter 4, available here.

BACTERIOLOGIC TESTING FOR INITIAL DIAGNOSIS

To assist in the diagnosis of pulmonary TB, at least three consecutive sputum specimens are needed, each collected in eight to 24-hour intervals, with at least one being an early morning specimen. Ideally, specimens should be collected before starting the patient on drug therapy because even a few days of treatment can inhibit the growth of, and prevent the isolation of, *Mycobacterium tuberculosis* complex (MTBC).

Samples submitted for the initial diagnosis of TB should undergo both AFB smear and culture testing. A nucleic acid amplification test, or NAAT, should be ordered on at least one respiratory specimen from a patient with signs and symptoms of pulmonary TB when a diagnosis of TB is considered, but not yet confirmed. NAAT results are typically available 24-48 hours after the test and inform physician decisions about patient treatment and any need for isolation, but do not replace the need for an AFB smear or culture. A NAAT should be obtained even if the patient is smear negative. Culture remains the gold standard for laboratory confirmation of TB and is required for drug-susceptibility testing and genotyping.

TB TESTING FOR RELEASE FROM ISOLATION

Sputum smear results are also used to evaluate infectiousness while the patient is on anti-TB treatment. Patients may be considered for release from isolation when ALL of the following criteria (one through five) are met:

1. For patients whose initial smear was:
    - AFB positive – they have completed two weeks of the standard four-drug anti-TB drug regimen; or
    - AFB negative – they have completed five to seven days of the standard four-drug anti-TB drug regimen
2. The patient is receiving treatment via directly observed therapy (DOT) and has been adherent
3. The patient has shown evidence of clinical improvement such as a decrease in symptoms, improvement in radiographic findings, or other medical determination of improvement
4. The patient has had three consecutive negative smears collected at least eight hours apart with at least one early morning specimen
5. The patient has no risk factors for drug-resistance, e.g. being a contact to an index case with drug-resistant TB

For patients with an AFB positive smear at baseline, begin weekly collection of sputum specimens as follows:

1. For patients with cavities upon chest x-ray (CXR) and/or baseline sputum smears that are 3+ (moderate) or 4 (heavy), wait until the patient has completed one to two weeks of treatment before collecting the first follow-up sputum specimen.
2. For patients without cavities upon CXR and/or baseline sputum smears that are 1+ (rare) or 2+ (few), a sputum specimen can be collected once the patient completes one week of treatment.
3. For both 1) and 2) above, if the first sputum is negative, obtain a second sputum specimen. If the second specimen is negative, obtain a third. If any one specimen is positive, wait one week and re-start the collection process.
4. Once three consecutive smear-negative specimens are collected:
    - Patients on isolation can be considered for release if criteria two through five in the previous section have all been met.
    - Sputum specimens can then be collected monthly (in sets of three) until conversion to culture negative is documented.

TB TESTING FOR RESPONSE TO TREATMENT

The best way to monitor treatment effectiveness for patients with a positive sputum culture is to collect sputa monthly for testing until culture conversion is documented. The conversion should be documented as of the date of the first negative culture as long as there are no subsequent positive cultures.

After three months of therapy, patients who have not achieved culture conversion or who remain symptomatic should be evaluated for drug-resistant disease or non-adherence to treatment.

Patients with multi or extensively drug-resistant (MDR or XDR) TB should have cultures performed monthly for the full course of treatment.

Resources

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CHAPTER 5, APPENDIX C: NUCLEIC ACID AMPLIFICATION TESTING (NAAT)

WHAT IS A NAAT FOR TB?

A nucleic acid amplification test, or NAAT, for tuberculosis (TB) is a molecular test used to detect the DNA (deoxyribonucleic acid) of Mycobacterium tuberculosis complex (MTBC) in a sputum or other respiratory sample. Because the amount of DNA in a sample is very small, NAA testing includes a step that amplifies (or copies) the genetic material. Polymerase Chain Reaction (PCR) is a common form of NAAT used in laboratory diagnosis. GeneXpert® MTB/RIF test is a PCR that simultaneously detects MTBC and the genetic mutation that confers rifampin (RIF) resistance.

WHAT ARE THE ADVANTAGES OF A NAAT FOR TB?

- ✓ A NAAT can detect MTBC genetic material even when very small amounts are present in the sample tested.
- ✓ NAAT results are typically available in 24 to 48 hours.
- ✓ Rapid results enable earlier diagnosis of TB, earlier initiation of treatment, a reduced period of infectiousness, and improved patient outcomes.
- ✓ The GeneXpert MTB/RIF NAAT also provides rapid identification of RIF resistance, a predictor of multi-drug resistant TB. In most cases, patients resistant to RIF are also resistant to isoniazid (INH).

DOES A NAAT FOR TB REPLACE AN AFB SMEAR OR CULTURE?

A NAAT does ***not*** replace the need for an acid-fast bacilli (AFB) smear or culture. Culture remains the gold standard for laboratory confirmation of TB and is required for drug-susceptibility testing and genotyping.

WHEN SHOULD A NAAT BE ORDERED?

- ✓ Order a NAAT on at least one respiratory specimen from a patient with signs and symptoms of pulmonary TB when a diagnosis of TB is considered, but not yet confirmed.
- ✓ If unable to access a laboratory which performs the NAAT, send a specimen to the Pennsylvania Department of Health Bureau of Laboratories (BOL). The BOL TB molecular testing guidelines are available at http://bit.ly/TBMolecularTesting and the BOL specimen submission form at http://bit.ly/BOLMicroSpecimen.

HOW ARE NAAT RESULTS INTERPRETED?

- ✓ If the NAAT and AFB smear are both positive, presume the patient has TB and begin anti-TB treatment while awaiting the culture results.
- ✓ If the NAAT is positive and the AFB smear negative, **the clinician should be highly suspicious of active TB** but use clinical judgement whether to begin anti-TB treatment while awaiting the culture results.
  - **In a patient with high suspicion of having TB, TB treatment should be initiated.**
  - In a patient with little suspicion of having TB, a single positive NAAT should be viewed with suspicion and the result interpreted in the context of other clinical, radiographic and laboratory findings. If TB is still not suspected, consider whether to do additional diagnostic tests including another NAAT.
- ✓ If the NAAT is negative and the AFB smear is positive, confirm that inhibition testing was performed as part of the NAAT. This is done automatically for PCR testing performed at the BOL and is part of the GeneXpert MTB/RIF test.
- ✓ If the NAAT and AFB smear are both negative, use clinical judgement whether to begin anti-TB treatment while awaiting the results of the culture and any other diagnostic tests.
  - A single negative NAAT result does not definitively exclude TB. The bacterial load in the sample may fall below the detectable limit of the NAAT. Currently available NAATs are not sufficiently sensitive (detecting 50% to 80% of AFB-smear negative, culture positive pulmonary TB cases) to exclude a diagnosis of TB in AFB smear-negative patients suspected of having TB.

RESOURCES FOR MORE INFORMATION

For more information about NAA testing, see the 2009 CDC Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis, available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm.

If you have any questions about NAA testing for TB, call the Pennsylvania TB Program at (717) 787-6267.

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Chapter 6: Treatment of Latent TB Infection (LTBI)

INTRODUCTION

PURPOSE

Use this chapter to understand and follow national and Pennsylvania guidelines to:

- Identify the high-risk groups who should be given priority for LTBI treatment.
- List the LTBI treatment regimens and doses;
- Select the appropriate LTBI treatment regimen for specific situations, such as when a patient is pregnant or is co-infected with *Mycobacterium tuberculosis* and human immunodeficiency virus (HIV);
- Monitor patients for side effects and adverse reactions;
- Monitor patients' adherence to treatment; and
- Determine whether and when therapy is completed.

POLICY

The shortest treatment regimen appropriate for the specific patient should be used to treat LTBI. Newer short-course regimens using isoniazid (INH) and rifapentine (RPT) once-weekly for 12 weeks (also known as 3HP) or rifampin (RIF) alone taken daily for 4 months have been shown to have higher completion rates with less liver toxicity than the older regimen of INH taken daily for 9 months.

Increased use of the 3HP regimen is encouraged in appropriate patients. Refer to Appendix B of this chapter for current guidance about the administration of 3HP via directly observed therapy (DOT) or, in certain circumstances, via a combination of DOT and self-administered therapy (SAT).

LTBI treatment should be started for patients at increased risk of progression to TB disease, and every effort should be made to ensure such patients complete treatment.

BACKGROUND

Treatment of LTBI is essential to controlling and eliminating TB in the United States because it substantially reduces the risk that LTBI will progress to TB disease.

The CDC estimates that up to 13 million people in the U.S. have LTBI, and that just 300,000 to 400,000 of those individuals are treated each year – far lower than the number needed to

eliminate TB in the U.S. It is estimated that approximately 80% of new TB cases in the U.S. are due to untreated LTBI progressing to active TB disease (also referred to as the reactivation of LTBI). As a result, the greatest reduction in future tuberculosis cases will come from expanded testing for and treatment of LTBI.

A key challenge in getting patients with LTBI to start and complete treatment has been the long duration of therapy. For many years, the standard of care in LTBI treatment was INH daily for 9 months, but the completion rates for such a long regimen are generally low. Also, the most concerning side effect with isoniazid – hepatoxicity – though relatively rare and manageable, can have severe consequences if not recognized promptly.

Because the newer short-course regimens (once-weekly 3HP for three months; RIF daily for four months) offer shorter duration of treatment, reduced hepatotoxicity and increased completion rates they are now preferred by the CDC over 9 months of INH.

WHOM TO TREAT

Once infected, certain groups are at high risk of developing TB disease. LTBI treatment should be started for patients at increased risk of progression to TB disease, and every effort should be made to ensure such patients complete treatment.

The strongest known risk factor for the progression of LTBI to TB disease is co-infection with HIV. Patients coinfected with HIV and LTBI have a 7 to 10 percent *yearly* risk of developing TB disease compared to a 10 percent *lifetime* risk for patients with LTBI alone.

Refer to Table 1 for a more complete list of groups who should be given high priority for LTBI treatment.

TABLE 1: **HIGH PRIORITY CANDIDATES FOR LTBI TREATMENT**

Groups Who Should be Given High Priority for LTBI Treatment
People who have a positive IGRA result or a TST induration of 5 or more millimeters • HIV infected persons • Recent contacts of persons with infectious disease • Persons with fibrotic changes on chest radiograph (CXR) consistent with prior TB disease • Patients with organ transplants • Persons who are immunocompromised for other reasons (including patients taking the equivalent of 15 mg/day of prednisone for a month or more)
People who have a positive IGRA result or a TST induration of 10 or more millimeters • People born in or who frequently travel to countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, and Guatemala, or other countries with high rates of TB • Injection drug users • Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, etc.) • Mycobacteriology laboratory personnel • Persons with medical conditions that increase the risk for progression to TB disease (diabetes mellitus, silicosis, recent infection with *Mycobacterium tuberculosis (M.TB)* within the past two years, bone marrow and organ transplant recipients, prolonged high-dose corticosteroid therapy and other immunosuppressive therapy, chronic renal failure, hemodialysis, some hematological disorders [e.g., leukemias and Hodgkin's disease], other specific malignancies [e.g., carcinoma of the head, neck, or lung], chronic malabsorption syndromes, weight 10% or more below ideal body weight, and intestinal bypass or gastrectomy • Children less than 5 years of age or children and adolescents exposed to adults in high-risk categories
People who have a TST induration of 15 or more millimeters The following groups may be considered for treatment of LTBI if their TST result is greater than or equal to 15 mm. These groups should be given a lower priority for prevention efforts than the groups listed above. • Persons with no known risk factors for TB disease • Healthcare workers who are otherwise at low risk for TB disease and who received baseline testing at the beginning of employment as part of a TB screening program

Some contacts who have a negative IGRA or TST result but are at high risk of progression to TB disease if infected should be evaluated for LTBI treatment after TB disease has been ruled out by clinical exam and a CXR. See the following section for more detail.

CLOSE CONTACTS AT HIGH RISK OF PROGRESSION

A contact is someone who has been exposed to *M.TB* infection by sharing air space with an infectious TB person. Susceptible contacts are those individuals who are more likely to progress to TB disease once infected. Vulnerable contacts are those individuals who could suffer severe morbidity if they developed TB disease. Persons who are susceptible and/or vulnerable to TB disease are candidates for window prophylaxis, or the treatment of presumptive LTBI during the interval between the time at which infection occurs and when it is detectable via an IGRA or TST. The CDC recommends that the window period be estimated at 8 to 10 weeks.

The following susceptible and vulnerable contacts with initially negative IGRA or TST test results should begin window prophylaxis LTBI treatment *after* TB disease has been ruled out by clinical examination and a CXR:

- Children less than 5 years of age
- Immunosuppressed persons
- Persons at increased risk for progression to TB disease once infected

If the second IGRA or TST result is negative and the contact is immunocompetent (including immunocompetent young children) and no longer exposed to infectious TB, treatment for LTBI may be discontinued, and further follow-up is not required. If the second test is negative but the contact is immunocompromised (e.g., HIV), a full course of LTBI treatment is recommended. If the second test result is negative but the person remains in close contact with an infectious patient, LTBI treatment should be continued if the contact is:

- less than 5 years old;
- aged 5–15 years, at the clinician's discretion; or
- HIV-seropositive or otherwise immunocompromised.

Contacts known to be, or suspected of being, immunocompromised should be given treatment for LTBI regardless of the IGRA or TST reaction.

LTBI TREATMENT REGIMENS AND DOSAGES

Treatment of LTBI is an essential part of the strategy to eliminate TB in the United States. Persons with LTBI who are considered at increased risk of progressing to TB should be encouraged to start treatment.

There are several treatment regimens available for the treatment of LTBI, and providers should discuss options with patients. DOT administration is recommended for persons at high risk for progressing to TB who are either suspected of being unlikely to adhere to treatment or on an intermittent dosing regimen. DOT is especially appropriate when a household member is on DOT for TB disease or in institutions and facilities where a staff member can observe treatment.

High-risk (under 5 years of age or immunocompromised) contacts of active cases should be started promptly on treatment for LTBI.

For more information on the treatment of LTBI, see the:

- "Treatment Regimens for Latent TB Infection" page on the Centers for Disease Control and Prevention (CDC) TB website at https://www.cdc.gov/tb/topic/treatment/ltbi.htm.
- Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent *Mycobacterium tuberculosis* infection. *MMWR Morb Mortal Wkly Rep.* 2018;67(25):723-726.
- Isoniazid-Rifapentine for Latent Tuberculosis Infection: A Systematic Review and Meta-analysis (Am J Prev Med 2018;55(2):244–252 Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine)

REGIMENS

Identify an appropriate regimen for the patient using the national guidelines provided in Table 2. In some instances – a contact to a drug-resistant index case or a patient who has an allergic reaction to rifampin – other medications may need to be used. In such cases, consult with the state TB consultant and/or the Global TB Institute at 1-800-482-3627.

TABLE 2: **RECOMMENDED DRUG REGIMENS FOR TREATMENT OF LTBI**

Priority Rank*	Drug	Interval and Duration	Comments	Recommendation/ Evidence
Preferred	INH + RPT (3HP)	Once weekly for 12 weeks in adults Once weekly for 12 weeks in children greater than 2 years of age	Missed doses or altered dosing intervals or amounts could jeopardize efficacy or safety; DOT or SAT may be used consistent with current TB Program policy. Effective February 2020, CDC and the National TB Controllers Association recommend 3HP to treat LTBI in adults and children greater than 2 years of age. Data on the safety and pharmacokinetics of rifapentine in children aged <2 years are not available. Refer to Appendix B of this chapter for current state TB program guidance about the administration of 3HP in children.	Strong/Moderate
Preferred	RIF	Daily for 4 months in adults Daily for 4 months in children	RIF is used for persons who are contacts of patients with INH-resistant, RIF-susceptible TB. Some antiretroviral drugs, such as the protease inhibitors and NNRTIs, have interactions with the rifamycins. Clinicians should consult Web-based updates (e.g., https://aidsinfo.nih.gov/guidelines/htnl/4/adult-and-adolescent-opportunistic-infection/0) or experts for the latest specific recommendations.	Strong/Moderate (HIV neg.) †

Priority Rank*	Drug	Interval and Duration	Comments	Recommendation/ Evidence
Preferred	INH + RIF	Daily for 3 months	This daily regimen of INH and rifampin is conditionally recommended for adults and children of all ages and for HIV-positive persons as drug interactions allow. It is not to be confused with the once-weekly, 12-dose regimen of INH and rifapentine**,	Conditional/Very low (HIV neg.) Conditional/Low (HIV pos.)
Alternative	INH	Daily for 6 months§	This regimen is strongly recommended for HIV-negative adults and children of all ages and conditionally for HIV-positive adults and children of all ages.	Strong§/Moderate (HIV neg.) Conditional/Moderate (HIV pos.)
Alternative	INH	Daily for 9 months §	This regimen is conditionally recommended for adults and children of all ages, both HIV-negative and HIV-positive. In HIV-infected patients, INH may be administered concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs).	Conditional/Moderate

Abbreviation: HIV = human immunodeficiency virus.

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness;
Alternative: excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

** Prescribing providers and pharmacists who are unfamiliar with rifampin and rifapentine might confuse the two drugs. They are not interchangeable and caution should be taken to ensure that patients receive the correct medication for the intended treatment regimen.

† No evidence reported in HIV-positive persons.

§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

Sources: Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. *MMWR* Recomm Rep 2020;69(No. RR-1):1–11. DOI: http://dx.doi.org/10.15585/mmwr.rr6901a1
Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent *Mycobacterium tuberculosis* infection. *MMWR Morb Mortal Wkly Rep*. 2018;67(25):723-726.

DOSAGES

Once the appropriate regimen has been identified, refer to Table 3 for the recommended dosages for each drug. The information in Table 3 is available on the CDC website at https://www.cdc.gov/tb/topic/treatment/ltbi.htm.

TABLE 3: **RECOMMENDED DOSES**

Drug	Preparation	Adults/ Children	Once weekly	
INH/RPT COMBINATION (3HP) §				
INH	Tablets (50 mg, 100 mg, 300 mg)	Adults and children aged 12 years and older (max.)	15 mg/kg rounded up to nearest 50 or 100 mg (900 mg)	
		Children aged 2 to 11 years (max.)	25 mg/kg (max 900 mg)	
RPT	Tablets (150 mg)	Adults and children aged 12 years and older (max.)	10.0 – 14.0 kg (300 mg) 14.1 – 25.0 kg (450 mg) 25.1 – 32.0 kg (600 mg) 32.1 – 49.9 kg (750 mg) 50.0 kg or more (900 mg)	
		Children aged 2 to 11 years (max.)	Same as RPT for adults and children aged 12 years and older	
Drug	**Preparation**	**Adults/ Children**	**Daily**	**Twice weekly†**
RIF (4 mos.)	Capsule (150 mg, 300 mg); powder may be suspended for oral administration	Adults (max.)	10 mg/kg (max 600 mg)	N/A
		Children (max.) Infants/toddlers/ meningitis*	15–20 mg/kg (max 600 mg) 20-30 mg/kg*	N/A N/A
INH + RIF (3 mos.)	**INH:** Tablets (50 mg, 100 mg, 300 mg) **RIF:** Capsule (150 mg, 300 mg)	Adults (max.)	**INH:** 5mg/kg (300 max mg) **RIF:** 10 mg/kg (max 600 mg)	N/A
		Children (max.)	**INH:** 10-20 mg/kg** (300 max mg) **RIF:** 15-20 mg/kg (max 600 mg)	N/A
INH (6 mos.)	Tablets (50 mg, 100 mg, 300 mg)	Adults (max.) Children (max.)	5 mg/kg (max 300 mg) 10-20 mg/kg** (max 300 mg)	N/A
		Adults (max.) Children (max.)	N/A	15 mg/kg (max 300 mg) 20-40 mg/kg** (max 900 mg)
INH (9 mos.)	Tablets (50 mg, 100 mg, 300 mg)	Adults (max.) Children (max.)	5 mg/kg (max 300 mg) 10-20 mg/kg** (max 300 mg)	N/A
		Adults (max.) Children (max.)	N/A	15 mg/kg (max 300 mg) 20-40 mg/kg** (max 900 mg)

All dose information was downloaded from https://www.cdc.gov/tb/topic/treatment/ltbi.htm on 02/21/20.

§ Per Pa TB Program policy, children less than 18 years of age should receive 3HP via DOT

† The twice-weekly regimens should only be used if no other regimen is appropriate. Intermittent regimens must be provided via directly observed therapy (DOT)

* The American Academy of Pediatrics acknowledges that some experts use rifampin at 20-30 mg/kg for the daily regimen when prescribing for infants and toddlers (Source: 2018 Redbook)

** The American Academy of Pediatrics recommends an isoniazid dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice-weekly regimen

DIRECTLY OBSERVED THERAPY (DOT)

DOT is not required for patients taking treatment for LTBI – except for some patients taking the once-weekly, 12-dose regimen of INH + RPT (3HP). Refer to Appendix B of this chapter for more information.

DOT may also be used at the clinician's discretion for patients at increased risk of progression from LTBI to TB disease. Refer to Chapter 8 - Directly Observed Therapy for more information.

SIDE EFFECTS AND ADVERSE REACTIONS

As is true with all medications, anti-TB medications are associated with a predictable incidence of side effects and adverse reactions, some mild, some serious.

Regardless of the LTBI treatment regimen selected (INH for 9 months, RIF for 4 months, or INH plus RPT for 12 weeks), patients should be seen by the TB nurse at least once a month so the patient can be assessed for treatment compliance and any signs or symptoms of side effects or adverse reactions. The patient can also be given the next month's supply of medication during the monthly visit.

If the patient is experiencing side effects or adverse reactions, the TB clinician should be consulted, and the patient may need to be monitored more frequently. Chemistries and CBC, AST/ALT, or other tests based on specific drugs should be done periodically. See **Table 5: Monitoring and Interventions for Side Effects and Adverse Reactions** in this chapter.

Side effects are generally mild, may resolve in time without any intervention and can often be anticipated by the prescribing physician or the TB nurse because they are known to commonly occur. Adverse reactions, however, are usually more severe, in rare instances can be fatal, and require intervention. For example, mild nausea in a patient taking INH may be considered a side effect while severe hepatitis is an adverse reaction. Descriptions of known side effects and adverse reactions for a specific prescription drug are based on substantial clinical evidence and can be found in the product package insert (PI) and the patient package insert (PPI).

Although it is important to be attuned to the potential for side effects and adverse reactions, it is at least equally important that treatment not be stopped without adequate justification. Mild side effects may resolve without any intervention or may be managed with treatment directed at controlling the symptoms. Adverse reactions can be severe and it is important to recognize adverse reactions that indicate when a drug should not be used. With more severe adverse

reactions, the offending drug or drugs must be discontinued. Proper management of more serious adverse reactions often requires expert medical consultation.

Serious adverse reactions are either life-threatening, require inpatient hospitalization or extends the length of current hospitalization, or results in death. Serious adverse reactions will be reported to the U.S Food & Drug Administration (FDA) via MedWatch at https://www.fda.gov/media/76299/download or by calling the FDA at 1-800-FDA-1088.

BASIC MONITORING STEPS

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

- All health care personnel providing treatment for LTBI should follow the current guidelines:
    - 2018 "Update of Recommendations for the Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* Infection", pages 723-726 at https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6725a5-H.pdf
    - 2011 "Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection", pages 1650-1653 at https://www.cdc.gov/mmwr/pdf/wk/mm6048.pdf
    - See the "Clinical and Laboratory Monitoring" section and Table 8: Medications to Treat LTBI – Doses, Toxicities and Monitoring Requirements of the 2000 LTBI treatment guidelines, "Targeting Tuberculin Testing and Treatment of LTBI" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf.
- It is also important to check for guideline updates posted on the CDC's Division of TB Elimination home page at http://www.cdc.gov/tb/ and the list of guidelines by date at https://www.cdc.gov/tb/publications/guidelines/list_date.htm.
- While on treatment, all patients should be evaluated in person at baseline (before starting treatment) and then at least monthly for side effects and adverse reactions. More frequent monitoring may be indicated with alternate treatment regimens.
- No more than a one-month supply of any medication will be given to a patient unless specifically ordered by the TB clinician and approved by the TB Program.
- The common side effects and adverse reactions reported for drugs used to treat for LTBI are listed in **Table 4**: **Reporting Reactions to Anti-TB Medications**. Educate patients to stop the prescribed TB medication(s) and promptly report to the prescribing clinic any of the symptoms or signs listed in Table 4 or any other unexplained illness.
    - If a patient reports a potential side effect or adverse reaction to the outreach worker, the outreach worker must notify the patient's TB public health nurse (PHN) immediately.
    - PHN must assess the patient's side effect or adverse reaction and notify TB clinician and other District Office staff as appropriate. PHN will continue to monitor the patient.

- If you suspect that an anti-TB drug may be causing a side effect or adverse reaction:
  - Refer to **Table 5: Monitoring and Interventions for Side Effects and Adverse Reactions**.
  - Consult with the patient's TB clinician and notify the nurse supervisor.
- If you suspect that an anti-TB drug may be interacting with other medications that the patient is taking, refer to pages 45–47 in the "Treatment of TB" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.
- Document the following patient information:
  - Review of symptoms, side effects, and adverse reactions (and any labs that were drawn)
  - Education given
  - Refill provided
  - Description of any problems encountered and action taken for that visit
  - Next appointment

REPORTING REACTIONS

The table below is intended for use by the PHN and/or outreach worker providing care to the patient. The patient should be instructed to contact the PHN if he or she experiences any of the side effects or adverse reactions listed in Table 4.

If a patient reports a potentially serious adverse reaction, the PHN should notify the patient's TB clinician immediately. In consultation with the TB clinician, the PHN should instruct the patient to stop TB medications until evaluated by the clinician.

If a patient reports a potentially less severe side effect, the PHN should notify the patient's TB clinician within 24 hours and monitor the patient.

TABLE 4: **REPORTING REACTIONS TO ANTI-TUBERCULOSIS MEDICATIONS**

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient's TB clinician. These signs and symptoms suggest potentially serious adverse reactions, including hepatotoxicity: • Jaundice • Dark urine • Vomiting • Abdominal pain • Fever • Visual changes • Marked clinical rash In consultation with the TB clinician, instruct the patient to stop TB medications until evaluated by the TB clinician.	Report the following signs and symptoms to the patient's TB clinician within 24 hours: • Anorexia • Nausea • Malaise • Peripheral neuropathy: tingling or burning sensation in hands or feet • Rashes
* These lists are not all-inclusive. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of TB" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and the 2016 official ATS/CDC/IDSA clinical practice guidelines: treatment of drug-susceptible tuberculosis at https://academic.oup.com/cid/article/63/7/e147/2196792.	

Source: California Department of Health Services(CDHS)/California TB Controllers Association(CTCA). TB case management core components. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. Last updated in 2011. Available at: https://ctca.org/wp-content/uploads/2018/11/ctca_case_management_5_.pdf

REPORTING SEVERE ADVERSE EVENTS

The CDC Division of TB Elimination (DTBE) urges health departments, hospices, hospitals, jails, prisons, and private medical offices to report all severe adverse events (e.g., liver injury, pancreatitis, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for LTBI.

- All adverse reactions should be reported to the community health nurse supervisor (CHNS) and the TB clinician.
- All severe adverse reactions will be reported to the U.S. Food & Drug Administration (FDA) via MedWatch at https://www.fda.gov/media/76299/download or by calling the FDA at 1-800-FDA-1088.

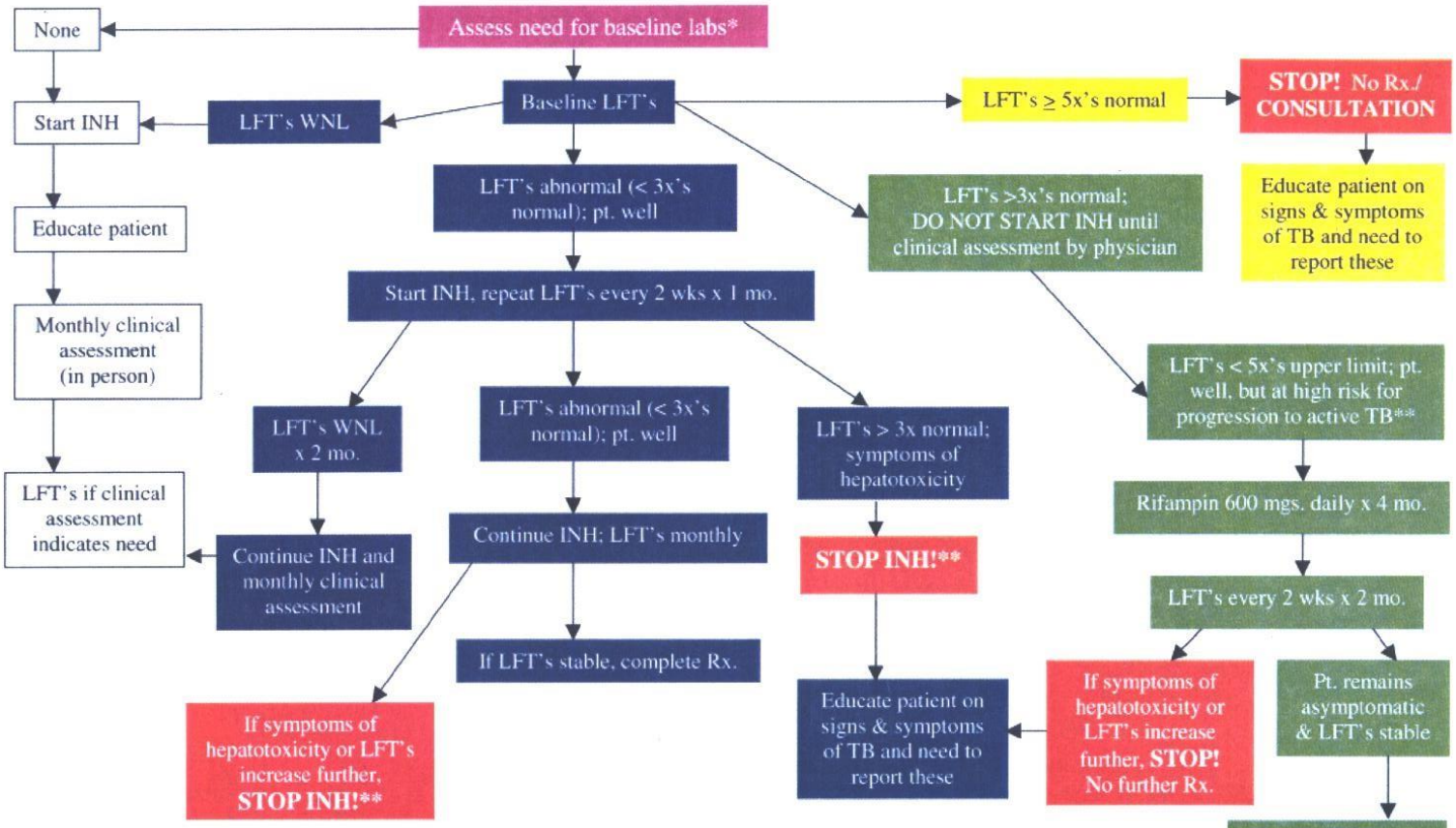
TABLE 5: **MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS**

Anti-TB Drug	Side Effects/Adverse Reactions	Monitoring	Comments
Isoniazid (INH) See Table 3 for dosages	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects Drug interactions resulting in increased phenytoin (Dilantin) or Disulfiram (Antabuse) levels	Clinical monitoring monthly Liver function tests AST, ALT, and serum bilirubin at baseline in selected cases HIV infection, history of liver disease, alcoholism, and pregnancy Repeat measurements if • Baseline results are abnormal • Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin) and adjust the dose if necessary.

Anti-TB Drug	Side Effects/Adverse Reactions	Monitoring	Comments
Rifampin (RIF) See Table 3 for dosages	• Rash • Gastrointestinal upset • Hepatitis • Fever • Bleeding problems • Thrombocytopenia • Renal failure • Flu-like symptoms • Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests AST, ALT, and serum bilirubin at baseline in selected cases HIV infection, history of liver disease, alcoholism, and pregnancy Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions	There are a number of drug interactions with potentially serious consequences, including significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to “Section 7: Drug Interactions” on page 45 in “Treatment of TB” at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf. Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC’s Division of TB “News and Updates” Web page at http://www.cdc.gov/tb/ to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Anti-TB Drug	Side Effects/Adverse Reactions	Monitoring	Comments
Rifapentine (RPT) See Table 3 for dosages	• Rash • Hepatitis • Fever • Thrombocytopenia • Orange-colored body fluids (secretions, urine, tears) With increased levels - Severe arthralgias Uveitis Leukopenia	See monitoring for Rifampin/Rifabutin Complete documentation of DOT visit on patient interview form Weekly report of LMP For women childbearing age weekly monitoring of side effects esp. hypotension/thrombo-cytopenia	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to “Section 7: Drug Interactions” on page 45 in “Treatment of TB” at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf. Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC’s Division of TB “News and Updates” Web page at http://www.cdc.gov/tb/ to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Assessing and Managing the Risk of Liver Disease in the Treatment of LTBI



*Serum AST, ALT, Total Bilirubin for patient whose initial evaluation suggests a liver disorder; is HIV infected, pregnant or is in postpartum period (3 mo. of delivery); has a history of liver disease, regular alcohol use, or chronic liver disease.

**Patients may be considered for treatment with daily Rifampin x 4 mo. especially if they are at high risk for progression to active disease. A CBC with platelet count should be drawn prior to initiation of Rifampin therapy.

Produced by the Department of State Health Services in collaboration with the Heartland National TB Center

Consultation to healthcare providers at 1-800-TEX-LUNG, www.HeartlandNTBC.org

ADHERENCE

Non-adherence with medication regimens is a major cause of LTBI treatment failure.

Monitor patients face to face for adherence to self-administered LTBI treatment regimens at least once a month throughout treatment. It is difficult to identify who will and who will not be adherent. If patients do not take medicine as directed, the effectiveness of the regimen decreases and the patient will be at greater risk of progressing to TB disease in the future and of infecting others with TB.

ASSESSMENT OF ADHERENCE

At each visit, the TB clinician or PHN should assess adherence by doing the following:

- The initial patient history must be carefully taken.
- Initial history intake may indicate that the patient is at-risk for non-adherence with medication ingestion.
- Inquire about missed doses since their last refill.
- Staff will encourage patients to bring their bottles of medicine to the appointment. Staff will count remaining pills and document.
- If adherence problems are identified, include patients in the problem-solving process.
    - Ask patients why they think that doses are missed and what could be done better: change the time of day, the location where they keep or take their pills, etc. (Encourage pill box).
    - Find out if there are barriers to obtaining refills in a timely manner that could be corrected.
    - Review with patients is their risk of developing TB if medicine is not taken.
    - Mutually agree on a plan to improve adherence.
    - Provide detailed documentation.
- Particular attention should be given to patients who receive LTBI therapy because they are close contacts of a case, children, persons who are HIV positive, and patients with other medical disorders which increase their risk of developing TB disease.
- DOT should be considered for patients who are at risk of non-adherence.
- The physician and nurse shall be jointly responsible for the decision to administer medication by self-administration or by DOT.

NON-ADHERENCE NOT DETECTED AT INITIAL VISIT

- The initial history and observations of the patient may not detect evidence of a lifestyle or other barriers to adherence to a treatment program. The patient who does not keep appointments, have laboratory work done as requested, take medication as directed, and assist the Department in locating close contacts for testing exhibits behavior which supports the impression of non-adherence.
- If the patient doesn't keep an appointment, the patient should be telephoned the same day or the next working day. Alternatively, the patient can be contacted by a home visit

the same day or the next day. The initial interview should have given the patient the information that return appointments are important. Be sure that the patient understood the appointment time and that the patient can get to the clinic. Negotiate with the patient the earliest return to the clinic.

STRATEGIES FOR ALTERING NON-ADHERENT BEHAVIOR

- The non-adherent patient who is on DOT needs strategies to maintain therapy other than education and appointment reminders.
- The same PHN should see the patient at each clinic visit. Appointment schedules should be arranged so that patients are not kept waiting.
- Reimold funds may be used to assist the TB patient with transportation, purchase of meals, and purchase of items which are incentives for compliance. Examples of incentives and enablers, along with information about the TB Program policy and procedures for requesting Reimold funds can be found in Chapter 17.

REFUSAL OF TREATMENT FOR LTBI

- If a person refuses treatment, document the refusal in the chart and in PA-NEDSS.
- For any refusal of treatment, send a letter emphasizing the importance of treatment and confirming the refusal. File a copy of the letter in the chart.
- Anyone who refuses treatment should be advised to seek medical care if they have symptoms suggestive of TB.

MISSED CLINIC APPOINTMENTS FOR LTBI TREATMENT

- Make one telephone call to the patient. If no response, send a missed appointment letter.
- If the patient doesn't respond to the telephone call or letter and is at increased risk of progression to TB disease, make a home visit as soon as possible to re-engage the patient.
- If there is no response to the above actions, discharge the patient from clinic with the approval of the CHNS and the TB clinician. Document all actions to contact the patient in the patient chart and in PA-NEDSS.

COMPLETION OF THERAPY

Determine whether the patient has completed therapy based on the total number of doses administered and the length of time in which they were completed (refer to Table 6). When patients have had lapses in therapy but are still able to complete the recommended number of doses in the allotted time period, encourage them to complete therapy.

For noncompliant patients, consult the TB clinician to determine course of therapy.

Assess patients who will not complete appropriate therapy within the time frame specified to determine whether to restart treatment. If the decision is made to retreat the patient, then restart

the entire regimen and follow the recommended treatment plan. Specific factors to consider when determining whether to restart treatment include the following:

- Individual's risk for developing TB disease
- Total number of doses of LTBI treatment administered
- Time elapsed since the last dose of treatment for LTBI
- Patient adherence issues (previous attempts at completion, willingness to continue, etc.)

Give non-adherent patients at very high risk of developing TB disease every opportunity to complete treatment for LTBI. Consider these patients for intermittent therapy with DOT and evaluate the use of incentives and enablers.

Treatment of LTBI in contacts is considered a priority in TB control activities. Make every effort to assure completion of treatment by contacts.

All contacts who are being treated for LTBI should be seen face-to-face by the TB nurse at least once every month. Incentives and enablers are recommended as aids to adherence, and the healthcare provider should educate the patient about TB, its treatment, and the signs and symptoms of adverse drug effects at each patient encounter.

TABLE 6: **CRITERIA FOR COMPLETION OF THERAPY**

Regimen	Age	Duration of Therapy	Number of Doses	All Doses Must be Completed Within
INH and RPT	Adult	12 weeks	12[1]	16 weeks
	Child *	12 weeks	12[1]	16 weeks
RIF daily	Adult	4 months	120	6 months
	Child	4 months	120	6 months
INH daily	Adult and child	9 months	270	12 months
INH daily	Adult	6 months	180	9 months
INH twice weekly	Adult and child	9 months	76	12 months
INH twice weekly	Adult	6 months	52	9 months
Definitions of abbreviations: INH = isoniazid; RIF = rifampin. * Not recommended under age 2; under 2 years old, use INH X 9 months				

[1] At minimum, patients taking INH + RPT to treat LTBI must complete 11 doses within 16 weeks to be considered as having completed treatment.

Sources: CDC. Targeted tuberculin testing and treatment of LTBI. *MMWR* 2000;49(No. RR-6):26–27; CDC. Regimens. In: Chapter 6: treatment of LTBI. *Core Curriculum on TB (2011)* [Division of TB Elimination Web site]. Updated November 2011. Available at: http://www.cdc.gov/tb/education/corecurr/index.htm.
See also Centers for Disease Control and Prevention (CDC). Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent *Mycobacterium tuberculosis*

infection. *MMWR Morb Mortal Wkly Rep*. 2018;67(25):723-726 at https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6725a5-H.pdf.

Make every effort to encourage patients to adhere to the LTBI treatment regimen. However, if a patient has failed three attempts to complete treatment, no further effort may be merited. The PHN should contact patients who interrupt therapy and are at high risk of developing TB disease (for example, contacts of patients with infectious TB, HIV-infected patients, or TB Class 4 patients) for reevaluation.

TREATMENT IN SPECIAL SITUATIONS

MANAGEMENT OF CLOSE CONTACTS OF DRUG-RESISTANT CASES

Close Contacts of Drug-Resistant TB Patients – For persons who have been exposed to INH-resistant, RIF-susceptible TB who are known or suspected to have LTBI, a 4-month regimen of daily RIF is recommended. When RIF cannot be used, rifabutin may be substituted.

Close Contacts of Multidrug-Resistant (MDR) TB Patients – For persons who have been exposed to a TB patient resistant to both INH and RIF and are known or suspected to have LTBI, alternative LTBI treatment regimens should be considered. Alternative regimens should include two drugs to which the TB strain is susceptible. A potential regimen should include daily fluoroquinolone. Many experts are now recommending a fluoroquinolone alone for treatment of LTBI in MDR contacts.

- The TB clinic physician is encouraged to discuss all aspects of the preventive treatment of contacts to drug resistant cases with the state TB consultant for adult or pediatric TB and/or the Global TB Institute.
- The drug(s) should be given in standard therapeutic doses in accordance with the information contained in Chapter 7, Treatment of TB Disease.
- Management of contacts with a high probability of infection with MDR-TB may include immigrants, refugees, and persons from areas of the world which have a high incidence of TB.
- Consult with the pediatric TB consultant about window prophylaxis treatment for children who are close contacts, especially those younger than 5 years of age.
- Contacts with known or suspected LTBI who are not immunosuppressed may be treated for 6 months or observed without LTBI treatment for 6 months.
- Contacts with a high risk of progression to TB disease should receive preventive LTBI treatment.
- All persons with suspected MDR LTBI should be monitored for 2 years regardless of the treatment regimen.
- Management of persons intolerant to INH can follow an approach similar to that taken for contacts of INH-resistant cases.

Advise the patient to seek medical attention if the signs and symptoms of TB develop. A CXR should be obtained.

PREGNANCY AND BREASTFEEDING

Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progressing to disease. Pregnant women should be targeted for testing only if they have a specific risk factor for LTBI or for the progression of LTBI to TB disease. Extensive use of INH during pregnancy has shown that although the drug readily crosses the placental barrier, it is not teratogenic, even when given during the first four months of gestation. Pregnant women taking INH should receive pyridoxine supplementation.

Breastfeeding is not contraindicated when the mother is being treated for LTBI. Infants whose breastfeeding mothers are taking INH should receive supplemental pyridoxine. Note that the amount of INH provided by breast milk is inadequate for treatment of the infant.

ALCOHOLISM

INH (and RIF) can cause hepatitis that may result in additional liver damage in patients with preexisting liver disease. Treatment with these drugs is initiated despite preexisting liver disease as clinically indicated.

Drug-induced hepatitis is defined as a serum aspartate aminotransferase (AST) level more than three times the upper limit of normal in the presence of symptoms or five times the upper limit of normal in the absence of symptoms.

Prior to treatment, serologic testing for hepatitis viruses A, B, and C should be considered, if clinically appropriate. Close monitoring, symptom review and repeat serologic testing, is essential in the management of a patient with an elevated serum AST.

To monitor for hepatitis:

- Conduct clinical monitoring on the initial visit and at least monthly
- Educate patients about symptoms and signs of adverse reactions, and instruct patients to stop treatment should symptoms occur and contact SHC
- If the patient is on DOT, assess for adverse reactions at each visit

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CHAPTER 6, APPENDIX A: QUICK START CHECKLIST

This check list is designed to assist community and public health nurses when treating a patient for LTBI. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Step	Date Completed
□ For patients with a newly positive interferon gamma-release assay (IGRA) or tuberculin skin test (TST), rule out a diagnosis of TB disease before diagnosing LTBI.	
□ If LTBI is diagnosed, recommend the shortest duration LTBI treatment regimen appropriate for the specific patient.	
□ Meet face-to-face with the patient at least once per month during LTBI treatment to: • Determine adherence to the prescribed regimen; • Complete clinical follow-up; and • Evaluate any side effects or adverse reactions experienced by the patient.	
□ As needed, provide enablers and/or incentives to the patient to facilitate their completion of LTBI treatment.	
□ Document whether the patient partially or fully completed LTBI treatment as prescribed.	

CHAPTER 6, APPENDIX B: UPDATED RECOMMENDATIONS FOR THE USE OF ISONIAZID PLUS RIFAPENTINE TO TREAT LATENT TB INFECTION (LTBI)

This document summarizes key updates by the Centers for Disease Control and Prevention (CDC) and the Pennsylvania Tuberculosis (TB) Program concerning the use of 3HP. The full text of the updated CDC recommendations was published in the June 29, 2018 issue of the CDC Morbidity and Mortality Weekly Report.

The key updates address the use of 3HP in children and in patients with human immunodeficiency virus (HIV) infection (including acquired immunodeficiency syndrome, or AIDS) and introduce the opportunity for self-administration.

BACKGROUND INFORMATION

Treatment of LTBI is essential to controlling and eliminating TB in the United States because it substantially reduces the risk that latent TB infection will progress to TB disease.

Since the CDC first recommended 3HP for the treatment of LTBI in 2011, additional research has been done in multiple patient populations to evaluate the efficacy, safety and treatment completion rates for 3HP. In 2017, a CDC Work Group did a systematic review and meta-analysis of published data concerning the 3HP regimen, the results of which were published in June 2018[1]. The meta-analysis determined that 3HP "is as safe and effective as other recommended [LTBI] regimens and achieves substantially higher treatment completion rates".

Based on all available data, the CDC continues to recommend 3HP for treatment of LTBI in adults and now recommends use of 3HP:

- In persons with LTBI aged 2 to 17 years;
- In persons with LTBI who have HIV infection, including AIDS, and are taking antiretroviral medications with acceptable drug-drug interactions with rifapentine; and
- By directly observed therapy (DOT) or self-administered therapy (SAT) in persons aged 2 years and older.

The CDC advises health care providers to choose the mode of administration (DOT or SAT) based on local practice, individual patient attributes and preferences, and other considerations

[1] Njie GJ, Morris SB, Woodruff RY, Moro RN, Vernon AA, Borisov AS. Isoniazid-rifapentine for latent tuberculosis infection: a systematic review and meta-analysis. Am J Prev Med 2018. Epub June 11, 2018. https://doi.org/10.1016/j.amepre.2018.04.30

including the patient's risk for progression to severe forms of TB disease[2]. The CDC also recommends that all individuals on 3HP be evaluated monthly to assess compliance with treatment and side effects, and that patients taking 3HP via SAT be encouraged to maintain a medication diary in which they record 1) each date they took their medication and 2) any difference in the day of the week they took their medication (e.g., the patient agreed to take their medication every Tuesday but took it on Wednesday in week 4).

Lastly, the updated CDC recommendations state that additional studies are needed to understand the:

- Pharmacokinetics, safety and tolerance of 3HP in children less than 2 years of age;
- Adherence to and safety of 3HP when self-administered by persons aged less than 18 years; and
- Safety of 3HP during pregnancy.

PENNSYLVANIA TB PROGRAM RECOMMENDATIONS

The Pennsylvania TB Program encourages increased use of the 3HP regimen in appropriate patients and recommends that 3HP be administered as follows:

- Patients less than 18 years of age should receive 3HP via DOT. Self-administered therapy (SAT) with 3HP has not been studied in persons younger than 18 years of age.
- Strong consideration of the patient's age, medical history, social circumstances, and risk factors for progression to severe TB disease should be given when making the decision regarding the administration of 3HP.
    - DOT is strongly recommended for patients on 3HP at high risk of progression to TB including, but not limited to: persons with conditions such as end stage-renal disease, diabetes mellitus, and organ transplantation; persons who use alcohol or illegal drugs; and persons with an incomplete TB treatment history. DOT is also highly recommended for patients who require translation services.
    - For patients aged 18 years and older at low risk of progression to TB, a combination of DOT and SAT may be considered, with each DOT visit including an in-person assessment of treatment compliance and side effects. Doses one, two, six and 10 of 3HP are provided via DOT with the patient self-administering doses three through five, seven through nine, and doses 11 and 12. Patients should have a final clinic visit upon completion of treatment.
- A combination of in-person DOT and video DOT may be utilized for patients meeting video DOT eligibility criteria.
- All patients on the DOT+SAT regimen will maintain a medication diary and record any side effects.
- The 3HP regimen is not approved for use by pregnant women.

[2] Groups at higher risk of progression to TB disease include, but are not limited to, children less than 5 years of age; persons with HIV infection; persons infected with Mycobacterium tuberculosis within the last 2 years; foreign-born persons; and persons with other immunocompromising conditions such as diabetes, end stage renal disease, or organ transplantation.

Clinicians with questions about 3HP or the most appropriate mode of administration for a specific patient can call the TB program at 717-787-6267 to request a consultation.

OTHER INFORMATION

The updated CDC recommendations also include the following information:

- Approximately 5% of patients discontinue 3HP because of adverse events. Side effects typically occur after the first three to four doses and usually resolve without treatment within 24 hours. However, if symptoms suggestive of a systemic drug reaction occur[3], patients should stop 3HP while the underlying cause is determined.
- Data published since 2011 confirm the effectiveness of 3HP in individuals with HIV infection who are not taking antiretroviral therapy and demonstrate the absence of clinically significant drug interactions between once-weekly rifapentine and either efavirenz or raltegravir in individuals with HIV infection treated with those antiretroviral medications. Simultaneous use of LTBI treatment and antiretroviral medications in patients with HIV infection should be guided by clinicians experienced in the management of both conditions.

[3] Such as fever, headache, dizziness, nausea, muscle and bone pain, rash and itching

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Chapter 7: Treatment of TB Disease

INTRODUCTION

PURPOSE

The overall goals for treatment of TB are to cure the patient and to minimize the transmission of *Mycobacterium tuberculosis* (*M. tuberculosis*) to others.

In the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment.

Successful treatment of TB has benefits both for the individual patient and the community in which the patient resides.

TB clinicians and nurses should understand and follow national and Pennsylvania (PA) guidelines when providing care to patients with TB disease:

- Follow basic treatment principles for TB disease.
- Select appropriate treatment regimens, dosages, and duration.
- Administer TB medications via directly observed therapy (DOT) as a best practice standard of care.
- Monitor patients for side effects and adverse reactions.
- Assess patients' response to treatment.
- Determine completion of therapy.
- Determine the need for post-treatment evaluation.
- Provide treatment in special situations, such as when a patient has drug-resistant TB or TB/HIV co-infection.
- Hospitalize and coordinate hospital discharges of patients with infectious TB.

POLICY

All patients with TB disease in Pennsylvania should receive and complete treatment in accordance with the national guidelines set forth in the Pennsylvania TB Manual, the Pennsylvania Department of Health (DOH) Public Health Policies, Procedures and Standing Orders and in accordance with Pennsylvania laws and regulations.

BASIC TREATMENT PRINCIPLES

Follow the basic treatment principles for TB disease, as outlined in Table 1.

TABLE 1: **BASIC TREATMENT PRINCIPLES FOR TUBERCULOSIS DISEASE**

Phase	Principles
At Start of Treatment	• **Patient-centered care and DOT.** An adherence plan should tailor treatment and supervision to each patient by considering his or her clinical and social circumstances (patient-centered care), as well as emphasizing DOT. • **Cultural competence.** It is imperative to become culturally competent and guide other healthcare providers toward culturally competent healthcare. A culturally competent system acknowledges cultural differences regarding healthcare and incorporates them into all levels of the healthcare delivery system, from policy to provider to patient. • **HIV testing.** HIV testing will be offered to all patients with TB disease. Document outcome in the patient chart. • **Medical supervision.** Patients with confirmed or suspected tuberculosis (TB) disease must be under the medical supervision of a provider who is licensed in the Commonwealth of Pennsylvania as a medical physician. • **Prompt start.** Start patients with confirmed or suspected TB disease promptly on appropriate treatment. It is not necessary to wait for laboratory confirmation.
Regimen During Treatment	• **Multiple drugs.** Treatment regimens must contain multiple drugs 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 resistance. **Never add a single drug to a failing regimen.** • **Single doses.** TB medications should be administered together as a single dose rather than in divided doses. A single dose leads to higher and potentially more effective peak serum concentrations and facilitates DOT. Although ingesting the medications with food will delay or moderately decrease the absorption of the medications, the effects are of little clinical significance. • **Pyridoxine to prevent neuropathy.** Pyridoxine (Vitamin B-6, 25 mg) is recommended for some individuals receiving isoniazid (INH) as part of their treatment regimen to prevent peripheral neuropathy. It should be used in persons at risk for neuropathy (women who are pregnant or breastfeeding or persons with nutritional deficiency, diabetes, HIV infection, renal failure, or alcoholism).
Persistent Positive Cultures	• **Evaluation when positive cultures persist.** Monitor for culture conversion and promptly evaluate patients with persistently positive cultures after 3 months of therapy to identify the cause. Treatment failure is defined as continued or recurrent positive cultures after 4 months of treatment.

Phase	Principles
At Completion of Treatment	• **Completion in terms of the number of doses.** The criteria for treatment completion are based upon the total number of doses observed via DOT and not solely on the duration of therapy.

TUBERCULOSIS INFECTIOUSNESS

- Patients with signs or symptoms of TB shall be given a surgical mask and instructed to keep it on during clinic visits and visits outside their residence, until they are considered not infectious. The patient will be informed when the physician determines the patient is no longer infectious. (See #4 below for the criteria used to determine infectiousness as listed in the CDC "Guidelines for Preventing the Transmission of Mycobacterium Tuberculosis in Healthcare Settings, 2005")
- Health care workers, including outreach workers, shall use particulate respirators to prevent the inhalation of *M. tuberculosis* when visiting the home of an infectious TB patient and while treating an infectious patient in the clinic.
- In general, patients who have suspected or confirmed active pulmonary, pleural or laryngeal tuberculosis should be considered infectious if they:
  - are coughing;
  - are undergoing cough-inducing or aerosol-generating procedures;
  - have sputum smears positive for acid-fast bacilli (AFB) and they are not receiving therapy, have just started therapy, or have a poor clinical or bacteriologic response to therapy; and/or
  - have cavitary disease on radiographic studies.
- Patients may be considered not infectious if they meet ALL THREE of the following criteria:
  - They have received adequate therapy for a minimum of 2 to 3 weeks.
  - They have a minimum of three (3) consecutive negative sputum smear results from sputum specimens collected at least 8 hours apart with one specimen obtained in the early morning.
  - They have a favorable clinical response to therapy (i.e., reduction in cough, weight gain, resolution of fever).

BASELINE LABORATORY STUDIES

- All TB patients shall have the following laboratory tests performed:
  - CBC
  - Platelet count (or a platelet estimate on smear)

- Blood chemistry screening to include an AST, ALT, alkaline phosphatase, total bilirubin, serum creatinine, BUN, and uric acid
- HIV test (unless patient opts out)

  Note: One of the NTIP objectives for 2025 is to increase the proportion of TB patients who have a positive or negative HIV result reported.

  The clinic nurse should have test results available for the TB clinician to review before medications are started.

- Visual acuity testing (reading small print, such as newspaper and Snellen eye chart) and color testing (Ishihara Color Chart) must be performed before ethambutol (EMB) is administered, and monthly while taking EMB, since EMB may affect eyesight.
  - These vision screening tests should be done in the clinic and documented in the medical record.
  - The tests should be repeated monthly while the patient receives EMB. Snellen readings should be recorded as 20/20, 20/30, 20/40 etc. with a notation of the number of missed letters viewed, e.g. 20/20 -1; 20/30 -2. Refer to Snellen Chart Instructions.
  - The Ishihara color plates are designed to read in a room that is adequately lit by daylight. When it is convenient only to use electric light, it should be adjusted as far as possible to resemble the effect of natural daylight. The plates are held 75 cm (approx. 2 feet) from the subject and tilted so that the plane of the paper is at right angles to the line of vision. Refer to Ishihara Instructions.
  - If the results are questionable, the patient should be referred to an ophthalmologist for further evaluation. The clinic nurse should notify the TB Program prior to any such referrals to obtain preauthorization.
  - Document results in the patient's chart.

DIRECTLY OBSERVED THERAPY (DOT)

DOT is the standard of care for TB disease. All TB patients should receive their anti-tuberculosis medications via DOT as specified in Chapter 8: Directly Observed Therapy of this manual.

Document all DOT doses in the patient's chart.

INTERMITTENT THERAPY

An intermittent therapy regimen may be used for patients with non-cavitary disease if clinically appropriate. Intermittent antibiotic therapy is any therapy regimen where the patient is not required to take medication every day for TB. Intermittent therapy must be given at least three times a week. A twice-weekly regimen is no longer recommended because of an increased incidence of relapse. Intermittent therapy is always given as DOT. Intermittent therapy is never

self-administered.

Intermittent administration of anti-TB medications is no longer recommended for HIV positive patients. The October 2016 ATS/CDC/IDSA guidelines for the treatment of drug-susceptible tuberculosis state that the “use of intermittent treatment regimens in HIV positive patients has been associated with high rates of relapse and the emergence of drug resistance”.

The state TB consultant does not recommend intermittent therapy for patients with cavitary disease.

CLINICAL MONITORING DURING TREATMENT

- All patients with TB disease shall be seen monthly by the TB clinic physician and monitored at least monthly by the nurse. Patients should be asked about any side effects or adverse reactions experienced while on treatment and the responses documented in the patient record. If the patient’s treatment regimen includes EMB monthly visual acuity and color testing must be done and documented in the patient record.

- INH-induced hepatitis: Patients taking INH should be monitored monthly for signs of hepatitis.

LABORATORY STUDIES DURING TREATMENT

- Patients taking INH, a rifamycin, or pyrazinamide for the treatment of TB disease should have monthly liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin).
- Other laboratory tests are not necessary during treatment unless the patient has signs or symptoms suggestive of toxicity to the medications. If symptoms suggestive of toxicity occur, the appropriate laboratory tests should be done. AST and bilirubin must be done for symptoms suggestive of hepatic toxicity, a platelet count for excessive bleeding or bruising and other tests as indicated.
- The medication which is suspected to cause the symptoms should be discontinued until the laboratory tests are interpreted by the clinician. Never leave the patient on one drug. Either stop all medications or continue the patient on two or more medications if the patient was initially started on two or more.
- For patients with an AFB positive smear at baseline, begin weekly collection of sputum specimens as follows:
    - For patients with cavities upon CXR and/or baseline sputum smears that are 3+ (moderate) or 4 (heavy), wait until the patient has completed one to two weeks of treatment before collecting the first follow-up sputum specimen.
    - For patients without cavities upon CXR and/or baseline sputum smears that are 1+ (rare) or 2+ (few), a sputum specimen can be collected once the patient completes one week of treatment.

- For both a) and b) above, if the first sputum is negative, obtain a second sputum specimen. If the second specimen is negative, obtain a third. If any one specimen is positive, wait one week and re-start the collection process.
- Once three consecutive smear-negative specimens are collected:
  - patients on isolation can be considered for release and/or
  - sputum specimens can then be collected monthly (in sets of three) until conversion to culture negative is documented.

TREATMENT REGIMENS AND DOSAGES

Use this information to:

- identify the appropriate regimen,
- determine the appropriate dosage for each drug, and
- determine the duration of treatment.

The information in this topic was provided using guidelines for treating drug-susceptible TB that have been developed by the ATS, CDC, and IDSA.

See the "Treatment in Special Situations" topic in this chapter for information on treatment when there is drug-resistant TB, HIV infection, liver disease, or renal disease; when the patient is taking tumor necrosis factor-alpha (TNF-α) antagonists; where there is culture-negative TB or extrapulmonary TB; when the patient is pregnant or breastfeeding; when the patient is of pediatric age; or when the patient has TB disease and nontuberculosis mycobacterium infection.

TABLE 2: **ABBREVIATIONS FOR FIRST-LINE DRUGS**

Ethambutol: EMB Isoniazid: INH Pyrazinamide: PZA	Rifabutin: RFB Rifampin: RIF Rifapentine: RPT

REGIMENS

Identify the appropriate regimen for the patient. There are four basic regimens recommended for treating adults with TB caused by organisms that are known or presumed to be susceptible to INH, RIF, PZA, and EMB. Children, depending on the circumstances, may not receive EMB in the initial phase of a six-month regimen, but the regimens are otherwise identical.

Each regimen has an initial phase of 8 weeks, followed by a choice of several options for a continuation phase of either 18 or 31-32 weeks. In **Table 3: Drug Regimens for Culture-Positive Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms**, the initial phase is denoted by a number (1, 2, 3, or 4), and the options for the continuation phase are denoted by the respective number and a letter designation (a, b, or c).

DOT is the standard of care for all anti-tuberculosis treatment regimens and should be used in accordance with the PA DOH Best Practice document. The recommended regimens, and the number of doses specified by each regimen, are described in Table 3.

Note: Two of the NTIP objectives for 2025 address TB treatment initiation.

1. **Treatment initiation:** For TB patients with positive AFB sputum smear results, increase the proportion who initiated treatment within 7 days of specimen collection.
2. **Recommended Initial Therapy:** For patients whose diagnosis is likely to be TB disease, increase the proportion who are started on the recommended initial 4-drug regimen.

TABLE 3: **DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS**

Initial Phase			Continuation Phase			Range of total doses (minimal duration)	Rating* (evidence)†	
Regimen	Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡§ (minimal duration)		HIV–	HIV+
1	INH RIF PZA EMB	Seven days/week for 56 doses (8 weeks) or 5 days/week for 40 doses (8 weeks)¶	1a	INH RIF	Seven days/week for 126 doses (18 weeks) or 5 days/week for 90 doses (18 weeks)¶	182–130 (26 weeks)	A (I)	A (II)
			1b	INH RIF	Three days/week for 54 doses (18 weeks)	110-94 (26 weeks)	A (I)	A (II)#
2	INH RIF PZA EMB	Seven days/week for 14 doses (2 weeks), then 3 days/week for 18 doses (6 weeks) or 5 days/week for 10 doses (2 weeks),¶ then 3 times/week for 18 doses (6 weeks).	2aΔ	INH RIF	Three days/week for 54 doses (18 weeks)	96–86 (26 weeks)	A (II)	B (II)#
3	INH RIF EMB	Seven days/week for 56 doses (8 weeks) or 5 days/week for 40 doses (8 weeks)¶	4a	INH RIF	Seven days/week for 217 doses (31 weeks) or 5 days/week for 155 doses (31 weeks)¶	273–195 (39 weeks)	C (I)	C (II)
			4b	INH RIF	Three days/week for 93 doses (31 weeks)	149–133 (39 week)	C (I)	C (II)

Definitions of abbreviations: DOT = directly observed therapy; EMB = ethambutol; INH = isoniazid; HIV = human immunodeficiency virus; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; D = should generally not be offered; E = should never be given.

† Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.

‡ When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice.

§ Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.

¶ Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is rated AIII.

Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/microliter.

$^{\Delta}$ This option should only be considered for a patient who is young, otherwise healthy and has a mild, early case of TB.

Source: ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195

DOSAGES

TABLE 4: **DOSES*OF FIRST-LINE ANTI-TUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN**

			Doses		
Drug	**Preparation**	**Adults/children**	**Daily**	**1x/wk.**	**3x/wk.**
INH	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml); aqueous solution (100 mg/ml) for intramuscular injection¶	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
		Children (max.)	10–15 mg/kg (300 mg)	—	—
RIF	Capsule (150 mg, 300 mg); powder may be suspended for oral administration; aqueous solution for intravenous injection	Adults‡ (max.)	10 mg/kg (600 mg)	—	10 mg/kg (600 mg)
		Children (max.)	15–20 mg/kg (600 mg) 20-30 mg/kg in infants and for TB meningitis (600 mg)	—	—
RFB	Capsule (150 mg)	Adults‡ (max.)	5 mg/kg (300 mg)	—	5 mg/kg (300 mg)
		Children	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown
PZA	Tablet (500 mg, scored)	Adults	See Table 5	—	See Table 5
		Children (max.)	15–30 mg/kg (2.0 g)	—	—
EMB	Tablet (100 mg, 400 mg)	Adults	See Table 6	—	See Table 6
		Children§ (max.)	15–20 mg/kg daily (1.0 g)	—	—

Source: ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195

TABLE 5: **SUGGESTED PYRAZINAMIDE DOSES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40 TO 90 KILOGRAMS**

Interval	Weight (kg)* 40–55 kg	56–75 kg	76–90 kg
Daily, mg (mg/kg)	1,000 (18.2–25.0)	1,500 (20.0–26.8)	2,000 † (22.2–26.3)
Three days/week, mg (mg/kg)	1,500 (27.3–37.5)	2,500 (33.3–44.6)	3,000 † (33.3–39.5)
* Based on estimated lean body weight. † Maximum dose regardless of weight.			

Source: ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195

TABLE 6: **SUGGESTED ETHAMBUTOL DOSES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40 TO 90 KILOGRAMS**

Interval	Weight (kg)* 40–55 kg	56–75 kg	76–90 kg
Daily, mg (mg/kg)	800 (14.5–20.0)	1,200 (16.0–21.4)	1,600 † (17.8–21.1)
Three days/week, mg (mg/kg)	1,200 (21.8–30.0)	2,000 (26.7–35.7)	2,400 † (26.7–31.6)
* Based on estimated lean body weight. † Maximum dose regardless of weight.			

Source: ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63,Issue 7, 1 October 2016, Pages e147–e195

DURATION OF TREATMENT

Use the treatment algorithm in **Figure 1: Treatment Algorithm for Tuberculosis** to determine the duration of treatment. The recommended regimens for treating patients with TB caused by drug-susceptible organisms have a duration of six to nine months. Each regimen has an initial phase of 8 weeks, followed by a continuation phase of either 18 or 31-32 weeks.

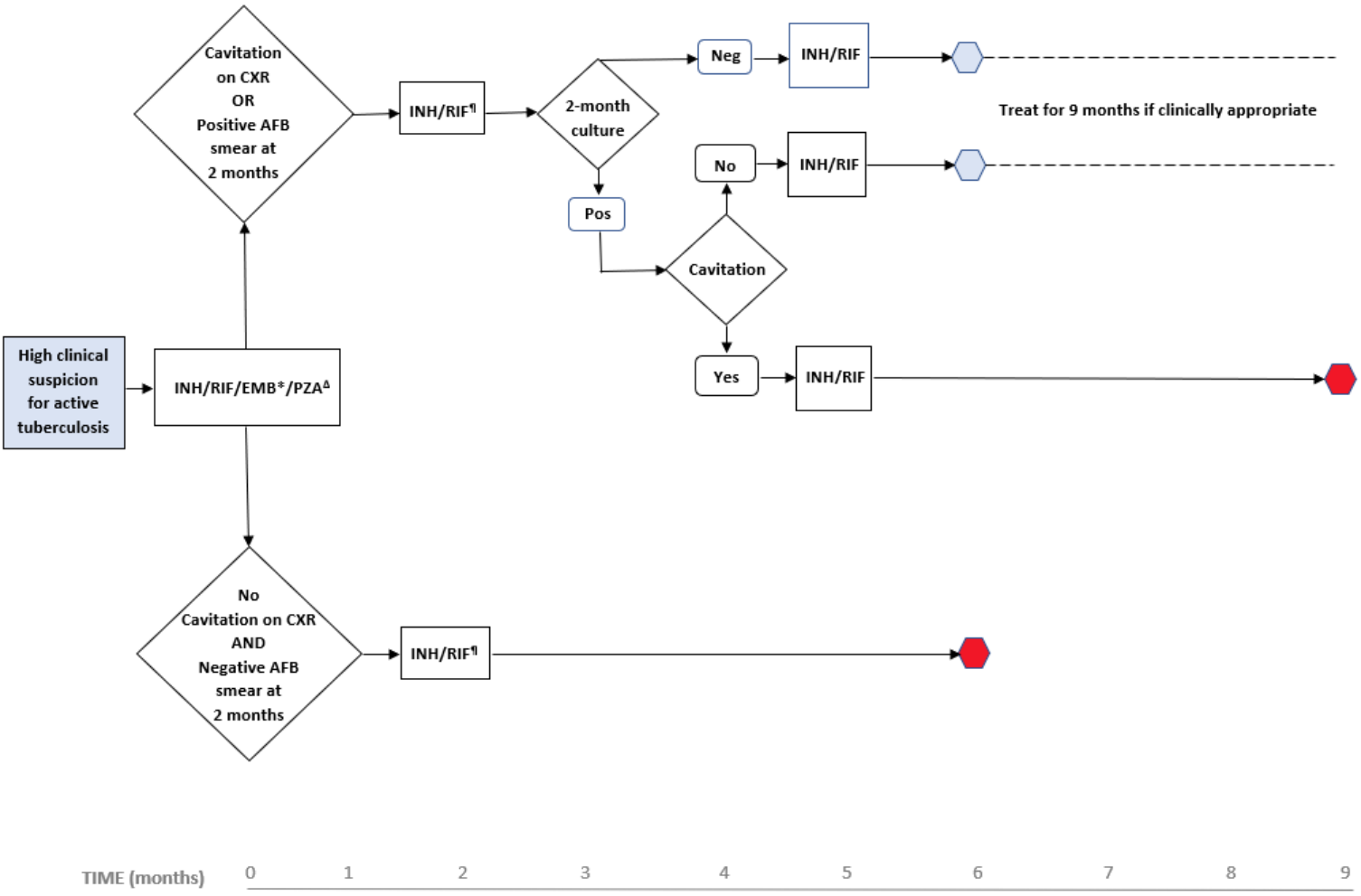
Figure 1 gives directions for treating patients with pulmonary and extrapulmonary TB. The standard duration of treatment for pulmonary TB is 26 weeks unless **both** the patient's chest x-ray (CXR) indicates cavitation is present **and** the patient is still culture positive after two months of treatment or has a co-morbidity such as diabetes in which case 40 weeks is recommended.

1. For tuberculous meningitis, the optimal length of therapy has not been established, although most experts recommend 9 to 12 months with 12 months preferred. For children with TB meningitis, use a 12-month regimen.
2. The recommended duration of treatment for TB of the bone or joint is 9 months.

3. In HIV-negative, culture-negative patients, treatment for 18 weeks may be adequate if there is clinical or radiographic improvement and no other etiology identified. However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of 26 weeks.
4. In some cases, either because of intolerance or drug-resistance, the above-described regimens cannot be used. In these instances, an alternative regimen may be required.

Source: ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195

FIGURE 1: **TREATMENT ALGORITHM FOR TUBERCULOSIS**



Definition of abbreviations: AFB = acid-fast bacilli; CXR = chest radiograph; EMB = ethambutol; HIV = human immunodeficiency virus; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* EMB may be discontinued when results of drug susceptibility testing indicate no drug resistance.

△ PZA may be discontinued after it has been taken for 2 months (56 doses).

¶ At 2 months, review drug susceptibility and culture results, if applicable, and review these results regularly throughout treatment if the patient is drug resistant.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):6.

SIDE EFFECTS AND ADVERSE REACTIONS

As is true with all medications, anti-TB medications are associated with a predictable incidence of side effects and adverse reactions, some mild, some serious.

While on treatment, the patient should be seen monthly by the TB clinic physician and monitored at least monthly by the nurse for treatment compliance and any signs and symptoms of side effects or adverse reactions.

If the patient is experiencing side effects or adverse events, the TB clinician should be consulted and the patient may need to be monitored more frequently. Chemistries and CBC, AST, ALT, or other tests based on specific drugs should be done. See **Table 8: Monitoring and Interventions for Side Effects and Adverse Reactions** in this section.

Side effects are generally mild, may resolve in time without any intervention and can often be anticipated by the prescribing physician or the TB nurse because they are known to commonly occur. Adverse reactions, however, are usually more severe, in rare instances can be fatal, and require intervention. For example, mild nausea in a patient taking INH may be considered a side effect while severe hepatitis is an adverse reaction. Descriptions of known side effects and adverse reactions for a specific prescription drug are based on substantial clinical evidence and can be found in the product package insert (PI) and the patient package insert (PPI).

Although it is important to be attuned to the potential for side effects and adverse reactions, it is at least equally important that treatment not be stopped without adequate justification. Mild side effects may resolve without any intervention or may be managed with treatment directed at controlling the symptoms. Adverse reactions can be severe and it is important to recognize adverse reactions that indicate when a drug should not be used. With more severe adverse reactions, the offending drug or drugs must be discontinued. Proper management of more serious adverse reactions often requires expert medical consultation.

Serious adverse reactions are either life-threatening, require inpatient hospitalization or extends the length of current hospitalization, or results in death. Serious adverse reactions will be reported to the U.S Food & Drug Administration (FDA) via MedWatch at https://www.fda.gov/media/76299/download or by calling the FDA at 1-800-FDA-1088.

BASIC MONITORING STEPS

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

- All health care personnel providing treatment for TB disease should follow the current guidelines, “Treatment of Drug-Susceptible Tuberculosis”, *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195 at https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf.

- It is also important to check for guideline updates posted on the CDC's Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/ and the list of guidelines by date at: https://www.cdc.gov/tb/publications/guidelines/list_date.htm.
- While on treatment, all patients should be evaluated in person at baseline (before starting treatment) and then at least monthly for side effects and adverse reactions.
- The common side effects and adverse reactions to drugs used for the treatment of TB diseases are listed in **Table 7: Reporting Reactions to Anti-tuberculosis Medications**. Educate patients to stop the medicine and promptly report any of the signs or symptoms listed in Table 7 or any unexplained illness to the prescribing clinic immediately.
    - If a patient reports a potentially serious adverse reaction, hold the medications, call the TB clinician immediately and alert the community health nurse supervisor.
    - If a patient reports a potentially less severe side effect, call the TB clinician immediately and monitor the patient.
    - If hepatotoxicity is suspected, complete the MedWatch form available at: https://www.fda.gov/media/76299/download.
- If you suspect that an anti-tuberculosis drug may be causing a particular side effect or adverse reaction refer to **Table 8: Monitoring and Interventions for Side Effects and Adverse Reactions**.
- If you suspect that an anti-tuberculosis drug may be interacting with other medications that the patient is taking, refer to pages 45–47 in the "Treatment of Tuberculosis" (*MMWR* 2003; 52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.
- Document the following patient information:
    - Review of symptoms, side effects, and adverse reactions (include any labs that were ordered/collected)
    - Education provided
    - Refill provided (number of pills on hand, number dispensed)
    - Description of any problems encountered and action taken for that visit
    - Next appointment

REPORTING REACTIONS

Table 7 is intended for use by the community health nurse (CHN) and/or outreach worker providing care to the patient. The patient should be instructed to contact the CHN if he or she experiences any of the side effects or adverse reactions listed in Table 7.

If a patient reports a potentially serious adverse reaction, the CHN should notify the patient's TB clinician immediately. In consultation with the TB clinician, the CHN should instruct the patient to stop TB medications until evaluated by the clinician.

If a patient reports a potentially less severe side effect, the CHN should notify the TB clinician within 24 hours and monitor the patient.

TABLE 7: **REPORTING REACTIONS TO ANTI-TUBERCULOSIS MEDICATIONS**

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient's TB clinician. These signs and symptoms suggest potentially serious adverse reactions, including hepatotoxicity: • Jaundice • Dark urine • Vomiting • Abdominal pain • Fever • Visual changes • Marked clinical rash In consultation with the TB clinician, instruct the patient to stop TB medications until evaluated by the TB clinician.	Report the following signs and symptoms to the patient's TB clinician within 24 hours: • Anorexia • Nausea • Malaise • Peripheral neuropathy: tingling or burning sensation in hands or feet • Rashes
* These lists are not all-inclusive. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of TB" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and the 2016 official ATS/CDC/IDSA clinical practice guidelines: treatment of drug-susceptible tuberculosis at https://academic.oup.com/cid/article/63/7/e147/2196792.	

Source: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). TB case management—core components. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. Last updated in 2011. Available at: https://ctca.org/wp-content/uploads/2018/11/ctca_case_management_5_.pdf

REPORTING SEVERE ADVERSE EVENTS

The CDC Division of TB Elimination (DTBE) urges health departments, hospices, hospitals, jails, prisons, and private medical offices to report all severe adverse events (e.g., liver injury, pancreatitis, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for TB.

- All adverse reactions should be reported to the community health nurse supervisor and the TB clinician.
- All severe adverse reactions will be reported to the U.S Food & Drug Administration (FDA) via MedWatch at https://www.fda.gov/media/76299/download or by calling the FDA at 1-800-FDA-1088.

TABLE 8: **MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS**

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Isoniazid (INH)	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects • Nausea • Vomiting • Dark urine	Clinical monitoring monthly Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy). **Per Standing Orders, Obtain Physician's order** to repeat measurements if: • Baseline results are abnormal • Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin) and adjust the dose if necessary.
Rifampin (RIF)	• Rash • Gastrointestinal upset • Hepatitis • Fever • Bleeding problems • Thrombocytopenia • Renal failure • Flu-like symptoms	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy). **Per Standing Orders, Obtain Physician's order** to repeat measurements if: • Baseline results are abnormal • Patient has symptoms of adverse reactions	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, warfarin, and many other drugs**.** Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline).

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (cont.)	• Orange-colored body fluids (secretions, urine, tears) • Sensitivity to sun		For more information, refer to the "Official ATS, CDC and IDSA Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis", Clinical Infectious Diseases, Volume 63, Issue 7, 1 October 2016, Pages e147–e195. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf Colors body fluids orange. May permanently discolor soft contact lenses.
Rifabutin (RFB)	• Rash • Hepatitis • Fever • Thrombocytopenia • Orange-colored body fluids (secretions, urine, tears) With increased levels of RFB: • Severe arthralgias • Uveitis • Leukopenia	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy). **Per Standing Orders, Obtain Physician's order** to repeat measurements if: • Baseline results are abnormal • Patient has symptoms of adverse reactions Use adjusted daily dose of RFB and monitor for decreased antiretroviral activity and for RFB toxicity if RFB taken concurrently with protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs)	Although drug interactions are less problematic with RFB, they still occur and close monitoring is required. Contraindicated for HIV-infected patients taking hard-gel saquinavir or delavirdine; caution is also advised if RFB is administered with soft-gel saquinavir. Similar to rifampin but less potent of an inducer, rifabutin reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). When used with efavirenz, the daily dose of RFB should be increased from 300 mg to 450 mg or 600 mg. May permanently discolor soft contact lenses. PI- Protease Inhibitors NNRTI – Non-Nucleoside Reverse Transcriptase I*nhibitors*

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifapentine (RPT)	Similar to those associated with rifampin	Similar to that for rifampin	Drug interactions involving RPT are being investigated and are likely to be similar to those of rifampin. RPT is an inducer of multiple hepatic enzymes and therefore may increase metabolism of co-administered drugs that are metabolized by these enzymes. For more information, refer to the "Official ATS, CDC and IDSA Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis", Clinical Infectious Diseases, Volume 63, Issue 7, 1 October 2016, Pages e147–e195. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/Clin-Infect-Dis.-2016-Nahid-cid_ciw376.pdf
Pyrazinamide (PZA)	• Gastrointestinal upset • Hepatitis • Rash • Photosensitive dermatitis • Hyperuricemia • Joint aches • Gout (rare) • Poor appetite	Clinical monitoring at weeks 2, 4, and 8 If the drug is used in patients with underlying liver disease, laboratory and clinical monitoring should be increased Baseline measurements of uric acid **Per Standing Order**. Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, or pregnancy). **Per Standing Orders, Obtain Physician's order** to repeat measurements if: • Baseline results are abnormal • Patient has symptoms of adverse reactions	Treat hyperuricemia only if patient has symptoms. Might make glucose control more difficult in persons with diabetes. Serum uric acid measurements are not recommended as a routine but may serve as a surrogate marker for compliance.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Ethambutol (EMB)	• Optic neuritis • Rash • Blurred vision • Changed color vision	Baseline tests of visual acuity (Snellen chart) At each monthly visit, patients should be questioned regarding possible visual disturbances, including blurred vision or scotomata Monthly testing of visual acuity and color discrimination is recommended for • Patients taking doses >15–25 mg/kg • Patients receiving EMB for >2 months • Patients with renal insufficiency	Optic neuritis may be unilateral; check each eye separately. Patients should be instructed to contact their physician or public health clinic immediately if they experience a change in vision. EMB should be discontinued immediately and permanently if there are any signs of visual toxicity.
Rifamate® (INH and RIF) Rifater® (INH, RIF, PZA)	See comments under individual drugs above		**Note:** The PA TB program neither stocks nor uses Rifamate and Rifater. Rifamate is a combination of INH and RIF. Rifater is a combination of INH, *RIF,* and PZA. Use of either of these medications has the advantage of having the patient take fewer units of medication. Patients cannot arbitrarily stop taking one medication while remaining on another when given a combination pill. Studies have shown side effects on these combination medications differ very little from the side effects noted from using individual doses of each drug.

Definitions of abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; EMB = ethambutol; HIV = human immunodeficiency virus; INH = isoniazid; NNRTIs = nonnucleoside reverse transcriptase inhibitors; PZA = pyrazinamide; PIs = protease inhibitors; RFB = rifabutin; RIF = rifampin; RPT = rifapentine.

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49 (No. RR-6):26–29, 38–39;
ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):19–25;
CDC. Update: Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States. *MMWR* 2003;52(No. 31):735–736; CDC.
Table 5: first-line anti-TB medications in Chapter 7: Treatment of TB Disease. CDC. *Core Curriculum on Tuberculosis (2013)* (Division of Tuberculosis Elimination website). Available at: http://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.pdf

NON-ADHERENCE

ENFORCEMENT OF DIAGNOSTIC TREATMENT REGIMENS FOR NON-ADHERENCE

- Patients who are infectious and do not follow isolation, diagnostic, and treatment regimens prescribed by the DOH to render them non-communicable are to be provided with an initial warning that a future failure to cooperate may prompt action by the department to enforce adherence.
    - It is preferred that the initial warning be given verbally by TB clinic staff and then followed-up in writing.
    - When feasible, another employee or clinician should be present for purposes of corroboration if court action is subsequently taken.
    - The warning and the way it was communicated are to be recorded in the patient's medical record and PA-NEDSS. Language and cultural barriers should be considered when issuing the warning and appropriate translation must be provided.
- If the patient remains non-adherent, a second more stringent letter shall be hand delivered to the patient with prior approval from legal counsel. This letter should be prepared and presented to the patient if the initial verbal/written warning is ignored. The patient should sign the letter acknowledging receipt and understanding of the letter. The patient's signature should be observed by two witnesses who also sign the letter in the space provided.
- All actions taken with respect to a non-adherent patient (such as attempts to locate, communication with family, etc.) and all departures by the patient from prescribed treatment or other directives are to be fully and legibly recorded in the patient's medical record and PA-NEDSS.

PERSISTENT NON-ADHERENCE

- The TB Program must be notified of any patient who misses more than three consecutive DOT visits.
- If significant non-adherence persists, such as repeated failures to take medications, adhere to isolation instructions, keep appointments, or provide specimens for laboratory tests, consider a letter to the patient consistent with the policy and procedures in effect in your jurisdiction.
- It is recommended that the letter be written by the TB clinic staff to suit the situation. Include a brief summary of the dates, times and circumstances pertaining to the missed doses. Be sure the letter is clear, concise and states the corrective action expected of the patient in terms he or she can readily understand.

- All actions taken with respect to a non-adherent patient (such as attempts to locate, communications with family, etc.) and all departures by the patient from prescribed treatment or other directives are to be fully and legibly recorded in the patient's medical record and PA-NEDSS.

  Note: ***Record keeping standards apply at all times, but adherence with these standards is critical in case legal action is deemed necessary.***

- If there is a significant violation of the directions given in the letter, a court order may be needed to more forcefully persuade the patient to comply with an appropriate medical care regimen. When the clinic staff believes a court order is necessary, the following preparations are recommended:
  - Determine the care regimen to be imposed (revising the violated regimen if appropriate)
  - Prepare a list of directions for the patient to follow that are to be included in the court order
  - Evaluate whether a request for Reimold funds to provide for nutrition, shelter or transportation is needed to help the patient remain on treatment
  - Consult with your legal advisor
- If a court order is ultimately secured and the patient violates the order, the clinic staff shall immediately inform the nurse supervisor, who will consult with the TB clinician and the legal advisor to determine whether confinement is indicated.

HOSPITALIZATION OR INCARCERATION FOR NON-ADHERENCE

- Hospitalization or incarceration of an infectious non-adherent patient for acute care is possible in a hospital or detention facility with respiratory isolation capability.
- If confinement of the patient is deemed necessary to ensure treatment adherence, follow the TB policy and procedures in effect for your local jurisdiction.

MEDICAL INTERPRETATION SERVICES

If the patient is not comfortable speaking in English, arrange for a professional medical interpreter who speaks the patient's primary language to be available via phone. Avoid asking a family member or friend to interpret unless no other option is available.

To arrange for a professional medical interpreter, follow the instructions provided by the DOH contractor for medical interpretation services.

Here are some do's and don'ts when interviewing a patient with the support of an interpreter:

- **Do** plan ahead. Before meeting with a patient, try to determine whether they are comfortable speaking in English. If not, arrange for a professional medical interpreter who speaks the patient's primary language to be available via phone.

- **Do** speak directly to the patient, not the interpreter.
- **Do** ask one question at a time.
- **Do** avoid using medical jargon.
- **Do** pay attention to nonverbal cues by the patient.
- **Do** encourage the patient to ask questions.
- **Do** respect the patient's privacy and modesty.
- **Don't** use family members – especially children – or a friend to interpret unless no other option is available.
- **Don't** ignore cultural differences e.g., some cultures view looking at someone directly as a sign of aggression.
- **Don't** rely on brochures to communicate – they can reinforce your conversation but should not replace it.
- **Don't** shout – not being comfortable speaking English doesn't mean the person is hard of hearing!

Also, be aware of the following behavioral cues when talking with a patient:

- If a patient shows signs of impatience or annoyance during your conversation, that may indicate intercultural misunderstanding.
- If a patient asks *you* personal questions, that may indicate a cultural need to establish trust and reassurance.
- Hesitation by the patient when talking with you may mean you've hit a cultural wall.
- Try to treat the patient the way he or she wants to be treated – not the way you like to be treated.
  If patients repeat your instructions exactly, it's possible they are repeating your words without understanding them. Rephrase your instructions and ask the patient to restate in his or her own words.

RESPONSE TO TREATMENT

The key measure of a patient's response to treatment is sputum culture conversion to negative.

For patients whose sputum smears are positive before treatment, begin follow-up weekly sputum collection as described in the "Laboratory Studies During Treatment" section of this chapter. Once three consecutive weekly specimens are smear negative, additional specimens should be collected monthly until conversion to culture negative is documented.

Patients with multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) should have cultures performed monthly for the entire course of treatment.

> **Note:** One of the NTIP objectives for 2025 is to increase the proportion of TB patients with positive sputum smear results who have document conversion to negative results within 60 days of treatment initiation.

In some cases, a patient may not be able to produce a sputum specimen after 8 weeks of treatment. If the patient has improved clinically and has shown chest radiograph improvement, treatment may be continued as if the patient had a negative sputum specimen at 8 weeks.

Important treatment decisions concerning the continuation phase regimen are based on the micro bacteriological status at the end of the initial phase of treatment, which is at the minimum of 8 weeks of treatment. The initial treatment period may extend beyond 8 weeks in some circumstances:

- Patients with cavitary disease with positive cultures at **8 weeks** should be evaluated to increase the continuation phase of therapy from 18 to 31-32 weeks for a total of nine months of treatment.
- Patients whose cultures have not become negative after **12 weeks** of therapy should be re-evaluated for potential drug resistant disease, as well as for potential inadequate drug levels and potential failure to adhere to the regimen.
- Patients who have positive cultures after **18 weeks** of treatment should be considered as having failed treatment and be managed accordingly.

For treatment decisions at the 12 to 18 weeks interval, a consultation with the state TB medical consultant or the Global TB Institute should be obtained. The consultants have expertise in the management of drug resistance and treatment failures.

Radiographic evaluations during treatment are of less importance than sputum evaluation.

Patients whose cultures remain positive or whose symptoms do not resolve after 12 weeks of therapy should be reevaluated for drug-resistant disease, potential inadequate drug levels and for compliance issues.

CULTURE POSITIVE AFTER THREE MONTHS

- The patient who is culture positive after 12 weeks of treatment must be reassessed. Because the results of the culture taken at the third month will not be available for a period of time, a positive smear is enough information to presume that the culture will be positive. If the initial culture showed the organisms sensitive to all first line drugs, the best explanation of the smear findings is that the patient has not taken sufficient medication. Infrequently, a patient with a large bacillary load will not improve the sputum smear after 12 weeks of therapy.
- A Molecular Detection of Drug Resistance (MDDR) test should be considered for a patient who is culture positive after three months. MDDR testing can quickly identify drug resistance so that an effective anti-TB regimen can be prescribed. Only specimens in which *M. tuberculosis* complex has been detected should be submitted to CDC for MDDR testing, and such specimens must be submitted by the state Bureau of Laboratories (BOL).
- If drug susceptibility results show resistance to any of the first-line drugs or if the patient remains symptomatic or smear- or culture-positive after 12 weeks consult the state TB medical consultant or the Global TB Institute.
- When the culture and sensitivities done in the third month are returned, a new medication program may be needed. The clinician must consult with the state TB medical consultant or the Global TB Institute if drug resistant organisms are isolated. Patients whose cultures are positive and whose smears are positive are probably infectious and must remain isolated until the smears show no acid-fast bacilli.

In patients with negative sputum cultures before treatment, the major indicators of response to therapy are the chest radiograph and clinical evaluation. The intervals at which chest radiography should be repeated depend on the clinical circumstances and the differential diagnosis that is being considered, but usually should be no more than every three months. If the radiograph does not improve after the patient has received three months of treatment, the abnormality may be the result of either previous (not current) TB or another process.

TREATMENT FAILURE

- Any patient whose sputum has not converted to negative (either smear or culture) after 26 weeks of treatment is a treatment failure. A current sputum specimen shall be submitted for smear, culture, and susceptibility testing. While the results are pending, the present medication regimen is continued. Consultation with the state TB medical consultant or the Global TB Institute shall be obtained.
- Two drugs not previously ordered may be given after consultation. The regimen should be adjusted after the cultures and sensitivities taken at six months are reviewed. Treatment must be by DOT. A treatment failure must be reported to the TB Program.

COMPLETION OF TREATMENT

- Completion of treatment occurs when the patient has taken the prescribed regimen of antibiotics, converted cultures and/or smears to negative, has cleared the symptoms of disease, and, for pulmonary disease, has a CXR which is stable.
- A patient who completes the 26 weeks of treatment is recommended to obtain a CXR at the conclusion of treatment, and – if the CXR has not returned to normal – again at 6 months post treatment.
- A patient who completes treatment should be told during their last clinic visit that if their TB symptoms reoccur, they should return to the clinic (or to the private physician). Symptoms suggesting TB recurrence are cough and sputum production for more than two weeks, weight loss, and fever.

Completion of treatment is determined based on a) the total number of doses administered b) within a recommended maximum timeframe. If there are no interruptions in drug administration, 26 weeks is usually the minimum duration of treatment for TB disease.

Eighteen (18) weeks of treatment may be adequate for HIV-negative, culture-negative patients, if there is clinical or radiographic improvement and no other etiology is identified.

Treating a patient for a defined duration, without accounting for the number of doses taken, can result in undertreatment.

Occasionally, either because of drug toxicity or nonadherence to the treatment regimen, the specified number of doses cannot be administered within the targeted period. In these cases, the goal is to deliver the specified number of doses within a recommended maximum timeframe. For example, for a six-month daily regimen, the total doses should be administered within nine months of beginning treatment. If treatment is not completed within this period, the patient should be assessed to determine the appropriate action to take, such as continuing treatment for a longer duration or restarting treatment from the beginning.

Interruptions in treatment may have a significant effect on the duration of therapy. Reinstitution of treatment must consider the extensiveness of the disease (e.g., cavitary versus noncavitary disease on chest radiograph, smears and cultures, immunologic status), the point in time when the interruption occurred, and the duration of the interruption. The earlier in treatment an interruption occurs and the longer the duration of the interruption, the more serious the effect and the greater the need to restart therapy from the beginning.

Note: A 2025 NTIP objective for patients with newly diagnosed TB disease – for whom 12 months or less of treatment is indicated – is to increase the proportion of such patients who do complete treatment within 12 months.

RELAPSE AFTER COMPLETION OF TREATMENT

- A patient whose TB is suspected of recurring twelve months or more after completing treatment should be carefully evaluated. If the patient took the initial course of treatment,

the organisms may still be sensitive to first line drugs and the initial treatment schedules shall be utilized until cultures and sensitivities are obtained.

- If relapse occurs and the nurse or clinician believes that the patient may not have taken or completed the initial course of treatment, directly observed therapy of at least two antibiotics not previously ordered shall be the method of treatment. Treatment can be changed when the results of culture and susceptibility studies are reviewed.
- Relapse is definite when cultures are positive. Worsening of a CXR with clinical symptoms suggests relapse. Biopsy findings of acid-fast bacteria and/or isolation of *M. tuberculosis* from an extra-pulmonary site also indicates relapse.
- Treatment is continued for at least eighteen months or at least twelve months after the last positive culture, if cultures are still positive after the initial six months of treatment.
- All patients being treated for relapse are recommended to be seen monthly by the physician.
- Patients treated for relapse must be questioned regarding any toxic manifestations of the drugs they are receiving. Any necessary clinical laboratory examinations should be performed.

WARNING: NEVER ADD A SINGLE NEW ANTI-TUBERCULOSIS DRUG TO A FAILING REGIMEN AS THIS WILL LEAD TO RESISTANCE TO THE NEW DRUG.

POST-TREATMENT EVALUATION

Routine follow-up after completion of therapy is not necessary for patients with a satisfactory and prompt bacteriologic response to a six- or nine-month regimen that included both isoniazid and rifampin.

The table below describes the clinician's responsibilities at completion of therapy for patients with a) drug-susceptible TB and b) drug-resistant TB.

TABLE 9: **CLINICIAN'S RESPONSIBILITIES AT COMPLETION OF THERAPY**

Drug Susceptibility	Clinician's Actions
Drug-susceptible organisms	Instruct the patient to promptly report the development of any symptoms, particularly prolonged cough, fever, or weight loss.
Organisms resistant to isoniazid, rifampin, or both	Individualize follow-up evaluation. May include x-ray and three sputa at conclusion of treatment, and at 6 months, 12 months and up to 24 months post treatment.

TREATMENT IN SPECIAL SITUATIONS

Treatment of TB in the following situations requires a high level of expertise or close consultation with an expert to provide appropriate management:

- Drug-resistant TB
- HIV infection
- Liver disease
- Renal insufficiency and end-stage renal disease (ESRD)
- TB associated with tumor necrosis factor-alpha (TNF-α) antagonists
- Culture-negative pulmonary TB
- Extrapulmonary TB
- Pregnancy and breastfeeding
- TB in children
- Mycobacterium bovis (*M. bovis*)
- TB and nontuberculosis mycobacterium (NTM) infection

DRUG-RESISTANT TUBERCULOSIS

Treatment of TB caused by drug-resistant organisms should be provided by, or in close consultation with, an expert in the management of these difficult situations. Second-line regimens often represent the patient's last hope for being cured and inappropriate management can have life-threatening consequences.

Drug-resistant TB disease can develop in two different ways, called primary and secondary resistance. Primary resistance occurs in persons who are initially exposed to and infected with resistant organisms. Secondary resistance, or acquired resistance, develops during TB therapy, either because the patient did not take the prescribed regimen appropriately or because of other conditions such as drug malabsorption or drug-drug interactions that lead to low serum levels. Please refer to table 2.7 on page 37 of Core Curriculum: "CDC *Core Curriculum on Tuberculosis (Sixth Edition,2013)* (Division of Tuberculosis Elimination" Web site; updated 2013). Available at: http://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.pdf.

Drug resistance is proven only by drug-susceptibility testing performed in a competent laboratory. A patient with a strain of *M. tuberculosis* resistant to both INH and RIF has multidrug resistant TB (MDR-TB). Refer to the 2019 clinical practice guidelines for the treatment of drug-

resistant tuberculosis[1] and seek a medical consultation with the Global TB Institute (GTBI) at Rutgers, a CDC-funded TB center of excellence.

The 2019 guidelines briefly mention the FDA approval of pretomanid in combination with bedaquiline and linezolid (often called the BPaL regimen) for the treatment of a specific limited population of adults with pulmonary extensively drug resistant (XDR-TB) or treatment-intolerant or nonresponsive MDR-TB.

The BPaL regimen should only be prescribed in consultation with the GTBI. Due to the potential for adverse events with BPaL, it is a best practice to review a BPaL treatment consent with the patient and have the patient sign the consent before starting treatment. (Sample text for a BPaL treatment consent is available from the PA TB Program. The treatment consent should be approved by local legal counsel before use.) A patient who is prescribed BPaL should also be asked to review and sign the BPaL Data Consent (see Appendix C). Failure to sign the Data Consent does not prevent the patient from receiving treatment with BPaL.

Acquired drug resistance usually develops when an inadequate drug regimen is prescribed (e.g., inappropriate drugs or insufficient dosage) or when there is a combined failure of both the patient and the provider to ensure that an adequate regimen is taken. A patient with acquired drug resistance may transmit his or her strain to others, who may then develop primary drug-resistant TB.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Management of TB in HIV positive patients is complex and requires expertise in the management of both TB and HIV disease. Because HIV-infected patients often take numerous medications, some of which interact with anti-tuberculosis medications, clinicians are strongly encouraged to consult with the state TB medical consultant or the Global TB Institute about appropriate treatment options.

It is especially important to use DOT and other adherence-promoting strategies with TB patients who are HIV positive.

TB patients who are also taking antiretroviral therapy for HIV may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations (paradoxical reactions) of TB while receiving anti-tuberculosis treatment. This is known as immune reconstitution inflammatory syndrome, or IRIS.

Note: drug regimens 1b and 2a in Table 3 in this chapter are not recommended for the treatment of TB in HIV+ patients.

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[1] Nahid P, Mase SR, Migliori GB, Sotgiu G, Bothamley GH, *et al*. Treatment of drug-resistant tuberculosis, an official ATS/CDC/ERS/IDSA clinical practice guideline. *Am J Respir Crit Care Med*, Vol 200, Issue 10, pp e93–e142, Nov 15, 2019 available at https://www.atsjournals.org/doi/full/10.1164/rccm.201909-1874ST#readcube-epdf.

For more information on Human Immunodeficiency Virus Infection refer to http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf, https://www.cdc.gov/tb/topic/treatment/tbhiv.htm, https://www.cdc.gov/tb/publications/factsheets/treatment/treatmenthivpositive.htm, https://www.cdc.gov/tb/education/ssmodules/pdfs/2017SelfStudy_Module4.pdf, and http://www.cdc.gov/mmwr/PDF/rr/rr5314.pdf

ALCOHOLISM

Because of the effectiveness of isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA), they should be used, if clinically appropriate, even if there is preexisting liver disease. Drug-induced hepatitis is defined as a serum aspartate aminotransferase (AST) level more than three times the upper limit of normal in the presence of symptoms or five times the upper limit of normal in the absence of symptoms.

TB itself may involve the liver, which may then cause abnormal liver function. Not all abnormalities in liver function tests noted at baseline should be attributed to causes other than TB. Liver abnormalities caused by TB will improve with effective treatment.

Prior to the initiation of treatment, serologic testing for hepatitis viruses A, B, and C should be considered. Close monitoring, symptom review and repeat serologic testing is an essential part in managing a patient with elevated serum AST.

To monitor for hepatitis:

- Conduct clinical monitoring on the first visit and repeat monthly to check for signs of hepatitis.
- Educate patients about symptoms and signs of adverse reactions and instruct patients to stop treatment should symptoms occur.
- Provide treatment via DOT and review for adverse reactions/symptoms during each visit.

For more information on alcoholism refer to http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.

LIVER DISEASE

Management of TB in patients with unstable or advanced liver disease is difficult. The likelihood of drug-induced hepatitis may be greater in these patients. The implications of drug-induced hepatitis for patients with marginal hepatic reserve are potentially serious, even life-threatening. Fluctuations in the biochemical indicators of liver function (with/without symptoms) related to the pre-existing liver disease confound monitoring for drug-induced hepatitis.

For all patients with pre-existing liver disease, frequent clinical and laboratory monitoring should be performed to detect drug-induced hepatic injury.

For more information on liver disease refer to http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.

RENAL INSUFFICIENCY AND END-STAGE RENAL DISEASE

Renal insufficiency complicates the management of TB because some anti-tuberculosis medications are cleared by the kidneys. Management may be further complicated by the removal of some anti-tuberculosis agents via hemodialysis. To facilitate DOT (three times per week) and avoid premature removal of the drugs, administer all anti-tuberculosis drugs **immediately after hemodialysis**.

For more information on renal insufficiency and end-stage renal disease refer to http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.

TUBERCULOSIS ASSOCIATED WITH TUMOR NECROSIS FACTOR-ALPHA ANTAGONISTS

TB is a potential consequence of treatment with tumor necrosis factor-alpha (TNF-α) antagonists such as the following:

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

These drugs work by blocking TNF-α, an inflammatory cytokine, and are approved for treating rheumatoid arthritis and other selected autoimmune diseases. Blocking TNF-α can allow latent TB infection (LTBI) to progress to TB disease. Healthcare providers should take steps to prevent TB in immunocompromised patients and remain vigilant for TB as a cause of unexplained febrile illness.

Patients should be screened for risk factors for *M. tuberculosis* infection and tested for infection before initiating immunosuppressive therapies, including TNF-α antagonists.

For more information about TB and TNF-α antagonists, see http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5330a4.htm.

CULTURE-NEGATIVE PULMONARY TUBERCULOSIS

A diagnosis of TB should not be ruled out if *M. tuberculosis* cannot be isolated from persons suspected of having pulmonary TB based on clinical features and chest radiographic examination. Alternative diagnoses should be carefully considered, and further appropriate diagnostic studies undertaken in persons with apparent culture-negative TB.

A diagnosis of culture-negative pulmonary TB can be made if all the following conditions are met:

- Initial AFB smears and cultures are negative
- Clinical or radiographic response occurs within two months of initiation of therapy
- No other diagnosis has been established

After the initial phase (first 8 weeks), continue treatment with an additional 10 weeks of isoniazid and rifampin during the continuation phase to complete a total of 18 weeks of treatment. HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of 26 weeks.

For more information on culture-negative pulmonary tuberculosis refer to http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.

EXTRAPULMONARY TUBERCULOSIS

The basic principles for treating pulmonary TB also apply to extrapulmonary forms of the disease. The addition of corticosteroids is recommended for patients with TB pericarditis and TB meningitis. Recommendations concerning duration of therapy are as follows:

- For bone or joint TB, use a minimum regimen of 9 months.
- For TB meningitis, use a minimum regimen of 12 months.
- Use a 26-week course of therapy for TB involving any site.
- Consider prolonging therapy for patients with TB in any site that is slow to respond.

Note: Affected lymph nodes may enlarge while patients are receiving appropriate therapy or after treatment has ended without any evidence of bacteriological relapse. On occasion, new nodes can appear during or after treatment as well.

For more information on extrapulmonary TB refer to
http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf,
http://www.cdc.gov/tb/pubs/TBfactsheets.htm and
http://www.phppo.cdc.gov/phtn/tbmodules/Default.htm

PREGNANCY AND BREASTFEEDING

Because of the risk of TB to the fetus, treatment in pregnant women should be initiated whenever the probability of maternal disease is moderate to high. The initial treatment regimen should consist of INH, RIF, and EMB. As PZA generally is not included in the initial treatment regimen, the minimum duration of therapy is 40 weeks. Although these drugs cross the placenta, they do not appear to have teratogenic effects.

Breastfeeding should not be discouraged in women being treated with first-line anti-tuberculosis agents because the small concentrations of drugs in breast milk do not produce toxicity in the nursing newborn. Conversely, drugs in breast milk should not be considered an effective treatment for TB in a nursing infant.

Pyridoxine supplementation (25 mg/day) is recommended for all women taking INH who are either pregnant or breastfeeding.

For more information on pregnancy and breastfeeding refer to
http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and
http://www.phppo.cdc.gov/phtn/tbmodules/Default.htm

TUBERCULOSIS IN CHILDREN

A pediatric patient is a person less than 10 years of age. TB clinic physicians are strongly encouraged to consult with the state pediatric TB medical consultant or the Global TB Institute when evaluating children for LTBI or TB disease.

The following recommendations have been developed for children:

- Because of the high risk of disseminated TB in infants and children younger than 5 years of age, treatment should be started as soon as the diagnosis of TB is suspected.
- Regimens recommended for infants, children, and adolescents with TB are generally the same as those for adults.
- Duration of treatment in children is six months.
  Exception: For disseminated disease and TB meningitis, use a 12-month regimen. For other exceptions, refer to "Duration of Treatment" in the "Treatment Regimens and Dosages" topics in this chapter.
- **DOT is required** when treating children. This includes monitoring the parent or guardian administering the medication to the child.

Due to the difficulty of isolating *M. tuberculosis* in a child with pulmonary TB, the choice of drugs for the child is frequently guided by the drug susceptibility test results of the presumed source case. If drug-resistant TB is suspected or the source case isolate is not available, specimens for microbiological evaluation should be obtained via early morning gastric aspiration, bronchoalveolar lavage, or biopsy.

For more information on tuberculosis in children refer to:
http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and
https://www.cdc.gov/tb/topic/treatment/children.htm

MYCOBACTERIUM BOVIS (*M. BOVIS*)

M. bovis is the most common of several mycobacteria included in the definition of the *M. tuberculosis complex* (the others include *M. africanum*, *M. microti*, *M. canetti*, *M. caprae*, *M. pinnipedii*, and *M. mungi).* In terms of their ability to cause clinical disease or be transmissible from person to person, all but *M. caprae* behave like *M. tuberculosis* and should be reported as tuberculosis.

While most laboratories do not distinguish between the mycobacteria in the *M. TB* complex, the state BOL has this capability.

The two most common reasons for someone to test positive for *M. bovis* are:

1. The consumption of unpasteurized dairy products such as milk or cheese. Pasteurization, a process of rapidly heating and cooling milk, eliminates disease-causing organisms such as mycobacteria.
2. Treatment with Bacillus Calmette-Guérin (BCG) for bladder cancer. BCG is prepared from an attenuated, or weakened, strain of *M. bovis*.

If not identified through lab testing, *M. bovis* BCG (also called *M. bovis* attenuated) can be identified by genotyping. Isolates testing positive for *M. TB* complex that are *M. bovis* BCG will have a genotype consistent with *M. bovis* as well as a MIRU that has an x, y, or z as the second character of the result and a spoligotype that ends in 600. TB program staff review genotyping results and will notify the public health nurse of any patients with a genotype consistent with *M. bovis* BCG.

M. bovis infection should also be considered in patients resistant to PZA.

Patients infected with *M. bovis* from consuming unpasteurized dairy products should be treated for TB disease. These cases should be counted as an active case of confirmed TB disease.

Patients undergoing treatment with BCG for bladder cancer should be treated for TB disease if it has disseminated to areas of the body other than the urinary tract system (comprised of two kidneys, two ureters, the bladder, and the urethra). Patients with disseminated *M. bovis* BCG should receive treatment for TB disease. All RVCT items in the surveillance system should be completed as for a case of TB disease –even though a case of *M. bovis* BCG will not actually be counted.

TB AND NONTUBERCULOSIS MYCOBACTERIUM (NTM) INFECTION

In rare cases, a patient may be coinfected with TB and NTM. In such cases, the treatment of the TB disease is unaffected by the NTM infection. However, the Pennsylvania Department of Health does not provide NTM treatment and patients coinfected with TB disease and NTM should be referred by the public health TB clinician or nurse to a pulmonologist or infectious disease specialist for the treatment of NTM.

For more information, refer to Chapter 14: Nontuberculosis Mycobacterium Infection.

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CHAPTER 7, APPENDIX A: QUICK START CHECKLIST

This check list is designed to assist public health nurses when treating a patient for tuberculosis disease. Its high-level list of tasks provides an overview and helps staff know where to access important instructions and identify available forms. The tasks listed below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Tasks for Diagnosis of Tuberculosis Disease	Instructions
Perform the initial assessment of the patient	Registration Health Assessment Physician referral Hospital Records Topics: Quick Start Check List, Initial Assessment
Evaluate the patient	Chapter 5: Diagnosis of LTBI and TB Disease Topic: Quick Start Check List
Follow basic principles for tuberculosis (TB) disease	Chapter 7: Treatment of Tuberculosis Disease Topic: Basic Treatment Principles
Plan and initiate treatment for TB disease: • Initiate medical treatment promptly scheduling patient to the next MD TB clinic if the suspicion of TB is high. A positive acid-fast bacilli (AFB) sputum smear result provides strong inferential evidence of TB • Patients with reported confirmed or suspected TB are contacted within 24 hours • Make a home visit or hospital visit to open a patient record. • If not available, obtain baseline biochemistry tests for toxicity monitoring (choose tests based on regimen and for special situations such as human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy): – Complete blood count – Platelets – Liver function tests – Uric acid measurements – Serum Creatinine – Total Bilirubin – Alkaline Phosphatase	Chapter 7: Treatment of Tuberculosis Disease Topics: Treatment Regimens and Dosages (Tables 3, 4, 5, and 6); **Treatment in Special Situations**

Tasks for Diagnosis of Tuberculosis Disease	Instructions
• Perform baseline visual acuity and color discrimination tests for toxicity monitoring if the patient is prescribed ethambutol • Assure that an appropriate treatment regimen, dosages, and duration are selected. The standard regimen for treating TB disease consists generally of an initial 8-week phase of 4 drugs: isoniazid, rifampin, pyrazinamide, and ethambutol followed by an 18-week continuation phase of isoniazid and rifampin (total of 26 weeks). • Assure that the following special situations are considered: – Drug-resistant TB – HIV infection – Alcoholism – Liver disease – Renal insufficiency and end-stage renal disease – TB associated with tumor necrosis factor-alpha antagonists – Culture-negative pulmonary TB – Extra-pulmonary TB – Pregnancy and breastfeeding – TB in children – *M. bovis* • Treatment plan is developed//Treatment Agreement is reviewed and signed by patient	
Monitor the patient regularly: • Assess adherence and drug toxicity at each directly observed therapy (DOT) visit • Conduct ongoing assessment and monitoring at least monthly for clinical response, drug toxicity, and adherence • Reassess treatment and, if concerned about response or drug toxicity, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs • Receive and review drug susceptibility results. If drug susceptibility results show drug resistance to first-line drugs, notify the CHNS, TB clinician, Pennsylvania (PA) TB Program and obtain a consultation from the PA TB medical consultant or the Global TB Institute (1-800-4TB-DOCS).	The CHN monitors at least monthly for drug toxicity, adherence and clinical response

Tasks for Diagnosis of Tuberculosis Disease	Instructions

Monitor the patient for drug toxicity:
• Assess drug toxicity at each DOT visit:
  – When baseline results are abnormal
  – The patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions
  – The patient has symptoms of adverse reactions
  – If the patient is taking ethambutol, question the patient monthly regarding possible visual disturbances, including blurred vision or scotomata
• Repeat liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) each month the patient is taking isoniazid, a rifamycin, or pyrazinamide.
• Due to the incidence of thrombocytopenia and other white and red blood count abnormalities with rifampin, the TB clinician may want to consider obtaining monthly CBC tests for patients taking rifampin or another rifamycin.
• Test visual acuity and color discrimination monthly when the patient is taking ethambutol
  – In doses >15–25 mg/kg
  – For >2 months
  – With renal insufficiency
• If a patient is taking aminoglycosides or other injectable drugs conduct baseline and monthly monitoring for auditory functioning.
	Chapter 7: Treatment of Tuberculosis Disease
	Topic: Side Effects and Adverse Reactions (Tables 7 and 8)
	
	Required Tests:
	• Snellen Chart
	• Ishihara test

Assess the patient's response to treatment:
• Talk with the nurse supervisor and TB clinic physician if unable to determine how to monitor the patient e.g., if the patient:
  – Is culture negative, or
  – Has no sputum specimens collected, or
  – Has AFB 3+ or 4+ results and/or cavitation on chest radiograph"
• If the patient initially had positive AFB sputum smear results then collect one sputum specimen at least weekly and submit them for testing until 3 consecutive negative AFB sputum smear results are reported
• If sputum smear results are positive after 2 months of treatment, notify the TB clinician
• If the patient initially has 3 negative AFB sputum smear results, then collect one sputum
	Chapter 7: Treatment of Tuberculosis Disease
	Topic: Response to Treatment

Tasks for Diagnosis of Tuberculosis Disease	Instructions
specimen weekly for a total of 5 sputum specimens. **Sputum Collection and Testing:** • When the patient has negative sputum smear results, then collect sputum each month and submit them for testing until 3 consecutive negative culture results are reported • For multidrug (MDR-TB) or extensively drug-resistant TB (XDR-TB) patients, monthly sputum specimens are required • For drug-susceptible TB patients who can produce sputum, monthly specimens are recommended until the first negative culture in a series of previously positive cultures is achieved. • For patients who are unable to raise sputum specimens consider sputum induction. • Take the following actions if cultures or smears remain positive and symptoms continue after 3 months of treatment: – Consult with the TB clinic physician, PA TB medical consultant, and/or the Global TB Institute about possible treatment failure – Evaluate the patient for drug-resistant TB. Contact the State Lab to repeat drug susceptibility testing – Continue to provide DOT	
Confirm the completion of treatment: • Verify completion of treatment 6 to 9 months after treatment was started depending upon: – Regimen – Adherence – Response to treatment – Number of weeks on DOT – Number of doses observed (DOT) • If treatment is not completed within the recommended time frame, contact the TB clinic physician, PA TB medical consultant, and/or the Global TB Institute to determine whether continuation of treatment is necessary and if so, for how long.	Chapter 7: Treatment of Tuberculosis Disease Topics: Completion of Therapy, Regimens (Table 3)

Pennsylvania TB Manual: CMHDs

Chapter 7, Appendix B

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Consent to Provide Data to the Centers for Disease Control and Prevention (CDC) About Treatment with Bedaquiline, Pretomanid and Linezolid (BPaL)

The Pennsylvania Department of Health (DOH) is required to report to the CDC essential information about the diagnosis and treatment of all patients with tuberculosis (TB). The CDC uses these data to monitor TB case and treatment trends in the United States. No patient is identified by name in this process.

In August 2019, the U.S. Food and Drug Administration (FDA) approved three drugs – bedaquiline, pretomanid and linezolid – to be used together (as the BPaL regimen) to treat adults with tuberculosis (TB) of the lungs that is extensively drug-resistant (XDR), treatment intolerant or nonresponsive multidrug-resistant (MDR) TB. The BPaL regimen cuts the length of treatment for these conditions from two or more years to six to nine months and greatly improves the chance for a cure.

BPaL provides important benefits but can cause serious side effects. Therefore, in addition to the required reporting of TB diagnosis and treatment data, the CDC is asking health departments to voluntarily report extra information about the use of the BPaL regimen including:

- The dates the patient started and stopped taking each of the three drugs (bedaquiline, pretomanid and linezolid);
- The patient's electrocardiogram (ECG) test results before starting treatment and at least 2, 12 and 24 weeks after starting treatment; and
- The amount of each of the three drugs in the patient's blood (i.e., therapeutic drug levels) if they are ordered by the prescribing TB clinician.

The extra information about the use of BPaL will be collected and reported to the CDC three times – when a patient begins treatment, finishes treatment and one year after the patient completes treatment.

I understand that if I do not consent to the DOH reporting the BPaL extra information to the CDC, it will not change my ability to receive treatment or the care I receive.

By signing this consent, I agree to allow the DOH to send the extra information about my treatment with BPaL to the CDC when I begin treatment with BPaL, when I finish treatment and one year after I complete treatment.

_____ _____

Patient signature Date

_____ _____

Clinic representative signature Date

Chapter 8: Directly Observed Therapy (DOT)

BACKGROUND

Treatment for tuberculosis (TB) disease lasts longer – typically a minimum of six months – and requires more drugs than treatment for most other infectious diseases. With a multi-drug regimen and long treatment period comes the risk that patients will become nonadherent, which can lead to disease relapse and the development of drug resistant TB.

DEFINITION

DOT is the standard of care recommended by the American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America (IDSA) for ensuring that patients adhere to therapy for active TB disease.

DOT is the process in which a trained health care worker observes a patient ingest each dose of TB medication. DOT ensures that a patient successfully completes treatment. Incomplete treatment can lead to relapse and the development of drug resistance. Drug resistant TB can be deadly and is a growing problem across the nation. It can result in hundreds of thousands of dollars in treatment costs and even death.

DOT should be started when treatment starts. To improve patient acceptance of DOT, the prescribing physician should explain that it is widely used in TB and – by reducing the potential for missed doses – is very effective in helping patients complete their treatment as quickly as possible. This message should also be reinforced by the public health nurse or DOT worker.

With each visit the public health nurse or DOT worker will have the opportunity to do one or more of the following:

- Educate the patient about TB
- Observe how the patient is tolerating and responding to treatment
- Offer incentives and/or enablers to facilitate and recognize compliance
- Help the patient connect with other social services as needed

DOT can be provided in a variety of settings including the TB clinic or physician office, the patient's home or workplace, a community-based organization site, a school, or any other site mutually agreeable to the patient and the DOT worker.

DOT FOR PRIVATELY MANAGED PATIENTS

DOT is traditionally done by health department staff. For TB cases that are privately managed, however, the local public health nurse (PHN) should contact the private physician to emphasize the importance of DOT and discuss whether the physician has the resources to provide DOT.

If the physician has sufficient staff resources to provide DOT, he or she must provide the local PHN with monthly documentation of the case information (i.e., RVCT data elements) necessary for CDC reporting. If the physician does not have sufficient resources to provide DOT, then the case should be referred to the local health department for TB treatment and case management.

For more information, refer to the TB Program Policy for state health centers (SHCs) or guidance for county and municipal health departments (CMHDs) on privately managed patients.

PENNSYLVANIA (PA) TB PROGRAM RECOMMENDATIONS

For the treatment of TB disease, the PA TB Program recommends:

- All patients with suspected or confirmed TB disease are to receive their TB medications via DOT for the full course of treatment. If resources are limited, prioritize the patient types listed in Table 1 on the next page for DOT.
- During the first two weeks of treatment, DOT must be provided seven days a week.
- After the first two weeks – and if approved by the TB clinician – DOT can be provided five days a week with the patient self-administering on weekends.
- Daily dosing is preferred over intermittent, but the ATS/CDC/IDSA guidelines allow for intermittent dosing three times a week for patients who are HIV negative and at low risk of relapse (i.e., patients with pulmonary tuberculosis caused by drug-susceptible organisms that at the start of treatment is noncavitary and/or smear negative). Intermittent dosing must be ordered by the treating physician and provided via DOT.
- Intermittent dosing should not be used for patients with cavitary disease.
- Each dose witnessed via DOT should be documented.
- Only those doses administered via DOT are counted towards treatment completion.
- If field resources are limited, the decision whether to provide DOT should be made on a case by case basis with the local TB clinician, nurse supervisor and the PA TB Program. Patients with the risk factors listed in Table 1 should be prioritized for DOT.
- Video DOT is an option for appropriate patients.
  - SHCs must comply with the TB program video DOT policy.
  - CMHDs are encouraged to develop and implement their own video DOT policy and protocols. A helpful resource is the CDC toolkit for “Implementing an Electronic Directly Observed Therapy (eDOT) Program” available at https://www.cdc.gov/tb/publications/pdf/TBeDOTToolkit.pdf.

For window prophylaxis, the PA TB Program recommends:

- DOT is the standard of care for children younger than 5 years of age receiving window prophylaxis (due to an increased risk of rapid progression to TB disease once infected). In most cases this doesn’t pose an additional burden on field resources since these children typically live with an adult receiving DOT for infectious TB disease.
- DOT is recommended for all other patients (including adults) on window prophylaxis.

For the treatment of latent TB infection (LTBI) with the once-weekly 12-dose regimen of INH and rifapentine (3HP), see the TB Program’s current recommendations concerning the use of 3HP.

Table 1: Risk Groups Prioritized for DOT

In the event limited staff resources prevent providing DOT to all appropriate patients, the PA TB Program follows the California Department of Public Health's (CDPH) guidelines that patients with certain risk factors be prioritized for DOT as listed in Table 1.

Table 1: Risk Groups to be Prioritized for DOT

High risk for transmission or acquired drug resistance	High risk for nonadherence	High risk for adverse events and/or poor treatment outcomes
• Cavitary pulmonary disease • Positive acid-fast bacilli (AFB) smear at diagnosis • Sputum conversion more than 2 months (60 days) after starting treatment or slow clinical improvement • Clinical deterioration while on treatment • Drug resistant TB • Receiving intermittent TB medication regimen • HIV infection, including those patients on anti-retroviral therapy	• Nonadherence with TB regimen, past or present • Patients court-ordered to complete their TB treatment • Too ill to self-manage • Psychiatric disorder or memory impairment • Poor or non-acceptance of TB diagnosis or treatment • Poor adherence to initial medical management • Recent history of alcohol or drug abuse • Homeless, shelter resident, or unstably housed • Current or recent history of incarceration	• TB disease relapse • Patients at higher risk for severe outcomes (e.g. those with end-stage renal disease, diabetes, or on a TNF-alpha antagonist) • Immunosuppression post organ transplant • Children

For more information, see the CDPH information sheet at
https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/TBCB-PMD-DOT.pdf

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CHAPTER 8, APPENDIX A: DOT FOR PRIVATELY MANAGED PATIENTS

Background:

The Centers for Disease Control and Prevention (CDC) recommends DOT as the most effective strategy to ensure patient adherence to treatment for active tuberculosis (TB). DOT is defined as the observation of the patient by a health care provider or other responsible person as the patient ingests every dose of TB medication. DOT should be used for *all* patients with TB disease, including children and adolescents as well as health care workers such as physicians, nurses and pharmacists. There simply is no way to accurately predict which patients will adhere to treatment without the use of DOT[1].

Purpose:

The purpose of this guidance is to establish a systematic approach to ensure all patients with TB disease diagnosed and managed by a private physician receive TB treatment via DOT.

Guidance:

- Privately managed TB cases are typically identified by reports electronically submitted via PA-NEDSS (e.g. lab results), outreach by the physician to the local state health center or county or municipal health department, or via word of mouth in the community.
- When a privately managed patient with active TB is identified, the local public health nurse (PHN) should contact the private physician promptly to open a dialogue and communicate the importance of DOT in the successful completion of TB treatment. Suggested talking points include:
    - DOT is universally recognized as the standard of care for all active TB cases.
    - The CDC strongly recommends DOT for all persons with active TB.
    - DOT improves treatment compliance, thereby decreasing the risk of disease transmission and/or the development of drug resistant TB.
    - The local state health center or county or municipal health department:
        - Assumes all responsibility for DOT and patient monitoring while the patient is receiving TB treatment;
        - Provides all TB medications free of charge; and
        - Keeps the private physician informed (with the patient's consent) about the patient's progress while on treatment.

[1] CDC. TB 101 for Health Care Workers, Lesson 6: Treatment of TB Disease

- If the physician commits to provide DOT and has the resources to do so, he or she must provide the PHN with documentation on a monthly basis of the case information (i.e. RVCT data elements) necessary for CDC reporting.
- If the physician doesn't have the resources to provide DOT, the PHN should recommend that the patient be referred to the local state health center or county or municipal health department for TB treatment and case management.
- If the private physician is unconvinced about the importance of DOT or is reluctant to give up responsibility for the patient's care and treatment, the PHN should ask the TB clinic physician to contact the private physician directly to discuss treatment and case management options. If that fails, the next step is for the PHN to work through their supervisory chain to request assistance from the state TB program. The request must include the following:
    - PA-NEDSS investigation number
    - Name and contact information of the private physician
    - Summary of the contact with the private physician regarding DOT
- Within three business days of receiving the request for assistance, the TB program will enlist the help of the state TB Medical Consultant to contact the private physician. A summary of the contact with the private physician will be provided to the local PHN by the TB program.
- For state health centers, a TB patient may continue to be managed by a private physician as long as the following conditions are met:
    - The private provider has discussed this option with the TB clinician or state TB consultant;
    - The TB clinician or state TB consultant prescribes the anti-tuberculosis medications;
    - The patient receives DOT from a community health nurse or outreach worker; and
    - The private provider consults monthly with the TB clinician or state TB consultant about the patient's response to treatment and any changes to the treatment regimen.
- The end goal of this process is to ensure that every patient with TB disease receives treatment via DOT, and that physicians aren't just educated about TB and its treatment but come to regard the state health centers or county or municipal health departments as valued partners in health care.

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Chapter 9: Infection Control

INTRODUCTION

Infection control measures are fundamental to reducing the spread of communicable diseases such as TB. Transmission of *M. tuberculosis* from person to person can occur in many locations, such as home, work, school, and healthcare facilities. It is impossible to prevent all exposure, however, the goal is to reduce the amount of transmission.

The Centers for Disease Control and Prevention (CDC) publication titled "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005" recommends that all healthcare settings have a TB infection-control program designed to ensure prompt detection of TB, appropriate use of airborne precautions, and prompt treatment of persons who have suspected or confirmed TB disease. The extent of infection control activities for an agency or facility is based on the results of its risk assessment. In areas where TB rates are lower, the TB risk is lower. This should affect which elements of the TB infection control plan are utilized.

In May 2019, the CDC updated the portion of the 2005 guidelines that addressed the frequency of TB screening, testing and treatment of health care personnel. A summary of the updated recommendations and associated reference materials can be found on the CDC website. For guidance on facility risk assessments and infection control practices please continue to refer to the 2005 guidelines.

The three components of an infection control program are administrative controls, environmental controls, and personal respiratory protection. Because each patient care setting and patient's home is different, each program will incorporate a different combination of control activities. In areas where TB rates are lower, the TB risk is lower. This should affect which elements of the TB infection control plan are utilized.

PURPOSE

Use this chapter to understand and follow national and Pennsylvania guidelines to:

- Review infection control measures and know where to go for further information;
- Alert local public health staff to the basic differences between masks and respirators;
- Evaluate when a patient is infectious and when he or she is noninfectious;
- Determine when to isolate patients, when to discharge them from hospitals, and when to permit them to return to work, school, or other settings;

- Review how to implement infection control measures in residential settings, patient care facilities, and transportation vehicles;
- Consult with facilities that are implementing infection control measures, including two-step testing.

POLICY

Infection control measures apply to three main settings:

- Healthcare facilities - where persons with infectious TB disease would seek care
- Congregate settings and residential facilities, whose residents are at increased risk for TB disease
- The TB patient's home

INFECTION CONTROL MEASURES

There are three types of infection control measures. The first are administrative controls, which are primarily aimed at early identification, isolation, and appropriate treatment of infectious patients. The second are environmental controls, which focus on preventing the spread and reducing the concentration of infectious droplet nuclei in the air. The third is personal respiratory protection, which may provide additional protection for healthcare workers in high-risk settings such as isolation rooms and cough-inducing or aerosol-generating suites.

The activities described below are more relevant to infection control in healthcare or residential facilities. Home settings are discussed separately in the "Residential Settings" topic in this chapter.

ADMINISTRATIVE CONTROLS

Administrative control measures are the first of three levels of measures designed to reduce the risk of TB transmission. Administrative controls are the first level of infection control because they include a variety of activities to identify, isolate, and appropriately treat persons suspected of having TB disease.

An effective TB infection control plan contains measures for reducing the spread of TB that are appropriate to the risk of a specific setting. Every healthcare setting should have a TB infection control plan that is part of an overall infection control program. A written TB infection control plan helps to ensure prompt detection, airborne precautions, and treatment of persons who have suspected or confirmed TB disease.

- **In TB infection control programs for settings in which patients with suspected or confirmed TB disease are expected to be encountered,** develop a written TB infection control plan that outlines a protocol for the prompt recognition and initiation of airborne precautions for persons with suspected or confirmed TB disease, and update it annually.

- **In TB infection control program for settings in which patients with suspected or confirmed TB disease are NOT expected to be encountered,** develop a written TB infection control plan that outlines a protocol for the prompt recognition and transfer of persons who have suspected or confirmed TB disease to another healthcare setting. The plan should indicate procedures to follow to separate persons with suspected or confirmed infectious TB disease from other persons in the setting until the time of transfer. Evaluate the plan annually, if possible, to ensure that the setting remains one in which persons who have suspected or confirmed TB disease are not encountered, and that they are promptly transferred.

ADMINISTRATIVE ACTIVITIES

Key activities to reduce the risk of transmission include the following:

- **Assign responsibility** to a specific person for designing, implementing, evaluating, and maintaining a TB infection control program for that facility.
- **Conduct a risk assessment.** The risk level for a specific facility will affect the extent of all other activities and will result in each facility having a different plan. Refer to Appendix B: TB Risk Assessment Worksheet in the 2005 CDC Guidelines at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.
- **Develop, implement, and enforce policies and procedures** to ensure early identification, evaluation, and treatment of infectious cases of TB.
- **Provide prompt triage** and management in the outpatient setting of patients who may have infectious TB.
- **Initiate promptly and maintain TB isolation** for persons who may have infectious TB and are admitted to an inpatient setting.
- **Plan effectively for the discharge** of the patient, coordinating between the local public health agency and the healthcare provider.
- **Implement environmental controls.** Develop, install, maintain, and evaluate the effectiveness of engineering controls.
- **Implement a respiratory protection program.** Develop, initiate, install, maintain, and evaluate the effectiveness of the respiratory protection program.
- **Implement precautions for cough-inducing procedures.** Develop, implement, and enforce policies and procedures to ensure adequate precautions when performing cough-inducing procedures.
- **Educate and train healthcare workers** about TB.
- **Counsel and screen healthcare workers.** Develop and implement counseling and screening program for healthcare workers about TB disease and latent TB infection (LTBI).
- **Evaluate promptly possible episodes of TB transmission.**

- **Coordinate activities** between the state and local public healthcare agencies.

For more comprehensive information, please refer to "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]:75–79) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

ENVIRONMENTAL CONTROLS

TB is caused by an organism called *Mycobacterium tuberculosis.* When a person with infectious TB disease coughs or sneezes, tiny particles called droplet nuclei that contain *M. tuberculosis* are expelled into the air. Environmental controls are used to prevent the spread and reduce the concentration of infectious droplet nuclei. Each facility should use different combinations of environmental controls, based on the results of its risk assessment.

It is important to note that without strong administrative controls, environmental controls are ineffective because cases would not be recognized or managed appropriately.

TABLE 1: TYPES OF ENVIRONMENTAL CONTROLS

Most Effective Control	Ventilation Controls direction of air flow to prevent contamination of air in areas surrounding a person with infectious tuberculosis (TB) Dilutes and removes contaminated air Exhausts contaminated air to the outside
Supplementary Controls	High-efficiency particulate air (HEPA) filtration Cleans the air of infectious droplet nuclei Ultraviolet germicidal irradiation (UVGI) Kills or inactivates TB bacilli in the air

PERSONAL RESPIRATORY PROTECTION

Although administrative controls and environmental controls are most effective in controlling the spread of TB, they do not eliminate the risk of transmission entirely. Personal respiratory protection, the third level of infection control, is also used in higher-risk settings.

The purpose of a respirator is to reduce exposure by filtering out TB bacilli from the room air before the air is breathed into a person's lungs. Respirators used for TB control should be approved for TB use by the National Institute for Occupational Safety and Health (NIOSH).

It is recommended that state health center (SHC) or county or municipal health department (CMHD) staff and visitors use personal respiratory protective equipment in settings that may be at higher risk for TB transmission, such as the following:

- Rooms where infectious TB patients are being isolated
- Areas where cough-inducing or aerosol-generating procedures are performed

- Other areas, which should be identified in the facility's risk assessment, where administrative and environmental controls are not likely to protect persons from inhaling infectious droplet nuclei

It is important to note that the precise level of effectiveness (of respiratory protection) in protecting healthcare workers from *M. tuberculosis* transmission in healthcare settings has not been determined. State health center nurses should refer to the DOH Respiratory Protection Program. For more information about respiratory protection programs, see the Centers for Disease Control and Prevention's (CDC's) "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]:75–79) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

The CDC guidelines recommend that healthcare facilities conduct annual training regarding multiple topics for healthcare workers (HCWs), including the nature, extent, and hazards of TB disease in the healthcare setting. Annual fit testing/training will be conducted in conjunction with other related training regarding infectious disease associated with airborne transmission.

Surgical-type masks are to be used by persons who are infectious or are suspected cases of TB disease when they are out of TB respiratory isolation. The purpose of the mask is to reduce transmission by reducing the number of TB bacilli coughed out into the room air. The infectious patient should not wear a respirator. For more information, see **Table 2: Using Masks and Respirators.**

In addition, training topics should include the following:

- Risk assessment process and its relation to the respirator program, including signs and symbols used to indicate that respirators are required in certain areas and the reasons for using respirators
- Environmental controls used to prevent the spread and reduce the concentration of infectious droplet nuclei
- Selection of a specific respirator for a given hazard (See "Selection of Respirators" on p. 78 of the 2005 CDC guidelines.)
- Operation, capabilities, and limitations of respirators
- Cautions regarding facial hair and respirator use
- Occupational Health and Safety Administration (OSHA) regulations regarding respirators, including assessment of employees' knowledge

Trainees should be provided opportunities to handle and wear a respirator until they become proficient. Trainees should also be provided with copies or summaries of lecture materials for use as references and instructions to refer all respirator problems immediately to the respiratory program administrator for your jurisdiction.

A fit test is used to determine which respirator fits the user adequately and to ensure that the user knows when the respirator fits properly. Fit testing provides a means to determine which respirator model and size fits the wearer best and to confirm that the wearer can don the

respirator properly to achieve a good fit. Annual fit testing and training is required for all PA DOH staff. This training is provided by appropriately trained personnel.

OSHA enforces CDC recommendations for respiratory protection, which includes the need for the following:

- Respiratory Protection Program
- Amended medical evaluation
- Training and recordkeeping
- Annual fit testing
- Fit checking

WHO SHOULD USE A MASK OR RESPIRATOR?

Using masks and respirators properly can reduce transmission of *Mycobacterium tuberculosis* and exposure to TB. Refer to **Table 2: Using Masks and Respirators** to determine when to use masks and respirators.

TABLE 2: USING MASKS AND RESPIRATORS

Mask (a regular "surgical" mask*)	Respirator (NIOSH-approved, N-95 or higher*)
Purpose To reduce transmission by capturing infectious droplet nuclei that an infectious patient releases before they get into the air.	Purpose To reduce exposure by filtering infectious droplet nuclei out of the air, before the wearer breathes the air into their lungs.
Who should wear a mask? • Patients with infectious TB or suspected infectious TB	Who should wear a respirator? • Staff • Visitors to TB isolation rooms (keep these visitors to a minimum)
A patient should wear a mask In a hospital setting when: • Suspected of having infectious TB and not yet placed in respiratory isolation • Leaving a respiratory isolation room for any reason **Note:** Infectious patients should NOT wear masks when in their TB isolation rooms. In a health clinic setting when: • Not in a TB isolation room • Returning to the clinic for evaluation	A staff person or visitor should wear a respirator In a hospital or clinic setting when: • Entering a TB isolation room • Performing cough-inducing or aerosol-generating procedures • Unlikely to be protected by administrative or environmental controls
A patient should wear a mask In a transportation setting when: • Traveling in a vehicle with other persons	A staff person or visitor should wear a respirator In some transportation settings when:

	• Riding in a vehicle with a patient with infectious TB
In the patient's home: **Note:** Infectious patients do NOT need to wear a mask when they are in their homes.	A staff person or visitor* should wear a respirator In a patient's home when: • Visiting the infectious patient inside a home/residence ***Note:** There should NOT be any visitors (excluding protected healthcare workers) to the home until the patient is released from TB isolation.
Definition of abbreviations: NIOSH = National Institute for Occupational Safety and Health; TB = tuberculosis. * There are some devices, such as the 3M 1860, which are both N95 respirators and surgical masks.	

Source: CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):38–40.

ISOLATION

To reduce disease transmission, a patient with TB disease may need to be isolated or have activities restricted.

Isolation: Isolation is used when people are ill. Isolation of people who have a specific illness separates them from healthy people and restricts their movement to stop the spread of that illness. Isolation allows for the focused delivery of specialized health care to people who are ill, and it protects healthy people from getting sick. People in isolation may be cared for in their homes, in hospitals, or at designated healthcare facilities. Isolation is a standard procedure used in hospitals today for patients with TB and certain other infectious diseases. In most cases, isolation is voluntary; however, many levels of government (federal, state, and local) have the basic legal authority to compel isolation of sick people to protect the public.

Restricted Activities: Until determined to be noninfectious, the patient is not permitted to return to work, school, or any social setting where the patient could expose individuals to airborne bacteria.

Quarantine: Although TB Control Program has used the word "quarantine" interchangeably with "isolation" and "restricted activities," the word "quarantine" when properly used is not a term applicable to TB Control. Quarantine applies to people who have been exposed and may be infected but are not yet ill. Separating exposed people and restricting their movements is intended to stop the spread of illness. Quarantine is not an appropriate TB Control measure for asymptomatic, exposed individuals.

DETERMINING INFECTIOUSNESS

Patients who have suspected or confirmed TB disease and who are not on anti-tuberculosis treatment should be considered infectious if they have any of the following:

- Presence of cough

- Cavitation on chest radiograph
- Positive acid-fast bacilli (AFB) sputum smear result
- Respiratory tract disease with involvement of the lung or airways, including larynx
- Failure to cover the mouth and nose when coughing
- Undergoing cough-inducing or aerosol-generating procedures (e.g., sputum induction, bronchoscopy, airway suction)

If a patient with one or more of these characteristics is on standard multidrug therapy with documented clinical improvement, usually in connection with smear conversion over several weeks, the risk of infectiousness is reduced.

DETERMINING NONINFECTIOUSNESS

Use the following criteria as general guidelines to determine when during therapy a patient with pulmonary TB disease has become noninfectious. Decisions about infectivity of a person on treatment for TB should depend on the extent of illness and the specific nature and circumstances of the contact between the patient and exposed persons. These guidelines can and should be modified on a case-by-case consultation with the TB clinician.

- Patient has negligible likelihood of multidrug-resistant TB (no known exposure to multidrug-resistant tuberculosis and no history of prior episodes of TB with poor compliance during treatment).
- Patient has received standard multidrug antituberculosis therapy for two to three weeks. (For patients with AFB sputum smear results that are negative or rarely positive, threshold for treatment is four to seven days.)
- Patient has demonstrated complete adherence to treatment (e.g., is receiving directly observed therapy).
- Patient has demonstrated evidence of clinical improvement (e.g., reduction in the frequency of cough or reduction of the grade of the AFB sputum smear result).
- All close contacts of the patient have been identified, evaluated, advised, and, if indicated, started on treatment for LTBI. This criterion is critical, especially for children younger than 5 years of age and persons of any age with immunocompromising health conditions.
- While in a hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they:
    - are receiving standard multidrug antituberculosis therapy;
    - have demonstrated clinical improvement; and
    - have had three consecutive AFB-negative smear results of sputum specimens collected eight to 24 hours apart, with at least one being an early morning specimen.

- Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected more than eight hours apart before being considered noninfectious.

AIRBORNE INFECTION ISOLATION IN A HEALTHCARE FACILITY

In airborne infection isolation (AII), the patient is placed in an AII room, usually within a hospital or healthcare facility. The main characteristics of an AII room (for new or renovated buildings) are that it has negative air pressure relative to the hall and 12 or more air exchanges per hour, of which at least two exchanges are outside air. For existing structures, six or more air exchanges per hour are acceptable.

The decisions to initiate and discontinue isolation should be made on a case-by-case basis in consultation with the TB clinician.

WHEN TO INITIATE AIRBORNE INFECTION ISOLATION

Suspected cases of laryngeal or pulmonary TB should be isolated immediately, before AFB sputum smear results are available.

Initiate TB AII precautions for any patient who meets the criteria in Table 4.

TABLE 4: INITIATION OF AIRBORNE INFECTION ISOLATION

Criteria for Initiation of Airborne Infection Isolation		
The patient has signs or symptoms of pulmonary, laryngeal, or multidrug-resistant tuberculosis (MDR-TB) disease	OR	The patient has documented infectious pulmonary, laryngeal tuberculosis (TB) disease or MDR-TB disease AND The patient has not completed treatment

Source: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):16, 44.

While in the hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they (1) are receiving standard multidrug antituberculosis therapy; (2) have demonstrated clinical improvement; and (3) have had 3 consecutive AFB-negative smear results of sputum specimens collected 8 to 24 hours apart, with at least one being an early morning specimen.

WHEN TO DISCONTINUE AIRBORNE INFECTION ISOLATION

The decision to release a patient with suspected or known MDR TB from isolation should be made in consultation with the state TB consultant and/or the Global TB Institute at Rutgers.

For patients placed in AII due to suspected infectious TB disease of the lungs, airway, or larynx, AII can be discontinued when the criteria in Table 5 are met.

TABLE 5: DISCONTINUATION OF AIRBORNE INFECTION ISOLATION OF SUSPECTED CASES OF TB

Criteria for Discontinuing Airborne Infection Isolation: Suspected Case of Tuberculosis of the Lungs, Airway, or Larynx		
Infectious tuberculosis (TB) disease is considered unlikely	AND	EITHER Another diagnosis is made that explains the clinical syndrome OR The patient has 3 negative acid-fast bacilli (AFB) sputum smear results,* has been on treatment delivered as directly observed therapy, and has demonstrated clinical improvement
* Each of the 3 sputum specimens should be collected 8 to 24 hours apart, and at least one (1) should be an early morning specimen (because respiratory secretions pool overnight). Generally, this will allow patients with negative AFB sputum smear results to be released from AII in 2 days.		

Sources: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):16, 43; ATS, CDC. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):9

Because patients with TB disease of the lungs, airway or larynx can still be infectious even with negative AFB sputum smear results, patients who meet the above criteria for release from AII should not be released to an area where other patients with immunocompromising conditions or children less than 5 years of age are housed.

CONFIRMED TB DISEASE

A patient with drug-susceptible TB of the lung, airway, or larynx who is on standard multidrug antituberculosis treatment and who has had a significant clinical and bacteriologic response to therapy (e.g., reduction in cough, resolution of fever, and progressively decreasing quantities of AFB on smear results) is probably no longer infectious. However, since the culture and drug susceptibility results are not usually known when the decision to discontinue AII is made, all patients with confirmed TB disease should remain in AII while hospitalized until ***all the criteria*** in Table 6 are met.

TABLE 6: DISCONTINUATION OF AIRBORNE INFECTION ISOLATION OF CONFIRMED CASES OF TB

Criteria for Discontinuing Airborne Infection Isolation: Hospitalized Patients with Confirmed, Drug-Susceptible TB of the Lungs, Airway, or Larynx
The patient has had 3 consecutive negative AFB sputum smear results collected 8 to 24 hours apart, with at least one being an early morning specimen AND The patient has received standard multidrug anti-tuberculosis treatment by DOT AND The patient has demonstrated clinical improvement

Source: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):43.

HOSPITAL DISCHARGE

The decisions to discharge an AFB sputum smear-positive patient or an MDR-TB patient should be made in consultation with the PA TB Program and – for an MDR patient – the state TB consultant.

DRUG-SUSCEPTIBLE TB DISEASE

If a hospitalized patient who has suspected or confirmed drug-susceptible TB disease is deemed medically stable (including patients with positive AFB sputum smear results indicating pulmonary TB disease), the patient can be discharged from the hospital before converting AFB sputum smear results to negative if ***all the criteria*** in Table 7 are met.

TABLE 7: HOSPITAL DISCHARGE OF DRUG-SUSCEPTIBLE CASES OF TB

Criteria for Hospital Discharge to Home: Patients with Suspected or Confirmed Drug-Susceptible TB
A specific plan exists for follow-up care with the local TB control program AND The patient has been started on a standard multidrug antituberculosis treatment regimen and DOT has been arranged AND No children less than 5 years of age or persons with immunocompromising conditions are present in the household AND All immunocompetent household members have been previously exposed to the patient AND The patient is willing to not travel outside the home except for healthcare-associated visits until the patient has negative AFB sputum smear results

Source: CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):43–44.

MULTIDRUG-RESISTANT (MDR) TB DISEASE

In most cases it is acceptable to discharge an MDR patient from the hospital when ***all the criteria*** in Table 8 are met. However, because the transmission of MDR TB can have severe consequences for immunocompromised individuals and children less than 5 years of age, the decision to discharge an MDR patient from the hospital to home must be made in consultation with the PA TB Program, the state TB consultant and/or the Global TB Institute, and the TB clinician and nurses for the jurisdiction that with provide follow-up care.

TABLE 8: HOSPITAL DISCHARGE OF MULTIDRUG-RESISTANT CASES OF TB

Criteria for Hospital Discharge to Home: Patients with Suspected or Confirmed Multidrug-Resistant TB
A specific plan exists for follow-up care with the local TB control program
AND
An appropriate treatment regimen has been initiated and DOT has been arranged
AND
No children less than 5 years of age or persons with immunocompromising conditions are present in the household
AND
All immunocompetent household members have been previously exposed to the patient
AND
Suitable arrangements have been made so that the regimen can be continued and properly monitored on an outpatient basis, specifically by DOT

RELEASE SETTINGS

Patients with suspected or confirmed infectious TB disease should not be released to healthcare settings or homes where the patient can expose others who are at high risk for progressing to TB disease if infected, such as HIV-infected persons or young children. Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected more than eight hours apart before being considered noninfectious.

Patients who have positive AFB sputum smear results should **not** be directly discharged from the hospital to **any** of the following living environments:

- Congregate living site (e.g., shelter, nursing home, jail, prison, group home, another hospital)
- Living situation where infants and young children also reside
- Living situation where immunosuppressed persons also reside
- Living situation where home health aides or other social service providers will be present in the home for several hours a day to care for the person or family member

RESIDENTIAL SETTINGS

Patients suspected of having infectious TB either are diagnosed during an outpatient workup, or if admitted to a hospital, are often sent home after starting treatment. Patients are sent home, even though they may still be infectious, because they are most likely to transmit TB to household members **before** TB has been diagnosed and treatment has started. However, TB patients and members of their household can take steps to prevent the spread of TB in their home until the patient becomes noninfectious.

ADMINISTRATIVE CONTROLS IN THE PATIENT'S HOME

Have a policy and procedure for managing infectious patients at home. To standardize care, the following information should be included:

- **Definition of key terms:** Infectious case and noninfectious case
- **Treatment of cases at home whenever possible:** Treat patients at home if their condition does not otherwise require hospitalization.
- **Window period treatment policy:** Ensure that candidates for window period treatment in the home have completed their evaluation and are on medication before the TB patient is discharged home (or as soon as possible if they were not hospitalized).
- **Education:** Educate infectious patients, family, care providers, and close contacts regarding the purpose of isolation, their responsibility to adhere to the isolation requirements, and the consequences of not voluntarily complying with isolation.
- **Home isolation:** Consider having infectious cases in isolation sign a Disease Treatment Agreement consistent with the policy and procedures in effect in your jurisdiction. This document should include any legal consequences should the patient fail to voluntarily comply with the terms of the agreement.

ENVIRONMENTAL CONTROLS IN THE PATIENT'S HOME

Generally, there are no special engineering recommendations. However, patients and their families can be advised to do the following:

- Have tissues available for patients to cover their mouths and noses when coughing or sneezing.
- Keep windows and doors open (weather permitting) to increase the ventilation and dilution of infectious droplet nuclei in the house.
- If a sputum sample needs to be collected at home, do so in a well-ventilated area away from other residents (e.g., bathroom with an exhaust fan). If possible, collect the sputum in an outdoor area away from open windows or doors.

RESPIRATORY PROTECTION IN THE PATIENT'S HOME

Patients:

- Patients do not need to wear masks at home.
- Give patients regular surgical-type masks and advise them to wear them at medical appointments until they are no longer infectious.
- Do not give patients respirators (N-95 or higher)

Healthcare Workers:

- Healthcare workers should wear respirators when entering the home or a closed area to visit with infectious patients.
- The respirators should be National Institute for Occupational Safety and Health (NIOSH)-approved (N-95 or higher).
- Healthcare workers should be provided with respirators after appropriate education and fit testing.

OTHER RESIDENTIAL SETTINGS

Motels:

Homeless persons with infectious TB may be housed in a motel that has outside access to rooms (not via hallways).

The motel manager must be advised of the following:

- The patient is in respiratory isolation.
- The manager should report to local SHC or CMHD staff if the manager becomes aware that the patient does not stay in the room or has guests.
- The manager should advise motel staff that they are not to enter the room while the patient resides at the motel. (Arrangements should be made that once a week, the patient sets out linens that need to be replaced. The staff can knock on the door and leave the linens for the patient to make his or her own bed.)
- Upon release from isolation, the room should be aired out for one day before staff enters to clean. Afterwards, routine cleaning done between guests is sufficient, and there are no additional special cleaning requirements.
- Local SHC or CMHD staff will be delivering medication to the patient (specify the frequency).
- Arrangements have been made for food delivery to the patient.

Healthcare Facilities or Residential Settings:

- Patients with infectious TB should be in appropriate respiratory isolation (airborne infection isolation rooms) when housed in healthcare facilities or residential settings.
- If a facility does not have the capability to provide appropriate respiratory isolation, the patient should be transferred to a facility that can accommodate respiratory isolation until the patient is noninfectious. Once noninfectious, the person may return to the original facility.

RETURN TO WORK, SCHOOL, OR OTHER SOCIAL SETTINGS

The decision of when to allow a patient to return to work, school, or other social settings should be made in consultation with the TB clinician.

The decision to permit a patient to return to work, school, or other social settings is based on the following:

- The characteristics of the patient with TB disease (e.g., whether the patient is likely to adhere to the regimen and follow treatment instructions)
- The characteristics of the TB disease itself (e.g., multidrug-resistant versus drug-susceptible TB, AFB sputum smear-positive versus smear-negative, cavitary versus noncavitary)
- The duration of current treatment (e.g., the patient has received standard multidrug antituberculosis therapy for two to three weeks or, if the patient has AFB sputum smears that are negative or barely positive, the minimum threshold for treatment is four to seven days)
- The environment(s) to which the patient will be returning

DRUG-SUSCEPTIBLE TB DISEASE

Patients with drug-susceptible TB are no longer considered infectious when they meet ***all the criteria*** in Table 9.

TABLE 9: RETURN OF DRUG-SUSCEPTIBLE CASES OF TB TO WORK, SCHOOL AND OTHER SETTINGS

Criteria for Return to Work, School, or Other Social Settings: Patients with Suspected or Confirmed Drug-Susceptible TB
The patient is on adequate therapy AND The patient has had a significant clinical response to therapy AND The patient has had 3 consecutive negative AFB sputum smear results collected 8 to 24 hours apart, with at least one being an early morning specimen

Source: CDC. Infectiousness. *Core Curriculum on Tuberculosis (2011)* November 2011.

MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB) DISEASE

Regardless of their occupation, patients known or likely to have pulmonary MDR-TB may be considered for return to work or school only if they meet ***all four of the criteria*** in Table 10.

TABLE 10: RETURN OF MULTIDRUG-RESISTANT CASES OF TB TO WORK, SCHOOL AND OTHER SETTINGS

Criteria for Return to Work, School, or Other Social Settings: Patients with Suspected or Confirmed Multidrug-Resistant TB
The resolution of fever and the resolution, or near resolution, of cough has occurred AND The patient is on current treatment with an antituberculosis regimen to which the strain is known or likely to be susceptible* AND The patient has had 3 consecutive negative AFB sputum smear results collected 8 to 24 hours apart, with at least one being an early morning specimen AND The patient has had a negative culture for *Mycobacterium tuberculosis*
* DOT is the standard of care for patients with MDR-TB.

TB INFECTION CONTROL IN PATIENT CARE FACILITIES

Patients with suspected TB may present for care in many different settings. The CDC has written a comprehensive set of guidelines for TB infection control in acute care hospitals and other medical settings. In addition to the CDC guidelines, various professional organizations or state regulations may have guidelines for managing TB patients.

TABLE 11: GUIDELINES FOR TB INFECTION CONTROL

Guidelines for Tuberculosis Infection Control
The following settings are addressed in the "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Facilities, 2005" (MMWR 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf. Some settings have additional guidelines as noted below.
Inpatient Settings • Emergency departments and urgent care settings • Intensive care units • Surgical suits • Laboratories • Bronchoscopy suites • Sputum induction and inhalation therapy rooms • Autopsy suites and embalming rooms

Guidelines for Tuberculosis Infection Control
• Outpatient Settings • TB treatment facilities • Medical settings in correctional facilities: Prevention and Control of Tuberculosis in Correctional Facilities. (ACET) (*MMWR* 1996;45[No. RR-8]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5509a1.htm • Medical offices and ambulatory care settings • Dialysis units
Nontraditional Facility-Based Settings • Homeless shelter clinics: Prevention and Control of Tuberculosis Among Homeless Persons (ACET) (*MMWR* 1992;41[No. RR-5]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/00019922.htm • Emergency medical services • Home-based healthcare and outreach settings • Long-term care facilities (e.g., hospices, skilled nursing facilities): Prevention and Control of Tuberculosis in Facilities Providing Long-Term Care to the Elderly (*MMWR* 1990;39[No. RR-10]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/00001711.htm

TRANSPORTATION VEHICLES

To prevent the transmission of *M. tuberculosis* while transporting patients, follow the respiratory precautions identified below.

PATIENT SELF-TRANSPORT

- Vehicle windows should be open and any recirculating air controls should be turned off.
- If possible, only household members should accompany the patient. Any members of the patient's household who accompany the patient do not need to wear surgical masks.
- If the only source for transport is a friend or relative who is not a member of the patient's household:
    - The person accompanying the patient should be given a respirator (N-95) to wear during transport (due to the confined space and lack of ongoing exposure).
    - The patient should sit in the back seat and wear a surgical mask.
    - Car windows should be opened and any recirculating air controls should be turned off.
- The patient should wear a surgical mask after leaving the vehicle.

TRANSPORT BY HEALTHCARE WORKERS

- Healthcare workers should wear respiratory protection (N-95) while in the vehicle.
- The patient should wear a surgical mask and sit in the back seat.

- Vehicle windows should be open and any recirculating air controls should be turned off.

TRANSPORT BY EMERGENCY MEDICAL SERVICES

Emergency medical services staff have specialized vehicles that may have the ability to separate the driver's compartment from the transport compartment and rear exhaust fans. Recommendations for these vehicles and staff are addressed in the Centers for Disease Control and Prevention (CDC) "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Facilities, 2005" (*MMWR* 2005;54[No. RR-17]:25–26, 88, 127) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

REFERENCES

- CDC. "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf
- CDC. "Guidelines for Environmental Infection Control in Health-care Facilities" (*MMWR* 2003;52[No. RR-10]) at http://www.cdc.gov/mmwr/PDF/rr/rr5210.pdf
- CDC. *Interactive Core Curriculum on Tuberculosis* at https://www.cdc.gov/tb/education/ce/interactive-corecurr.htm
- CDC. "Respiratory Protection in Health-Care Settings" (*TB Elimination Fact Sheet* April 2010) at https://www.cdc.gov/tb/publications/factsheets/prevention/rphcs.pdf
- CDC. Module 4: "Treatment of TB Infection and Disease" (*Self-Study Modules on Tuberculosis*) at https://www.cdc.gov/tb/education/ssmodules/pdfs/2017SelfStudy_Module4.pdf
- CDC. Module 5: "Infectiousness and Infection Control" (*Self-Study Modules on Tuberculosis*) at https://www.cdc.gov/tb/education/ssmodules/pdfs/TB_SelfStudyModules_2015_Module05.pdf
- OSHA. "Respiratory Protection" [Web page] at https://www.osha.gov/SLTC/respiratoryprotection/guidance.html
- OSHA. "Tuberculosis: OSHA Standards" [Web page] at http://www.osha.gov/SLTC/tuberculosis/standards.html

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DEPARTMENT OF HEALTH

Chapter 10: Contact Investigation

INTRODUCTION

PURPOSE

The Centers for Disease Control and Prevention (CDC) have described the conduct of contact investigations as the one of the highest priorities of a tuberculosis (TB) control program – second only to the identification and treatment of individuals with TB disease.

A contact investigation is the process of identifying, examining, evaluating, and treating all persons who are at risk for infection with *M. tuberculosis* due to recent exposure to a newly diagnosed or suspected case of pulmonary, laryngeal, or pleural TB. The primary goals of a contact investigation are to:

- Stop further transmission of TB by finding and treating previously undetected cases of TB disease, and
- Prevent future cases of TB disease by finding and treating persons with latent TB infection (LTBI).

Except in rare cases, every case of TB begins as a contact to a person with active pulmonary, laryngeal, or pleural TB disease. Nationally, approximately 20% to 30%[1] of all TB contacts have LTBI and are at risk of progressing to TB disease if not diagnosed and treated for LTBI. One percent of all TB contacts have TB disease at the time of the contact investigation and need treatment.

Identifying and treating individuals with TB disease and LTBI through the proper conduct of contact investigations would lead to substantial personal and public health benefits and facilitate progress toward eliminating TB in the United States.

[1] CDC. "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC" (*MMWR* 2005;54 [No. RR-15]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

POLICY

- A contact investigation is required for all laboratory confirmed cases of infectious TB, including TB disease of the lungs, airways, or larynx.
- A contact investigation should be started for all suspected cases of infectious TB, even before the case is confirmed. This includes persons with acid fast bacilli (AFB) positive sputum smears, abnormal chest x-ray (CXR) findings consistent with TB disease and any other test results that suggest TB disease. If it is later determined that the suspect case does not have infectious TB disease, the contact investigation should be stopped.
- A contact investigation should be started as soon as a suspected or confirmed case of infectious TB is reported to health authorities. The initial steps of the investigation include reviewing the patient's medical information and interviewing the patient within 1 to 3 days of the case being reported.

RESPONSIBILITY

28 Pa Code § 27.161b requires that "a human household contact or other close human contact shall be required to have a TB test or a chest x-ray, or both. If the person refuses, enforcement shall be accomplished as designated in § § 27.82 and 27.83 (relating to request to submit to examination; and court ordered examinations). If evidence of tuberculosis in contacts is found on chest x-rays or by symptoms, laboratory studies shall be conducted to determine if the contacts represent a public health threat".

Public health departments – the local state health center (SHC) or county or municipal health department (CMHD) – have overall responsibility for conducting and overseeing contact investigations for all suspected and confirmed cases of infectious TB in their jurisdiction, regardless of whether the case was identified by a public provider, private physician or medical staff at health care facilities such as hospitals, long-term care facilities and schools.

The local public health nurses (PHNs) will work with private physicians and medical staff at health care facilities to plan and conduct the contact investigation and will coordinate with other public health staff to ensure that contacts who live outside the jurisdiction are tested and evaluated for TB. The state TB program manager, state medical consultant(s) and the Global TB Institute at Rutgers are available for consultation in planning contact investigations.

The state TB program manager should be notified immediately of all contact investigations that may involve significant numbers of contacts such as those occurring in schools, colleges, large industries, hospitals, nursing homes, correctional facilities, etc.

Tuberculosis disease which occurs in a federal, state or local government institution (correctional facility, public welfare institution, hospital) must be reported to the state TB program.

- PHNs must coordinate with the staff of the institution to assure that a contact investigation is completed, either by a collaborative effort between the local health department and the institution or by the institution in consultation with the local health department.
- If contact investigations by the institution are delayed or not started, public health nursing staff must notify their supervisor, who will notify the state TB program manager.

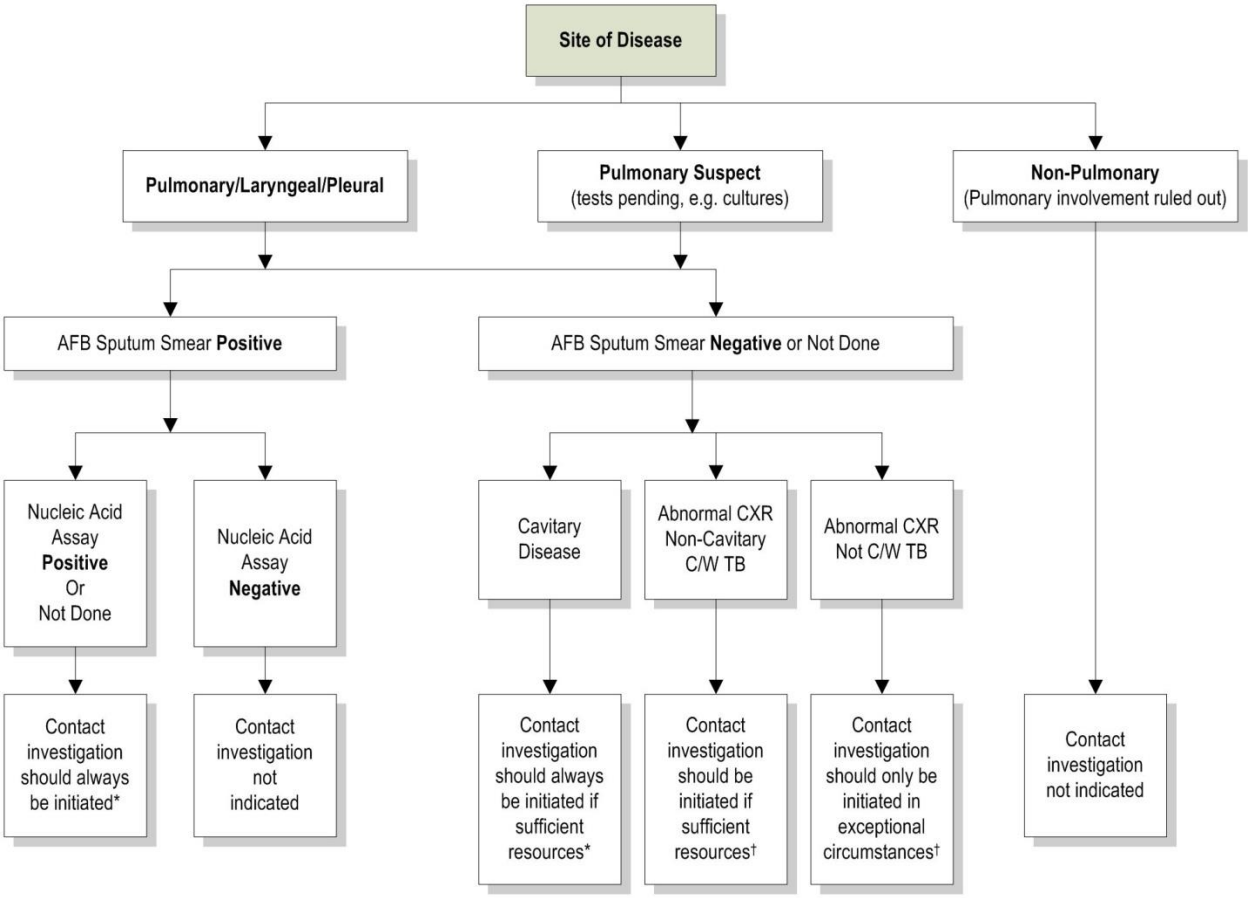
Private physicians may conduct a contact investigation for their patients **but the local public health staff is responsible for ensuring that a complete contact investigation is done** and should offer to conduct the investigation for the physician.

DECIDING TO INITIATE A CONTACT INVESTIGATION

Consider a contact investigation for any patient with confirmed or suspected pulmonary, laryngeal, or pleuropulmonary TB. Refer to Figure 1 to help determine whether to start a contact investigation.

FIGURE 1: **DECISION TO INITIATE A CONTACT INVESTIGATION**

HOW TO PRIORITIZE A CONTACT INVESTIGATION



Definitions of abbreviations: AFB = acid-fast bacilli; C/W = consistent with; CXR = chest radiograph; TB = tuberculosis.

* Use time frames from the middle column of Table 2 in the "Time Frames for Contact Investigation" topic.

† Use time frames from the right-hand column of Table 2 in the "Time Frames for Contact Investigation" topic.

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):5, available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.htm.

At times, limited resources or competing demands may prevent health departments from promptly completing a contact investigation for all confirmed or suspected cases of infectious TB. In these situations, public health staff need to decide which contact investigations are assigned the highest priority. Generally, the highest priority should be assigned to those contact investigations where the case is likely to be highly infectious, is in a congregate or other setting where the likelihood of transmission is high, or where the contacts are at increased risk for rapid progression to TB disease.

HIGHLY INFECTIOUS CASES

Highly infectious cases generally have one or more of the following characteristics:

- Pulmonary, laryngeal or pleural TB
- AFB positive sputum smear results
- A positive NAAT
- Cavities on CXR
- Frequent or long-term coughing, sneezing, or singing – actions that spread droplets containing *M. tuberculosis* in the air

SETTINGS WHERE TRANSMISSION OF TB IS LIKELY

Transmission is more likely in settings where there is a high concentration of *M. tuberculosis* in the air. The concentration of *M. tuberculosis* bacteria in the air is affected by:

- Room size
- Ventilation
- Air-cleaning system

M. tuberculosis is more likely to be transmitted in small, crowded spaces that lack ventilation than in large well-ventilated spaces. Settings with air-cleaning systems such as high-efficiency particulate air (HEPA) filters and ultraviolet lights can decrease the concentration of *M. tuberculosis* bacteria in the air.

In addition to the above criteria, the activities in a given setting should also be considered. For example, medical procedures such as bronchoscopy, sputum induction, TB wound irrigation or autopsy of TB cases can all aerosolize TB bacteria and increase the concentration of M. tuberculosis in the air. Contact investigations involving settings where these procedures are done should be assigned a high priority.

CONTACTS AT HIGH RISK OF RAPID PROGRESSION TO TB DISEASE

Contacts infected with *M. tuberculosis* who are at particularly high risk for rapidly progressing to TB disease include:

- Children less than 5 years of age; and
- Persons with weakened immune systems due to
    - HIV infection; or
    - Immunosuppressive therapy (including TNF-alpha antagonists, prolonged use of high-dose adrenocorticosteroids, or medications received after organ transplantation to reduce the risk or organ rejection)

Contact investigations including the above high-risk patients should be given priority for initiation and completion.

CONTACT INVESTIGATION PERSONNEL

A TB contact investigation involves many different steps and procedures. Depending on the size of the investigation and the resources available, the investigation may be done by one or two individuals or a contact investigation team.

The public health staff involved in a contact investigation may include:

- Nurse case managers
- Field investigators
- Outreach workers
- Epidemiologists and surveillance staff
- TB program manager
- TB medical consultant

Ideally, one person should be assigned responsibility for the overall management of the investigation to ensure all activities are completed and done properly. In some situations, infection control professionals or other staff from the facility where exposure occurred may also participate in the contact investigation.

KNOWLEDGE AND SKILLS NEEDED TO DO A TB CONTACT INVESTIGATION

The person in charge of the overall contact investigation (the "contact investigator") and other members of the contact investigation team should have the following knowledge and skills:

- A basic understanding of TB transmission and pathogenesis.
    - A useful resource is *CDC Tuberculosis Self-Study Module 1: Transmission and Pathogenesis of Tuberculosis*. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/2017SelfStudy_Module1.pdf
- Effective communication skills to build trust and rapport with the case patient during interviews.
    - A helpful resource is the *Effective Interviewing for Tuberculosis Contact Investigations* video and checklist issued in 2019 by the Global TB Institute at Rutgers and available at: http://globaltb.njms.rutgers.edu/educationalmaterials/productfolder/ci_video.php

- Data collection, management and analysis. Contact investigations typically involve a large amount of demographic, medical and epidemiological data that needs to be systematically collected, organized and analyzed. The contact investigator needs to decide which data need to be collected, who is responsible for collecting it and how, and how the data is to be safeguarded and managed.
- An understanding of TB genotyping. Genotyping is done for each culture-positive case of TB and identifies the specific strain of *M. tuberculosis* that has infected the patient. Because genotyping is done on positive cultures, the resulting information isn't available to the investigator until later in the contact investigation. When the genotyping data is available, it can confirm, disprove or detect connections among TB cases. For example, two cases with the same genotype may not know one another but may have been exposed to the same infectious case of TB years earlier. Genotyping data is also key to identifying an emerging outbreak of TB cases.
    - For more information on genotyping, see *CDC Tuberculosis Self-Study Module 9: Tuberculosis Outbreak Detection and Response.* Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/Module9.pdf

SYSTEMATIC APPROACH TO A CONTACT INVESTIGATION

Contact investigations should be done using a systematic process that includes the following 10 steps:

1. Review all existing information about the case
2. Do an initial calculation of the infectious period and estimate the patient's degree of infectiousness
3. Interview the case patient
4. Review the information gathered to date and prepare a plan for the contact investigation
5. Refine the patient's infectious period and degree of infectiousness
6. Prioritize contacts
7. Conduct field visits
8. Conduct contact assessments
9. Determine whether to expand or conclude an investigation
10. After completing the contact investigation, evaluate the contact investigation activities and results and note improvements for future investigations

Highlights of key steps are described in the following pages. For an in-depth review of each of the above steps, refer to *CDC Tuberculosis Self-Study Module 8: Contact Investigations for Tuberculosis, pages 16-56.* Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/Module8.pdf

CALCULATING THE INFECTIOUS PERIOD

The infectious period is the time during which a case is potentially capable of transmitting *M. tuberculosis*. Because there is no well-established method of determining the start, duration and end of the infectious period, it must be estimated. Estimating the infectious period helps the investigator focus on those contacts who were most likely exposed to *M. tuberculosis* while the case was infectious.

Estimating the Start of the Infectious Period

For TB cases that have positive sputum smears or evidence of cavitation on their CXR, the minimum start date of the infectious period is usually three months before the onset of coughing or other respiratory symptoms, or three months before the first finding consistent with TB disease (e.g., an abnormal CXR consistent with TB disease), whichever is earlier.

- Example 1: The patient recalls that his or her symptoms began on November 1. In this case, it is estimated the start of the infectious period was August 1.
- Example 2: The patient doesn't remember when his or her symptoms began or was never symptomatic. However, a CXR taken on September 1 indicated a cavity in the right lung. In this case, it is estimated the start of the infectious period was June 1, or three months before the CXR was done.

For TB cases with TB symptoms and negative sputum smears, the start date of the infectious period would be three months before the onset of symptoms or three months before the first finding consistent with TB disease, whichever is earlier.

For TB cases with no symptoms, negative sputum smears and no cavities, the start of the infectious period is 1 month (4 weeks) before TB disease was first suspected by a healthcare provider.

These recommendations are summarized in Table 1.

Public health nurses are encouraged to confer with the local TB clinician if they have any concerns about estimating the start of the patient's infectious period.

Table 1: Recommendations for Estimating the Start of the Infectious Period

Characteristics of TB Case			Recommended Minimum Beginning of the Infectious Period
Respiratory TB Symptoms	Sputum Smear Positive	Pulmonary Cavity on Chest X-ray	
Yes	No	No	3 months before symptom onset or first finding consistent with TB disease, whichever is earlier
Yes	Yes	Yes	3 months before symptom onset or first finding consistent with TB disease, whichever is earlier
No	No	No	1 month (4 weeks) before date of suspected diagnosis
No	Yes	Yes	3 months before first finding consistent with TB disease

Estimating the End of the Infectious Period

TB patients rapidly become less contagious while receiving treatment, but the exact rate of decrease cannot be predicted for individual patients, and a subjective determination is required for each.

In general, **for the purposes of a contact investigation**, the infectious period is over when exposure to contacts has ended (e.g., the patient is isolated under airborne infection isolation procedures) **OR** when the index patient meets **all three** of the following criteria:

1. The TB patient is on an appropriate treatment regimen – such as RIPE therapy (rifampin, isoniazid, pyrazinamide and ethambutol) for pan-susceptible patients – for at least two weeks
2. The TB patient has diminished symptoms
3. The TB patient exhibits mycobacteriologic response (e.g., decrease in grade of sputum smear positivity detected on sputum-smear microscopy)

There are three important exceptions:

- **Multidrug-resistant TB (MDR-TB) and extensively-resistant TB (XDR-TB):** Extend the infectious period if the treatment regimen is ineffective.
- **Signs of infectiousness:** Any TB case with signs of continued infectiousness should be continually reassessed for recent contacts.
- **High-risk contacts:** Apply more stringent criteria for setting the end of the infectious period if high-risk contacts are involved. A patient returning to a congregate living setting,

or to any setting in which high-risk persons might be exposed, should have at least three consecutive negative AFB sputum smear results from sputum collected more than eight hours apart (with one specimen collected during the early morning) before being considered noninfectious.

Figure 1.1 shows an example of how to determine an initial estimate for the beginning and the end of the infectious period for a patient with a positive sputum smear result and symptoms of TB disease.

Figure 1.1 – Example of determining the start and end of the infectious period for a smear positive patient (case) with TB symptoms

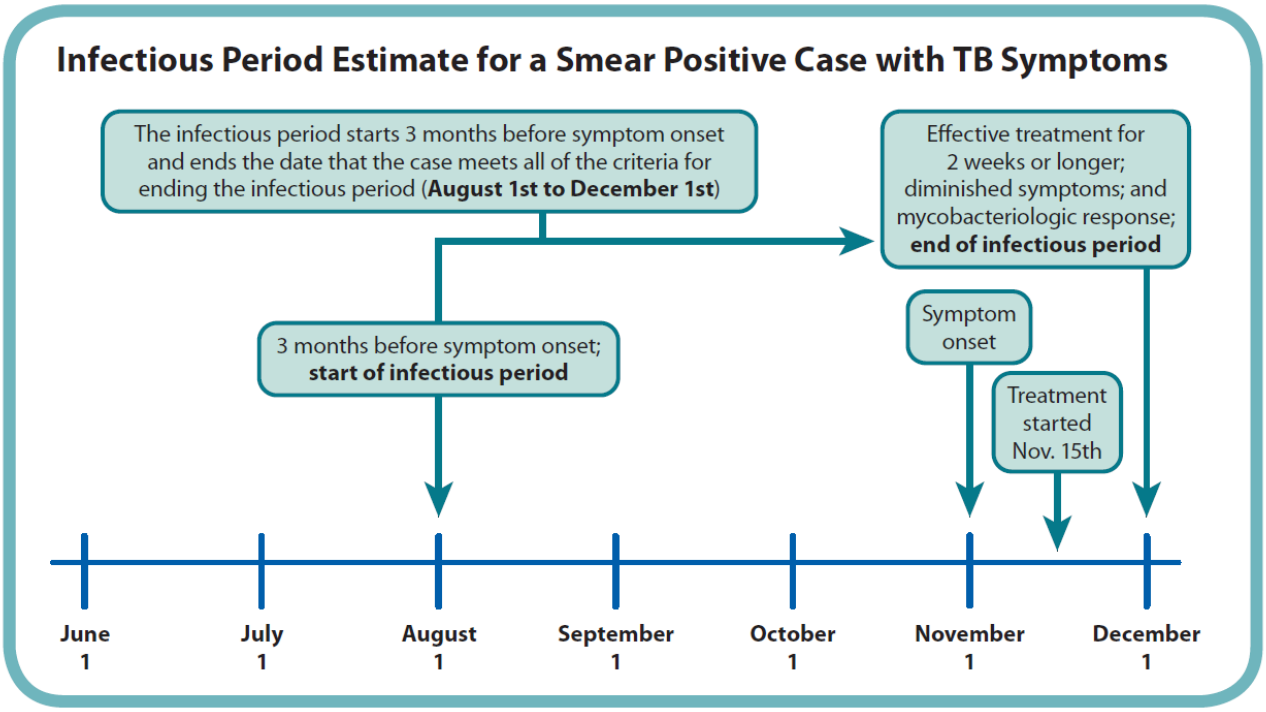
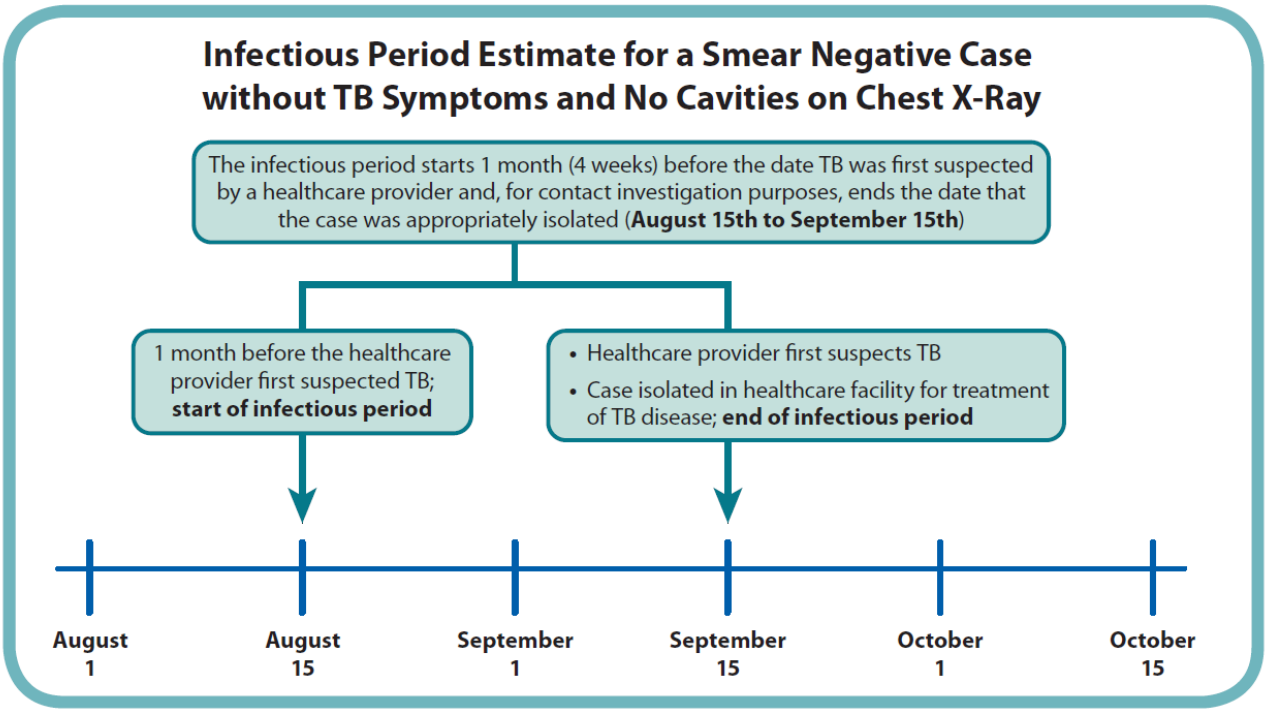


Figure 1.2 shows an example of how to determine an initial estimate for the beginning and the end of the infectious period for a patient with a negative sputum smear result, no TB symptoms and no cavities on CXR.

Figure 1.2 –Infectious period estimate for a smear negative patient (case) without TB symptoms and no cavities on chest x-ray



Estimating the Patient's Degree of Infectiousness

The greater the degree of a patient's infectiousness, the more likely that transmission occurred.

An initial estimate of the degree of infectiousness can be made during the pre-interview phase of the contact investigation and revised after the patient interview and as the investigation continues.

Table 2 lists the factors that should be considered when estimating the patient's degree of infectiousness.

Table 2: Factors Associated with Infectiousness and Noninfectiousness

Factors Associated with *More* Infectiousness	Factors Associated with *Less* Infectiousness
Presence of a cough	No cough
Cavity in the lung	No cavity in the lung
Acid-fast bacilli on sputum smear	No acid-fast bacilli on sputum smear
TB of the lungs, airway or larynx	Extrapulmonary (non-respiratory) TB
Patient not covering nose or mouth when coughing or sneezing	Patient covering mouth or nose when coughing or sneezing
Not receiving adequate treatment of having prolonged illness	Receiving adequate treatment for two weeks or longer
Undergoing cough-inducing procedures	Not undergoing cough-inducing procedures
Positive sputum cultures	Negative sputum cultures

INTERVIEWING THE PATIENT

The foundation of an effective contact investigation is the patient interview, and it is very important that the investigator is trained and skilled in conducting patient interviews. If the case investigator does not establish trust and rapport with the patient, he or she is unlikely to obtain the information necessary to identify and medically evaluate persons who were exposed to *M. tuberculosis* during the case patient's infectious period. For more information, see the 2019 video *Effective Interviewing for Tuberculosis Contact Investigations* by the Global TB Institute at Rutgers: http://globaltb.njms.rutgers.edu/educationalmaterials/productfolder/ci_video.php. A companion interview guide is included as Appendix B to this chapter.

> **Note:** One of the National TB Indicators Project (NTIP) objectives for 2025 is to increase the proportion of TB patients with AFB-positive sputum smear results who have contacts elicited.

To gather information about contacts who may have been exposed to M. tuberculosis, the investigator should ask the patient:

- **Where** he or she spent time during the infectious period, and for each place:
  - The amount of time spent there
  - Physical characteristics of the place e.g., room size, crowding, and ventilation
- **What** activities or events he or she participated in during the infectious period, including:
  - On a typical day

    - Any special events or holiday celebrations
    - Any volunteer activities especially in day care, a school, a hospital or nursing home
- **Whom** he or she spent time with during the infectious period, particularly:
    - Any children less than 5 years of age
    - Anyone with a medical condition that weakens the immune system
    - Anyone who had TB symptoms such as coughing, weight loss, and fatigue
- For each contact listed, the investigator should obtain locating information such as a phone number or home or workplace address.

During the interview, the investigator needs to be sensitive to situations where the case patient may be reluctant to identify contacts who live in the United States illegally or who misuse alcohol or illegal drugs. The investigator needs to reassure the case patient that all information is kept confidential and explain the importance of testing contacts to eliminate further spread of TB disease.

Additional goals of the interview are to:

- Describe the contact investigation process. A case patient who understands why and how a contact investigation is done is more likely to provide information.
- Educate the case patient about TB disease. The case patient may have little or no knowledge of TB, may have misconceptions about TB, or may be reluctant to seek information due to stigma about the disease.
- Confirm or correct information obtained during the pre-interview phase of the investigation, especially about any personal history of TB disease and/or TB symptoms and any contact during their lifetime with other individuals who had TB.

The initial patient interview should be done 1 to 3 days after the health authority receives notice of an infectious case. A second interview should be scheduled 1 to 2 weeks later, which allows the patient time to adjust to their TB diagnosis and treatment. Additional interviews can be scheduled as needed or conducted during routine visits to provide directly observed therapy (DOT) and assess the patient's response to treatment.

All interviews should be done in person and can occur in the hospital, TB clinic, the patient's home, or any other location that is convenient for the patient and that respects his or her privacy. Unless there are extenuating circumstances, at least one interview should be done in the patient's home so that the investigator can look for clues that young children or other adults live with or frequently visit the patient and may have been exposed to TB.

For more information about strategies for conducting effective patient interviews see *CDC Tuberculosis Self-Study Module 8: Contact Investigations for Tuberculosis*. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/Module8.pdf.

FLIGHT INVESTIGATIONS

For patients suspected or confirmed of having infectious pulmonary TB, be sure to ask about any travel during the estimated infectious period. If the patient travelled by air during the past six months on a flight lasting eight hours or more, ask the patient for specifics, including the date of the flight, the airline, the flight departure and destination cities and where the patient sat on the plane. Notify the state TB program manager immediately and provide him or her with the flight information. The TB program manager will then contact CDC's Division of Global Migration and Quarantine (DGMQ) office at the Philadelphia International Airport and a DGMQ officer will schedule a teleconference with the state and local public health personnel familiar with the case to review the facts and determine next steps.

REVIEW INFORMATION AND DEVELOP AN INVESTIGATION PLAN

After the case investigator has interviewed the patient, he or she should meet with his or her supervisor to review all the information obtained to date and develop a plan for the remainder of the investigation. For a large, challenging (e.g., the index case is multi drug or extensively drug-resistant) or complicated (e.g., contacts have been identified in multiple jurisdictions) investigation, a contact investigation team may be established.

As part of the planning process, the investigator or team should:

- Refine the calculation of the infectious period and degree of infectiousness for the case based on any new information obtained after the initial estimates were prepared
- Prioritize contacts for assessment
- Prioritize places where contact with the case occurred for field visits
- If appropriate, (e.g., a high-volume contact investigation, a contact investigation in a school, or for a multi-drug or extensively-drug resistant case) establish a communication plan among all personnel involved in the conduct of the contact investigation
- Clarify any jurisdictional issues
- Establish timeframes and methods for investigation activities, data collection and management
- Determine stakeholders in the investigation
- Determine potential media interest in the investigation
- Schedule case conferences or meetings to review progress and resolve challenges

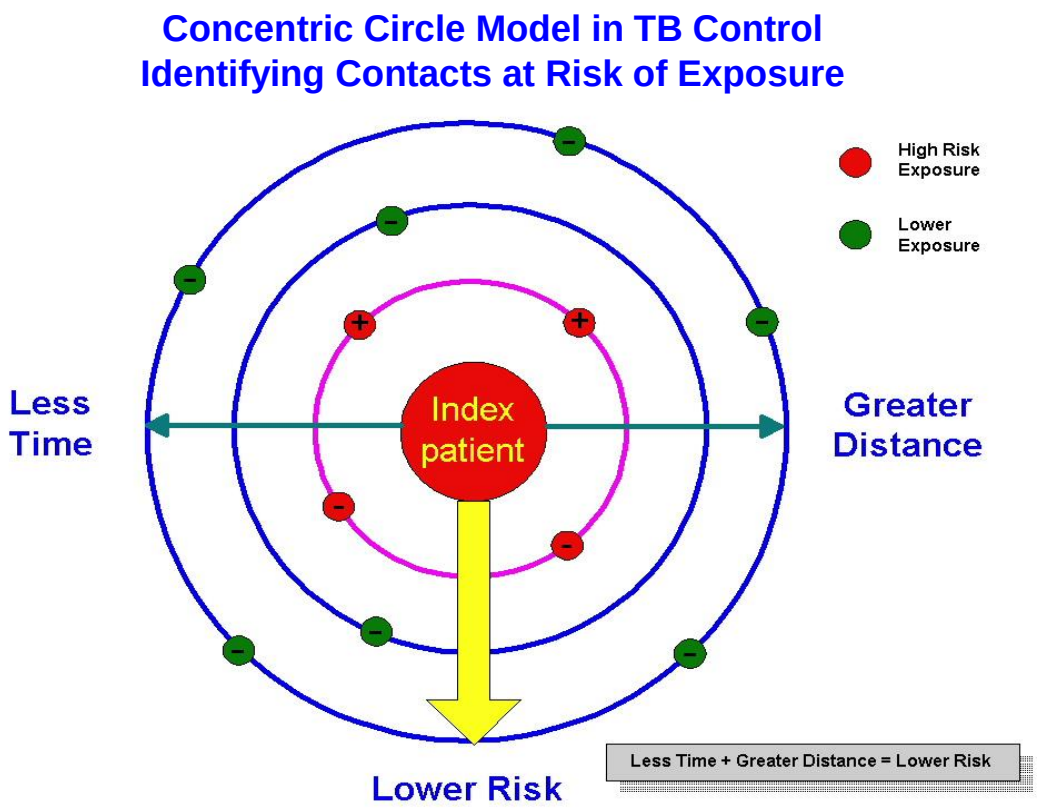
The investigation plan should be written and include where to conduct field visits, which contacts are considered a priority for assessment, and a timeline for accomplishing these tasks. If the health department has multiple TB cases requiring contact investigations, the information in the plan should be used to help prioritize which contact investigations require immediate attention and resources. The plan should be considered a work in progress and be updated as needed throughout the investigation.

PRIORITIZE CONTACTS

During the planning meeting, the investigator should use information from the initial interview of the index patient to prioritize contacts for assessment. The priority assigned to each contact should be based on:

- How much time (duration and frequency) the contact spent with the index patient;
- The distance from the index patient during exposure as well as environmental factors (outdoors, indoors with ventilation, indoors without ventilation, etc.); and
- Any medical conditions of the contact that place him or her at increased risk for progressing to TB disease once infected.

These concepts are illustrated in the concentric circle model.



The priority assigned to each contact should be based on both:

- The infectiousness and likelihood of transmission by the case; and
- The contact's risk of progressing to TB disease once infected.

The assignment of contacts as high, medium or low priority should be done in consultation with supervisory clinical and management staff or during a case conference with the contact investigation team. Dividing contacts into these three levels provides a system to reach high-priority contacts first, then medium-priority contacts, and finally low-priority contacts. The priority scheme directs resources to the following essential actions:

- Identification of contacts who are secondary active TB cases;
- Identification of contacts who have recent *M. tuberculosis* infection—the most likely to benefit from treatment; and
- Identification of contacts who are most likely to progress to TB disease if they are infected (i.e., high-risk contacts) or who could suffer severe morbidity if they had TB disease (i.e., vulnerable contacts).

Tables 3, 4, and 5 on the following pages provide a summary of contact priorities based on the above criteria.

INDEX PATIENT WITH POSITIVE ACID-FAST BACILLI SPUTUM SMEAR RESULTS OR CAVITARY TUBERCULOSIS

TABLE 3: **PRIORITIZATION OF CONTACTS TO SMEAR-POSITIVE OR CAVITARY CASES**

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
• Household contacts • Contacts less than 5 years of age • Contacts with human immunodeficiency virus (HIV) infection or other immunocompromising condition • Contacts with exposure during a medical procedure such as bronchoscopy, sputum induction, or autopsy • Contacts with exposure in a congregate setting • Contacts whose exposure exceeds duration/environment limits per unit time established by the health department for high-priority contacts*	• Contacts not in high-priority groups • Contacts 5–15 years old • Contacts whose exposure exceeds duration/ environment limits per unit time established by the health department for medium-priority contacts*	• Contacts not in high-priority groups • Contacts not in medium-priority groups
* Observe environmental characteristics, such as room size, crowding, and ventilation to estimate the risk of TB transmission; air volume, exhaust rate, and circulation assist in predicting the likelihood of transmission in an enclosed space.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54 (No. RR-15):12. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

INDEX PATIENT WITH NEGATIVE ACID-FAST BACILLI SPUTUM SMEAR RESULTS

TABLE 4: **PRIORITIZATION OF CONTACTS TO SMEAR-NEGATIVE CASES**

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
• Contacts less than 5 years of age • Contacts with human immunodeficiency virus (HIV) infection or other immunocompromising conditions • Contacts exposed during a medical procedure such as bronchoscopy, sputum induction, or autopsy	• Contacts not in high-priority groups • Household contacts • Contacts exposed in a congregate setting • Contacts whose exposure exceeds duration/environment limits per unit time established by the by the local TB control program for medium-priority contacts *	• Contacts not in high-priority groups • Contacts not in medium-priority groups
* Observe environmental characteristics, such as room size, crowding, and ventilation to estimate the risk of TB transmission; air volume, exhaust rate, and circulation assist in predicting the likelihood of transmission in an enclosed space.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):13. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

INDEX PATIENT WITH NEGATIVE BACTERIOLOGIC RESULTS AND ABNORMAL CHEST RADIOGRAPHS NOT CONSISTENT WITH TUBERCULOSIS

TABLE 5: **PRIORITIZATION OF CONTACTS TO CASES WITH NEGATIVE BACTERIOLOGIC RESULTS AND ABNORMAL CHEST RADIOGRAPHS NOT CONSISTENT WITH TUBERCULOSIS**

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
	• Household contacts • Contacts less than 5 years of age • Contacts with human immunodeficiency virus (HIV) infection or other medical risk factor • Contacts exposed during a medical procedure such as bronchoscopy, sputum induction, or autopsy	• Contacts not in medium-priority groups

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):14. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

CONDUCT FIELD INVESTIGATIONS

Field investigations include visiting the patient's home or shelter, workplace (if any), and the other places where the patient spent time while infectious. The purpose of the field investigation is to identify contacts and evaluate the environmental characteristics of the place in which exposure occurred.

During field investigations, the investigator should:

- **Observe environmental characteristics** such as room size, crowding, and ventilation. Air volume, exhaust rate, and circulation predict the likelihood of transmission in an enclosed space. In large indoor settings, the degree of proximity between contacts and the index patient can influence the likelihood of transmission. The volume of air shared between an infectious TB patient and contacts dilute the infectious particles. Local circulation and overall room ventilation also dilute infectious particles, but both factors must be considered because they can redirect exposure into spaces that were not visited by the index patient.
- **Identify additional contacts** (especially children) and their locating information, such as phone numbers and addresses.
- **Look for evidence of other contacts** who may not be present at the time of the visit (for example, pictures of others who may live in or visit the house, shoes of others who may live in the house or toys left by children).
- **Interview and test high- and medium-priority contacts** who are present and arrange to let them know of the results.
- **Educate the contacts** about the purpose of a contact investigation, the basics of transmission, the risk of transmitting *M. tuberculosis* to others, and the importance of testing, treatment, and follow-up for LTBI and TB disease.
- **Refer contacts who have TB symptoms** for a medical evaluation, including sputum collection.

The investigator and other healthcare personnel should remember to follow infection control precautions while visiting a potentially infectious TB patient at home or in any other location. These precautions may include wearing personal protective equipment (i.e. N95 or N100 respirators).

Another critical consideration during field investigations is safety. The investigator should become familiar with policies and recommendations of local law enforcement agencies and health department administration regarding personal safety. Current information on local high-risk areas for crime can be very valuable in planning and conducting safe field visits.

General safety precautions that are recommended for the investigator and other healthcare workers include the following:

- Wearing a photo ID

- Working in pairs when visiting a potentially dangerous area
- Informing supervisor/office staff of your itinerary and expected time of return, especially if you anticipate problems

TIME FRAMES FOR INTERVIEWING THE INDEX PATIENT AND INVESTIGATING POTENTIAL TRANSMISSION SITES

Because of the urgency of finding other infectious cases associated with the index patient, the first interview should be done within one to three business days of the index patient being diagnosed, as outlined in **Table 6: Time Frames for Investigating the Index Patient and the Sites of Transmission**.

TABLE 6: **TIME FRAMES FOR INVESTIGATING THE INDEX PATIENT AND THE SITES OF TRANSMISSION**

Suspects Expected to Be Cases of Tuberculosis		
Activity	**Suspects with Indications of Infectiousness**	**Suspects Without Indications of Infectiousness**
Initial Index Patient Interview Number of days following notification within which the index patient should be interviewed in person, and may occur in the hospital (however, not by telephone)	≤1 Business Day of Reporting	≤3 Business Days of Reporting
Residence Visit Number of days following the first index patient interview within which the place of residence of the index patient should be visited	≤3 Business Days After First Interview	3 Business Days After First Interview
Field Investigation Number of days following initiation of the contact investigation within which all potential settings for transmission should be visited	5 – 7 Business Days After the Start of the Investigation	5 – 7 Business Days After the Start of the Investigation
Index Patient Re-interviews Length of time after the first interview within which the index patient should be re-interviewed one or more times for clarification and additional information	1 or 2 Weeks After First Interview	1 or 2 Weeks After First Interview

Suspects Expected to Be Cases of Tuberculosis		
Activity	**Suspects with Indications of Infectiousness**	**Suspects Without Indications of Infectiousness**
Reassessment of Index Patient Information about the index patient should be reassessed at least weekly until drug-susceptibility results are available for the *M. tuberculosis* isolate or for 2 months following notification, whichever is longer.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):7–8. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

CONTACT EVALUATION AND TREATMENT

In addition to the investigation of the index patient and transmission sites, a contact investigation also involves contact follow-up.

Every new case of TB was initially a contact to someone with infectious TB, which highlights why the proper evaluation and treatment of contacts is an essential component of the contact investigation process.

Note: The NTIP objectives for 2025 include three objectives concerning the evaluation and treatment of contacts:

- Examination – For contacts to AFB sputum-smear positive TB cases, increase the proportion who are examined for LTBI and TB disease.
- Treatment Initiation – For contacts to AFB sputum-smear positive TB cases (who are) diagnosed with LTBI, increase the proportion who start treatment.
- Treatment completion – For contacts to AFB sputum-smear positive TB cases who have started treatment for LTBI, increase the proportion who complete treatment.

Refer to **Table 7: Time Frames for Contact Evaluation and Treatment** to monitor the progress of the investigation and determine whether additional resources are needed for finding, evaluating, and treating the high- and medium-priority contacts.

TABLE 7: **TIME FRAMES FOR CONTACT EVALUATION AND TREATMENT**

Type of Contact	Business Days from Listing of a Contact to Initial Encounter*	Business Days from Initial Encounter to Completion of Medical Evaluation†	Business Days from Completion of Medical Evaluation to Start of Treatment
High-Priority Contact Index patient with AFB **positive** sputum smear results or cavitary disease on CXR	**3 Business Days After Being Listed in the Investigation**	5 Business Days	10 Business Days
High-Priority Contact Index patient with AFB **negative** sputum smear results	**3 Business Days After Being Listed in the Investigation**	10 Business Days	10 Business Days
Medium-Priority Contact Regardless of AFB sputum smear or culture result	**3 Business Days After Being Listed in the Investigation**	10 Business Days	10 Business Days

* "Encounter" means a face-to-face meeting, which gives the PHN an opportunity to determine whether the contact is generally healthy or ill. The initial encounter also provides opportunities to administer a TB test and to schedule further evaluation.

† The medical evaluation is complete when the contact's diagnosis of tuberculosis infection or TB disease has been determined. A normal exception to this schedule is the delay in waiting for final mycobacteriology results, but this applies to relatively few contacts.

Source: Adapted from CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR*2005;54(No. RR-15):9. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

CONTACT EVALUATION, TREATMENT, AND FOLLOW-UP

Complete evaluation, treatment, and follow-up for high- and medium-priority contacts, as specified in the contact investigation plan. The Centers for Disease Control and Prevention (CDC) recommends the following:

- Complete an initial assessment of each high- and medium-priority contact that includes a face-to-face encounter in which an impression of each contact's general health is formed and a TB test is administered.
- Medically evaluate each high- and medium-priority contact to determine whether TB disease or LTBI is present or absent.

- Timely initiation of treatment is especially important for high-priority contacts and for contacts likely to progress to TB disease if they are infected (i.e., high-risk contacts) or contacts who could suffer severe morbidity if they had TB disease (i.e., vulnerable contacts). Use the same diagnostic methods for all contacts, except when they have medical or constitutional conditions making TB more likely or more difficult to diagnose. In contacts of an infectious case who are foreign-born or BCG-vaccinated, interpret a positive TST as evidence of recent *M. tuberculosis* infection. Evaluate these contacts for TB disease. If a diagnosis of TB disease is excluded, encourage them to complete the shortest regimen of LTBI treatment appropriate for the specific patient.

Use the tables on the following pages to determine the evaluation activities for contacts in these different risk groups and priority rankings:

1. **Table 8: Immunocompromised Contacts and Children Less than 5 Years of Age**
2. **Table 9: Immunocompetent Adults and Children 5 and Older (High and Medium-Priority Contacts)**
3. **Table 10: Contacts with Prior Positive Tuberculin Skin Tests**

IMMUNOCOMPROMISED CONTACTS AND CHILDREN LESS THAN 5 YEARS OF AGE

Refer to Table 8 to select evaluation, treatment, and follow-up activities for contacts who are immunocompromised and/or less than 5 years of age.

Evaluate these contacts with medical history, physical examination, CXR, and IGRA or TST. Based on the results of these evaluations, take the actions in Table 8.

The American Thoracic Society (ATS), the Centers for Disease Control and Prevention (CDC), and the American Academy of Pediatrics (AAP) recommend that contacts less than 5 years of age be treated for presumptive LTBI – even if their first IGRA or TST is negative – once a diagnosis of TB disease has been eliminated. In those instances where these high priority contacts may not be evaluated in TB clinic for a month or longer, discuss with the TB clinician the feasibility of starting LTBI preventative treatment (also known as window prophylaxis) immediately.

TABLE 8: **EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPROMISED CONTACTS AND CHILDREN LESS THAN 5 YEARS OF AGE**

If the contact's medical evaluation or TB test results show:		Then take this action or these actions:
Symptoms consistent with TB disease and/or abnormal CXR		Fully evaluate for TB disease
No symptoms consistent with TB	A. IGRA is positive or 1st TST ≥5 mm	Complete a full course of treatment for LTBI

If the contact's medical evaluation or TB test results show:		Then take this action or these actions:
disease and normal CXR	B. IGRA or 1st TST was done 8-10 weeks since last exposure and either the IGRA was negative or the 1st TST result was <5 mm	If not HIV-infected, no further evaluation required If HIV-infected, no further evaluation required; consider a full course of treatment for LTBI
	C. IGRA or 1st TST was done less than 8 weeks since last exposure and either the IGRA was negative or the 1st TST result was <5 mm Upon retest:	Begin (window prophylaxis) treatment for LTBI and retest 8–10 weeks post exposure
	If the 2nd IGRA is positive or the 2nd TST result was ≥5 mm	Complete a full course of treatment for LTBI
	If the 2nd IGRA is negative or the 2nd TST result was <5 mm	• If not HIV-infected, no further evaluation required • If HIV-infected, no further evaluation required; consider a full course of treatment for LTBI
Definitions of abbreviations: HIV = human immunodeficiency virus; IGRA = interferon gamma release assay; TB = tuberculosis; TST = tuberculin skin test.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):15–16. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

IMMUNOCOMPETENT ADULTS AND CHILDREN 5 YEARS OF AGE AND OLDER

Refer to Table 9 to select evaluation, treatment, and follow-up activities for high- and medium-priority contacts who are immunocompetent and/or 5 years of age or older.

Evaluate high- and medium-priority contacts with medical history, exposure history, and an IGRA or TST. Based on the results of these evaluations, take the actions in Table 9.

TABLE 9: **EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPETENT ADULTS AND CHILDREN 5 YEARS OF AGE OR OLDER (HIGH- AND MEDIUM-PRIORITY CONTACTS)**

If the contact's medical evaluation or test results show:		Then take this action or these actions:
Symptoms consistent with TB disease		Fully evaluate for TB disease
No symptoms consistent with TB disease	A. IGRA is positive or 1st TST ≥5 mm	Evaluate with a physical examination and CXR: • If CXR abnormal, fully evaluate for TB disease • If CXR normal, complete a full course of treatment for LTBI
No symptoms consistent with TB disease	B. IGRA or 1st TST was done 8-10 weeks since last exposure and either the IGRA was negative or the 1st TST result was <5 mm	No further evaluation or treatment required
No symptoms consistent with TB disease	C. IGRA or 1st TST was done less than 8 weeks since last exposure and either the IGRA was negative or the 1st TST result was <5 mm Upon retest: If the 2nd IGRA is positive or the 2nd TST result was ≥ 5mm If the 2nd IGRA is negative or the 2nd TST result was <5mm	Retest 8–10 weeks post exposure Evaluate with a physical examination and CXR: • If CXR abnormal, fully evaluate for TB disease • If CXR normal, complete a full course of treatment for LTBI No further evaluation or treatment required
Definitions of abbreviations: CXR = chest radiograph; IGRA = interferon gamma release assay; TB = tuberculosis; TST = tuberculin skin test.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):17. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

CONTACTS WITH A PRIOR POSITIVE TB TEST

Refer to Table 10 to select evaluation, treatment, and follow-up activities for contacts who have a prior positive TB test (IGRA or TST).

For contacts, evaluate them with medical and exposure history. Based on these histories, take the actions in Table 10.

TABLE 10: **EVALUATION, TREATMENT, AND FOLLOW-UP OF CONTACTS WITH PRIOR POSITIVE TUBERCULIN SKIN TESTS**

If the contact's medical evaluation shows:		Then take this action or these actions:
Symptoms consistent with TB disease		Fully evaluate for TB disease
No symptoms consistent with TB disease	Immunocompromised or less than 5 years of age	Evaluate with a physical examination and CXR: If CXR or physical examination is indicative of TB disease, fully evaluate for TB disease If results do not indicate TB disease: • If contact previously completed treatment, consider retreatment • If treatment was **not** completed previously, complete a full course of LTBI treatment
No symptoms consistent with TB disease	Immunocompetent and 5 years of age or more	If contact previously completed treatment for LTBI, no further evaluation or treatment required If contact has **not** completed treatment for LTBI, consider LTBI treatment
Definitions of abbreviations: CXR = chest radiograph; TB = tuberculosis.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):19. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

LOW-PRIORITY CONTACTS

Refer to Table 11 to select evaluation, treatment, and follow-up activities for low-priority contacts. Evaluate low-priority contacts with medical and exposure history.

TABLE 11: **EVALUATION, TREATMENT, AND FOLLOW-UP OF LOW-PRIORITY CONTACTS**

If evaluation or test results show that a contact has:		Then take this action or these actions:
Symptoms consistent with TB disease		Fully evaluate for TB disease
No symptoms consistent with TB disease	8–10 weeks since last exposure	Test with an IGRA or TST

If evaluation or test results show that a contact has:		Then take this action or these actions:
No symptoms consistent with TB disease	<8 weeks since last exposure	Wait 8–10 weeks after last exposure, and then test with an IGRA or TST
No symptoms consistent with TB disease	IGRA is positive or TST ≥5 mm	Evaluate with physical examination and CXR: If CXR is abnormal, fully evaluate for TB disease If CXR is normal, consider treatment for LTBI
No symptoms consistent with TB disease	IGRA is negative or TST <5 mm	No further evaluation or treatment required
Definitions of abbreviations: CXR = chest radiograph; IGRA = interferon gamma release assay; TB = tuberculosis; TST = tuberculin skin test.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):22. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

WHEN TO EXPAND A CONTACT INVESTIGATION

GUIDELINES FOR EXPANDING AN INVESTIGATION

Throughout the contact investigation process, it's important to continually review findings to determine whether it's necessary to expand the scope of the investigation. Any decision to expand a contact investigation should be based on the TB test results for the medium and high priority contacts. If evidence emerges indicating recent transmission of TB, then it's likely the scope of the investigation needs to expand.

Evidence of recent transmission of TB disease includes:

- TB disease in any contact
- LTBI in contacts less than 5 years of age
- A change in contacts' IGRA or TST result from negative (i.e., for the initial test) to positive (i.e., 8 to 10 weeks after the last exposure to the case)
- A greater than expected rate of TB disease among the priority contacts. An infected contact who develops TB disease is referred to as a secondary case of TB. A separate contact investigation should be considered for each secondary case of TB. Secondary transmission of TB may also indicate that a TB outbreak is occurring, especially if the genotypes match.
- A greater than expected prevalence of LTBI among case contacts, with prevalence defined as the percentage of persons with LTBI in a defined population. A commonly used threshold for expanding a contact investigation is a LTBI prevalence rate of 10% or more among case contacts.

- If TB disease occurs in a contact who was originally considered a low priority for evaluation, this may indicate a need to expand the contact investigation.
- Generally, if any of the above examples of recent transmission are detected, then expanding the contact investigation to include contacts originally assigned a lower priority should be considered.
- When results from an investigation indicate that it should be expanded, but resources are insufficient, contact the next higher level in public health administration (e.g., the local nurse supervisor and the state TB program manager).
- Do not expand a contact investigation to lower-priority contacts unless:
  - There is evidence of recent transmission; or
  - There is a unique situation that has been reviewed with the state TB program and the state TB medical consultant and the latter has recommended expansion of the contact investigation.
- Review the incoming results of the contact investigation at least weekly to reassess the scope and elements of the plan.

OVERVIEW OF ONGOING CONTACT INVESTIGATION ACTIVITIES

Ongoing contact follow-up includes testing, medical evaluation, and treatment. Information from contact follow-up guides decisions about whether to expand a contact investigation. Refer to **Table 12: Overview of Ongoing Management Activities and Maximum Time Frames** to monitor the progress of ongoing contact follow-up and to determine when to decide whether to expand the investigation.

TABLE 12: **OVERVIEW OF ONGOING MANAGEMENT ACTIVITIES AND MAXIMUM TIME FRAMES FOR THE COMMUNITY HEALTH NURSE**

Activity	Purpose	Maximum Time Interval
Review all documentation	To ensure that contact list is complete	Ongoing
Review and assess completeness of each contact's medical follow-up and treatment plan	To ensure appropriate and complete medical follow-up	5 business days after each contact's medical evaluation is completed*
Review and assess the timeliness of initiating the treatment plan	To avoid delays in treatment initiation, particularly in high-risk contacts	10 business days after each contact's medical evaluation is completed*
Determine if transmission occurred	To decide whether to expand investigation	At completion of follow-up testing, or if secondary cases are identified

Activity	Purpose	Maximum Time Interval
Obtain and review drug-susceptibility results	To determine if contacts are receiving appropriate treatment for LTBI	1 to 2 months after the index patient's initial sputum collection date
Repeat the TB test if contact initially tests negative	To determine if contact has converted (TB Class I to TB Class II)	8 to 10 weeks after each contact's initial TB test or last exposure to the index patient†
Reevaluate contacts whose TB test was initially negative and started on LTBI treatment (Window Period Treatment for a TB Class I Contact)	To determine if treatment for LTBI should be continued	8 to 10 weeks after each contact's initial TST or last exposure to the index patient before the end of the infectious period†
Assess contacts' adherence with medical follow-up and TB medication	To remove barriers and ensure timely and complete evaluation and follow-up	Monthly, at time of each visit
Ensure contacts are monitored for adverse reactions and toxicity of LTBI treatment regimens	To prevent development of adverse effects and toxicity from drug regimens	At least monthly while on LTBI treatment in either nurse directed or MD TB clinics
Evaluate problems and concerns that arise and may delay or hamper contact investigation	To remove barriers and ensure timely and complete evaluation and follow-up	Whenever problems are identified
Collect and analyze data to evaluate the contact investigation	To provide epidemiologic analysis of investigations and to measure performance using indicators that reflect performance objectives	Ongoing
Ensure the data for all contacts is complete in PA-NEDSS so the TB program manager can accurately complete the *Aggregate Reports for Tuberculosis Program Evaluation (ARPE)* form	To report on investigation to the Centers for Disease Control and Prevention	Ongoing

Activity	Purpose	Maximum Time Interval
* The medical evaluation is complete when the contact's status relative to *M. tuberculosis* infection or TB disease has been determined. A normal exception to this schedule is the delay in waiting for final mycobacteriology results, but this applies to relatively few contacts. † Third TB test: In rare circumstances, an infectious index patient with advanced disease can stay infectious for several months. In these circumstances, the second TB test for negative contacts should be performed in the usual time frame (8 to 10 weeks). This will identify any contacts who have already converted so they can be evaluated for treatment. However, any household members whose second TB test is negative and have continued exposure to the infectious index patient should have a third TB test 8 to 10 weeks after the index patient becomes noninfectious. This is especially true for contacts who are infants in a household where a resident is culture positive after 3 months or has multidrug-resistant TB. For example, a household member with continued exposure to an infectious index patient had a negative second TB test on 3/12/2007. The last date the index patient was infectious was 3/5/2007. The household member should have a third TB test 8 to 10 weeks from 3/5/2007.		

Source: Adapted from: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). Contact investigation guidelines. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. November 12, 1998:18. Available at: http://www.ctca.org/fileLibrary/file_363.pdf.

DATA MANAGEMENT AND EVALUATION OF CONTACT INVESTIGATIONS

Data collection related to contact investigations has three (3) broad purposes:

1. Management of care and follow-up of individual index patients and contacts
2. Epidemiological analysis of an investigation in progress and overall investigations
3. Program evaluation via performance indicators that reflect performance objectives

The public health nurse and the state TB program both have roles in collecting and analyzing the data related to contact investigations. These activities include the public health nurse entering contact investigation data into PA-NEDSS and the state TB program staff analyzing and summarizing data before it is forwarded to CDC.

INDEX PATIENT AND CONTACT DATA

For each index patient all RVCT information should be entered in PA-NEDSS:

TABLE 13: **DATA ABOUT THE INDEX PATIENT**

Identifiers/Demographic Information	Name and aliases For minors and dependents: guardian information Date of birth Social security number Current locating information and emergency contacts Residences during infectious period if unstably housed Sex Race Ethnicity Country of birth Time in the United States, if foreign born Primary language and preferred language Methods of translation or interpretation
Transmission Settings and Associated Time Frames	Living situation(s) Employment or school Social/recreational activities Congregate settings (e.g., jail, homeless shelter) Substance abuse with social implications
Tuberculosis Information	Healthcare provider for TB (e.g., public health, private, both, other) Anatomic site of disease
Definitions of abbreviations: AIDS = acquired immunodeficiency syndrome; CXR = chest radiograph; HIV = human immunodeficiency virus; *RVCT = Reports of Verified Cases of Tuberculosis*; TB = tuberculosis.	

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *M. tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):21. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

The following information should be added for each contact to the index case:

TABLE 14: **DATA ABOUT EACH CONTACT**

Investigator and Dates	Contact manager or investigator Date listed How or why contact was listed (e.g., named by index patient) Dates of interviews Start and end dates for exposure (updated as new information arrives)

Identifiers	Name and aliases For minors and dependents: guardian information Social security number Date of birth Locating information and emergency contacts Sex Race Ethnicity Country of birth Time in United States, if foreign born Primary language and preferred language Methods of translation or interpretation
Exposure	Relationship/connection to index patient Social affiliations (e.g., work, school, church, clubs, activities) Environmental information about exposure settings (e.g., size, ventilation) Frequency, duration, and time frame of interactions
Medical History and Risk Factors	Prior history of TB disease or LTBI, and documentation BCG vaccination and date Medical risk factors for progression of LTBI to TB disease† Population risk factors for prevalent *M. tuberculosis* infection†
Evaluation for Tuberculosis Disease and LTBI	Healthcare provider for TB (e.g., public health, private, both, other) Symptoms suggesting TB disease TSTs, with dates, reagents and lot numbers, reaction measurement IGRA results CXR results with dates Bacteriologic results with dates HIV infection status Final diagnostic classifications for LTBI or TB disease
Treatment Information for Contacts with LTBI	Dates of treatment Treatment regimen (medications, dosing schedule, any changes to these) Methods of supervising treatment (DOT, etc.) Adverse reactions (specify each) Interruptions in regimen and dates Outcome of treatment (completion, etc., consistent with *ARPE*†) If treatment not completed, reason†
Definitions of abbreviations: *ARPE* = *Aggregate Report for Program Evaluation*; BCG = Bacille Calmette-Guérin; CXR = chest radiograph; DOT = directly observed therapy; HIV = human immunodeficiency virus; IGRA = interferon gamma release assay; TB = tuberculosis; TST = tuberculin skin test. † As defined by CDC *ARPE* for contact investigations.	

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC*MMWR* 2005;54(No. RR-15):21. Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

EVALUATION OF A CONTACT INVESTIGATION

At the completion of a contact investigation, a review and evaluation of the investigation activities should be done by the contact investigator or contact investigation team and the appropriate supervisor(s). Evaluating the effectiveness of a contact investigation plan can be very helpful in improving the contact investigation process and, by extension, the overall effectiveness of the TB control program.

The objective of the review is to identify what went well, what didn't, and how the investigator or investigation team would do things differently in the future. The findings should be documented in a succinct report so that what was learned can be applied to future contact investigations.

TB OUTBREAK INVESTIGATION

If data from a contact investigation or surveillance indicate a potential outbreak, conduct an outbreak investigation. A TB outbreak warns of potential extensive transmission. An outbreak implies that 1) a TB patient was infectious, 2) contacts had significant exposure to the infectious case, and 3) the interval since exposure has been sufficient for infection to progress to disease. An outbreak investigation involves several overlapping contact investigations, with a surge in the need for public health resources. More emphasis on active case finding is recommended, which sometimes means that more contacts than usual should have CXRs and specimen collection for mycobacteriology.

For more information about the conduct of an Outbreak Investigation, see Chapter 13.

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CHAPTER 10, APPENDIX A: QUICK START CHECK LIST

This check list is designed to help public health nurses – whether at a SHC or CMHD – conduct a contact investigation. The tasks below should be performed by licensed nursing, medical, and laboratory staff.

Completion of the check list requires a thorough understanding of the instructions in this chapter and familiarity with applicable local protocols and standing orders.

Contact Investigation Tasks	Date Completed or Updated
Evaluate the Need for a Contact Investigation	
• Gather and review the index patient's medical records (from hospital, clinic, and/or healthcare provider)	☐
• Decide if a contact investigation is indicated. A contact investigation is not needed if the index case has only extrapulmonary TB and is noninfectious	☐
• Prepare a preliminary estimate of the index patient's a) infectious period and b) degree of infectiousness following the instructions in this chapter	☐
• If an investigation is indicated, start the contact investigation within 10 days of the case report	☐
Interview the Index Patient	
• Conduct the first interview **within ≤1 business day of the case report**	
• Visit the index patient's residence within **≤3 business days after first interview,** if not already done in the first interview	
• Re-interview the index patient **within 1 to 2 weeks after the first interview**	
• During the interviews, gather information on the following: ○ Additional medical history ○ Residence(s) ○ Transmission sites, including dates and times ○ Contacts	☐ ☐ ☐ ☐

Contact Investigation Tasks	Date Completed or Updated
After Interviewing the Index Patient	
Based on the information obtained during the case interview, update the patient's estimated: • Infectious period and • Degree of infectiousness	☐ ☐
List and Prioritize Contacts	
• During the index patient interview, list names and locating information of named contacts (plan to update this list throughout the investigation) • Assign an initial priority classification to each contact (plan to revise as needed when new information is received) • Review all documentation to ensure that the contact list is complete	☐ ☐ ☐
Complete the Field Investigation (Site Visits)	
• Visit all potential transmission sites **within 5-7 days after starting the investigation**	☐
Evaluate Contacts	

• Meet face-to-face with each high- and medium-priority contact within 3-5 business days. This assessment includes the following:
  ○ An impression of each contact's general health
  ○ Administration of an IGRA or a TST
• Assure that medical evaluations* are completed and window prophylaxis is started for latent TB infection (LTBI) in high-priority contacts who are children and/or have high-risk factors for progression to TB disease within 5-10 business days after initial encounters
• Assure that medical evaluations* are conducted of other high-priority contacts to index patients with AFB **positive** sputum smear results within 5-10 business days after initial encounters
	☐
	☐
	☐
	☐
	☐

Contact Investigation Tasks	Date Completed or Updated
• Assure that medical evaluations[1] are conducted of high-priority contacts to AFB **negative** sputum smear index patients and medium-priority contacts within 10-15 business days after initial encounters • Review and assess the completeness of contacts' medical follow-up and treatment plans **within 5-10 business days after their medical evaluations**	☐ ☐
Initiation of Treatment for LTBI	
• Educate the contact that treating LTBI prevents TB disease. • Ensure that treatment for LTBI is started for high-priority contacts that are children and/or have high-risk factors **within 5-10 business days after initial encounters**. • Ensure that treatment for LTBI is started for adult high- and medium-priority contacts without high-risk factors **within 10-15 business days of their medical evaluations** • Review and assess the timeliness of initiating the treatment plans for contacts **within 10 business days after their medical evaluations**	☐ ☐ ☐ ☐
Review Data and Documentation Weekly Throughout the Contact Investigation	
• Review documentation to ensure that the contact list is complete • Collect and analyze data on contacts and IGRA and TST test results • Reassess contact priorities • Evaluate whether there is a need to expand the contact investigation	☐ ☐ ☐ ☐

[1] *A medical evaluation for IGRA or TST positive contacts includes a medical history and CXR. HIV screening of these patients is strongly recommended. For contacts with symptoms of TB disease, the evaluation must also include a medical history and bacteriology tests.*

Contact Investigation Tasks	Date Completed or Updated
Enter Contacts in PA-NEDSS	
• Enter information for all identified contacts in PA-NEDSS including, but not limited to: ○ Demographics ○ Relationship to index case ○ Address/phone number(s)	☐ ☐ ☐
○ Test results including IGRA or TST and CXR (if indicated) ○ Treatment information if diagnosed with LTBI or TB disease	☐ ☐
Monitor Contacts on Treatment for LTBI	
• Assure that contacts are assessed at least monthly for: ○ Clinical follow-up ○ Adherence to LTBI treatment ○ Adverse reactions to LTBI treatment	☐ ☐ ☐
Retest Contacts	
• Contacts whose results were initially negative, repeat IGRA or TST **8 to 10 weeks after last exposure to the index patient during the infectious period** • **After retesting**, reevaluate contacts who were initially IGRA or TST negative and started on LTBI treatment to determine if treatment should be continued • **After retesting**, determine if transmission occurred and whether to expand the investigation	☐ ☐ ☐
Report on the Contact Investigation	
• Enter data in PA-NEDSS to include any additional test results and treatment information once the second phase of TB testing is **completed.**	☐

Contact Investigation Tasks	Date Completed or Updated
Confirm Contacts' Completion of Treatment for LTBI	
• Verify completion of treatment depending on regimen, adherence, and number of doses. • Provide the patient with a LTBI Treatment Summary letter and advise the patient to keep the letter as proof of treatment.	☐ ☐
Update Report on the Contact Investigation	
• Report data in PA-NEDSS **after contacts complete treatment for LTBI**	☐

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CHAPTER 10, APPENDIX B: TB PATIENT INTERVIEW CHECK LIST

Step	Date Completed
Pre-Interview Activities	
• Review the patient's medical record, including information about the diagnosis and medical history; social history and language or cultural barriers; and locating information • Estimate the preliminary infectious period • Develop an interview strategy • Arrange a date/time/location for the interview Note: If the patient is hospitalized do not wait until he or she is discharged – interview the patient as soon as possible and meet with the hospital medical staff to coordinate the patient's care after discharge.	☐ ☐ ☐ ☐
The Interview: Introduction	
• Introduce yourself to the patient and provide your identification • Explain the purpose of the interview • Discuss patient confidentiality, reassuring the patient that his or her identity and diagnosis will only be shared on a need-to-know basis • Build trust and rapport with the patient	☐ ☐ ☐ ☐
Collect and Confirm Patient Information	
• Collect and confirm the following information: • Name/alias(es)/nickname(s) • Age/date of birth • Address and phone number(s) • Country of birth • Other locating information (workplace and other frequented sites) • Next of kin • Physical description	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Step	Date Completed
• Known exposure to TB • Symptom history • Recent hospitalization(s) • Medical provider for TB • Other medical conditions • Lifestyle factors • Outpatient/DOT plan • Barriers to adherence • Access to transportation	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
TB Education and Information	
• Assess the patient's knowledge of TB • Discuss the basis of the TB diagnosis – bacteriology, chest x-ray (CXR), symptom history, infectiousness • Educate the patient about TB transmission; exposure vs. transmission; disease intervention behaviors; treatment plan (TB disease is treatable and curable); DOT and the importance of treatment adherence; the need for follow-up medical appointments; and the reason for identifying and evaluating contacts – especially children • Review with the patient the importance of accurately determining the infectious period and update the calculation as needed	☐ ☐ ☐ ☐
Identification of Contacts	
• Focus on contacts during the infectious period • Explain high vs. low risk contacts • Stress the importance of identifying all contacts • Collect information on contacts in the patient's household or residence; social and recreational; workplace; school; place of worship; other congregate settings to • Discuss visits to exposure sites and sharing information on a need-to-know basis • Referral method for contact notification	☐ ☐ ☐ ☐ ☐ ☐
Collect Contact Information	
• Name/alias(es)/nickname(s)	☐

Step	Date Completed
• Age/date of birth • Country of birth • Race/gender • Physical description • Address and phone number(s) • Other locating information • Dates of first and last exposure during the infectious period • Hours of exposure per week during the infectious period	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
Interview Conclusion	
• Ask for and answer the patient's questions • Review and reinforce the treatment adherence plan • Confirm the next appointment • Arrange to re-interview the patient and make a home visit (if not already completed) • Leave your business card or name and phone number with the patient • Thank the patient and conclude the interview	☐ ☐ ☐ ☐ ☐ ☐

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Until further notice, refer to the CDC website for current guidance about COVID-19 mRNA vaccines and TB testing.

Chapter 11: Targeted Testing for TB

INTRODUCTION

PURPOSE

Targeted testing refers to the screening of asymptomatic adults in populations at increased risk for tuberculosis using either an interferon-gamma release assay (IGRA) blood test or the Mantoux tuberculin skin test (TST).

This chapter summarizes national and Pennsylvania state guidelines concerning targeted testing to screen for latent TB infection (LTBI).

BACKGROUND

The Centers for Disease Control and Prevention (CDC), the U.S. Preventive Services Task Force (USPSTF) and other U.S. and international health organizations agree that a key strategy for reducing the transmission, morbidity and mortality of active TB disease is the identification and treatment of LTBI.

After nearly two decades of decline, the U.S. TB incidence rate has stalled at about three cases per 100,000 persons. A key factor in the lack of further progress is the number of people in the U.S. estimated by the CDC to have LTBI – as many as 13 million, or about 1,400 people with LTBI for each case of TB disease – representing a vast reservoir of potential new cases of TB disease.

Without treatment, about 10 percent of people with LTBI will develop TB disease in their lifetime. For certain groups, however, the risk is much higher:

- Individuals with untreated LTBI and uncontrolled diabetes have about a 30 percent risk of developing TB disease in their lifetime.
- Persons with untreated LTBI and HIV have a 7 to 10 percent risk of developing TB disease per year.

Fortunately, LTBI treatment is approximately 90 percent effective in preventing the progression to active TB disease.

U.S. epidemiologic data indicates that more than 85 percent of new TB cases are due to the progression from LTBI to TB disease (sometimes referred to as the reactivation of LTBI), and about 70 percent of TB cases occur in non-U.S. born people.

Since 2007, overseas screening of U.S. bound immigrants and refugees has included routine culture and drug susceptibility testing in addition to smear microscopy, resulting in the

identification and treatment of smear negative/culture positive TB cases before U.S. arrival and a corresponding decrease in the importation of TB cases. However, overseas screening procedures do not require the treatment of LTBI prior to U.S. arrival and therefore do not prevent the importation of LTBI.

POLICY

In Pennsylvania, there are four primary groups for TB testing:

- Persons who show or report signs and symptoms of TB are evaluated for TB disease as described in Chapter 5, Diagnosis of LTBI and TB Disease, and reported as suspected cases of TB as described in the “Reporting TB” section in this chapter.
- Close contacts to infectious TB cases are evaluated as described in Chapter 10, Contact Investigation.
- Targeted testing for LTBI is conducted among persons at increased risk for LTBI and/or progression to TB disease.
- Other individuals may be tested for TB as mandated by local administrative or legal requirements.

2016 RECOMMENDATIONS FOR TB SCREENING

In September 2016, the USPSTF recommended screening for LTBI among asymptomatic adults ages 18 and older in populations at increased risk, including:

- People who were born in, or are former residents of, countries with a high prevalence of TB; and
- People who live or have lived in high-risk group settings such as nursing homes or other long-term care facilities, homeless shelters and correctional facilities.

The USPSTF also assigned a "B" grade to testing for TB in populations at increased risk. Under current law, preventive services with a USPSTF grade of A or B are covered without cost-sharing (e.g., co-payment or deductible) by many health insurance plans or policies.

In supporting the USPSTF position, the CDC added its recommendation that the following groups also be tested for TB:

- People who have spent time with a person who has infectious TB;
- People with certain health conditions that weaken the immune system, including human immunodeficiency virus (HIV) infection, diabetes, substance abuse (e.g. smoking, alcohol abuse, or injection drug use) and severe kidney disease;
- People taking medications that suppress the immune system such as corticosteroids and TNF inhibitors; and
- Health care personnel and others who work in places at high risk of TB transmission.

The USPSTF recommendation is likely to reduce cost barriers to TB testing and the availability of blood tests using the interferon-gamma release assay (IGRA) methodology and shorter treatment regimens, such as the 12-dose once-weekly regimen, have the potential to overcome other barriers including the need for multiple clinic visits when testing with the TST and LTBI treatment regimens which last up to nine months.

IDENTIFYING GROUPS AT INCREASED RISK

The CDC states that persons at risk for developing TB disease generally fall into one of the following two categories:

- Those who have an increased likelihood of exposure to persons with TB disease; and
- Those with clinical conditions or other factors associated with an increased risk of progression from LTBI to TB disease.

Persons who are both at increased likelihood of exposure to TB disease and have a clinical condition or other factor that increases their risk of progression have a higher risk of developing TB disease than those who fall into one category or the other. For example, an individual born in a high-TB-prevalence country who is HIV positive is at much higher risk of having active TB than a US-born individual with HIV infection.

Table 1: Persons at Increased Risk for LTBI and/or Progression to TB Disease

Increased Risk of LTBI	Increased Risk For Progression to TB Disease
• High-priority contacts of persons who have smear-positive pulmonary or laryngeal TB • Infants, children, and adolescents exposed to adults in high-risk categories • Non-U.S. born person from, or recent traveler to, high prevalence countries including Mexico, the Philippines, Vietnam, India, China, Haiti, or other countries with high rates of TB • Migrant workers • Persons with high rates of TB transmission: – Homeless persons – Injection drug users – Persons with human immunodeficiency virus (HIV) infection • Persons living or working in congregate settings such as: – Hospitals, especially staff in nursing, emergency departments, and laboratories – Long-term care facilities – Homeless shelters – Residences for acquired immunodeficiency syndrome (AIDS) patients – Correctional facilities	• Persons with HIV infection • Infants and children aged <5 years • Persons infected with *Mycobacterium TB* within the previous 2 years • Persons with a history of untreated or inadequately treated TB disease • Persons with radiographic findings consistent with inactive or past TB disease • Persons dependent on addictive substances (tobacco, alcohol, or injectable drugs) • Persons with any of the following conditions or other immunocompromising conditions: – Silicosis – Diabetes mellitus – End-stage renal disease (ESRD)/chronic renal failure, hemodialysis – Hodgkin's Disease, leukemia – Other malignancies (e.g., carcinoma of head, neck, or lung) – Body weight ≥10% below ideal body weight – Use of immunosuppressive agents such as corticosteroids or tumor necrosis factor-alpha (TNF- α) antagonists – Organ transplantation – Intestinal bypass or gastrectomy – Chronic malabsorption syndromes

Adapted from: CDC. Guidelines for preventing the transmission of *Mycobacterium TB* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent TB infection. *MMWR* 2000;49(No. RR-6):7–9. CDC. Latent TB Infection: Guide for Diagnosis and Treatment, Sec. 1.3 Identifying Persons at Risk. https://www.cdc.gov/tb/publications/ltbiapp/identifying.htm. Accessed October 17, 2017.

TB SCREENING: RISK ASSESSMENT TOOL

Mass screening of the general population for TB is an inefficient method of finding infection and disease, and a poor use of limited financial and human resources. Screening should be prioritized to identify infected persons at increased risk of disease who would benefit from preventive therapy.

To assist clinicians in determining which patients are at risk and should be tested, the Pennsylvania (PA) TB Program has developed the following tools:

- Adult TB Risk Assessment and Adult TB Risk Assessment User Guide
- Pediatric TB Risk Assessment and Pediatric TB Risk Assessment User Guide

See Appendix A of this chapter for more information.

HEALTH CARE PERSONNEL

TB screening of health care personnel in inpatient and outpatient settings should be done in accordance with "Tuberculosis Screening, Testing and Treatment of U.S. Health Care Personnel: Recommendations form the National Tuberculosis Controllers Association and CDC, 2019" (*MMWR* 2019;68:439–443 at http://dx.doi.org/10.15585/mmwr.mm6819a3.

The risk assessment tools provided by the CDC and the PA TB Program ask the same three questions (temporary or permanent residence in a country with a high TB rate, current or planned immunosuppression, and close contact with someone with infectious TB) and either may be used.

TB TESTS

There are two types of tests for TB – the interferon gamma-release assay (IGRA) blood test and the tuberculin skin test (TST). Currently, two different IGRA blood test brands are available – QuantiFERON® (Qiagen) and T-Spot® (Oxford Immunotec).

The advantages and disadvantages of both test types are summarized in the chart on the following page.

Test Type	Advantages	Disadvantages
IGRA	• An IGRA has greater specificity than a TST, so there are fewer false positive results with an IGRA in individuals who have had the Bacille Calmette-Guérin (BCG) vaccine or who are infected with nontuberculosis mycobacteria. • Cost effective – greater specificity means fewer patients are treated unnecessarily for LTBI • Requires one patient visit to collect the blood sample for the test • Results can be available within 24 hours • Does not boost responses to subsequent tests • Preferred over a TST for children 2 years of age and older with prior BCG vaccination	• Blood samples must be processed within 8-30 hours of collection • Test accuracy can be affected by errors in collecting or transporting the blood sample, or in running or interpreting the assay • Typically costs more than tuberculin
TST	• Costs less than an IGRA • Preferred over an IGRA in children less than 2 years of age	• The TST is less specific than an IGRA. False positive TST results can occur in individuals vaccinated with BCG or infected with nontuberculosis mycobacteria • Requires two patient visits – one to place the test and one to read the results • Results must be read between 48 and 72 hours after the test was placed • The TST can boost the results of subsequent tests

Both the IGRA and TST tests can detect the presence of *Mtb* in the body, but neither test can differentiate between LTBI and active TB disease nor predict which patients with LTBI will progress to active TB disease.

Patients with documented evidence of either a previous IGRA or TST positive test result or a history of TB should not be tested with an IGRA or TST. Once a patient tests positive, they will always test positive – even after completing treatment for LTBI or TB disease.

Individuals with a positive IGRA or TST test result, or individuals with a negative IGRA or TST test result who are at high risk of TB exposure (e.g., close contacts of sputum-smear positive cases TB cases, especially young children or persons with weakened immune systems) should be evaluated for TB as described in Chapter 5, Diagnosis of LTBI and TB Disease.

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CHAPTER 11, APPENDIX A: ADULT AND PEDIATRIC RISK ASSESSMENT TOOLS AND USER GUIDES

This appendix includes the following PA TB Program documents:

- Tuberculosis (TB) Risk Assessment – Adult
- TB Risk Assessment Guide – Adult
- TB Risk Assessment – Pediatric
- TB Risk Assessment Guide – Pediatric

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Tuberculosis (TB) Risk Assessment - Adults

- Use this tool to identify asymptomatic **adults** for TB testing.
- **Do not repeat TB testing** unless there are **new** risk factors since the last test.
- Do not treat for latent TB infection (LTBI) until a diagnosis of active TB disease has been excluded:
  - For patients with TB symptoms or an abnormal chest x-ray consistent with active TB disease, evaluate for active TB disease with a chest x-ray, symptom screen, and – if indicated – sputum AFB smears, cultures and nucleic acid amplification testing (NAAT). A negative interferon gamma release assay or tuberculin skin test does not rule out active TB disease.

TB testing is recommended if any of the 3 boxes below are checked.

☐ **Birth, travel or residence** in a country with an elevated TB rate for at least a month

- Includes any country **other than** the United States, Canada, Australia, New Zealand, or a country in western or northern Europe.
- If resources require prioritization within this group, **prioritize** those patients with at least one medical risk for progression to TB disease (see the Pennsylvania Adult TB Risk Assessment User Guide for a list).
- An interferon gamma release assay test is preferred over a tuberculin skin test for non-U.S. born persons 2 years of age or older.

☐ **Immunosuppression,** current or planned

Examples include HIV infection, organ transplant recipient or treatment with a TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent to a prednisone dose of 15 mg/day for one month or longer), or other immunosuppressive medication.

☐ **Close contact** to someone with infectious TB disease during lifetime

If TB test is positive, rule out active TB disease before diagnosing LTBI.

☐ **No risk factors identified;** TB testing is not indicated at this time

Provider: _____ **Patient Name:** _____

Assessment Date: _____ **Date of Birth:** _____

For more information about using this tool see the Pennsylvania Adult TB Risk Assessment User Guide on our website.
Adapted for local use from the California Tuberculosis Risk Assessment tools at www.ctca.org

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Tuberculosis (TB) Risk Assessment Guide - Adults

Avoid testing persons at low risk

Routine testing of persons without risk factors is not recommended and may result in unnecessary evaluations and treatment because of falsely positive test results.

Prioritize persons at risk for progression

If health system resources do not allow for testing of all non-U.S. born persons from a country with an elevated TB rate, prioritize patients with at least one of the following medical risks for progression:

- diabetes mellitus
- smoker within past 1 year
- end stage renal disease
- leukemia or lymphoma
- silicosis
- cancer of head or neck
- intestinal bypass/gastrectomy
- chronic malabsorption
- body mass index ≤20
- history of chest x-ray findings suggestive of previous or inactive TB (no prior treatment). Includes fibrosis or non-calcified nodules but not a solitary calcified nodule or isolated pleural thickening. Test for TB infection and if positive evaluate for active TB disease.

U.S. Preventive Services Task Force (USPSTF)

The USPSTF has recommended testing persons born in or former residents of a country with an elevated TB rate and persons who live in or have lived in high-risk congregate settings such as correctional facilities, nursing homes and homeless shelters. Because the increased risk of exposure to TB in congregate settings varies substantially by facility and local health jurisdiction, clinicians are encouraged to follow local recommendations when considering testing persons from these congregate settings.

The USPSTF did not review data supporting testing among close contacts to persons with infectious disease or among persons who are immunosuppressed because these persons are recommended to be screened by public health programs or clinical standards of care.

Children

This risk assessment tool is intended for adults. A separate risk assessment tool for children is also available on our website.

Mandated testing

Certain populations may be mandated for testing by statute, regulation, or policy. This risk assessment does not supersede any mandated testing for healthcare workers, school employees or volunteers, and residents or employees in congregate settings such as correctional institutions, nursing homes, homeless shelters and others.

Age as a factor

Age (among adults) is not considered in this risk assessment. However, younger adults have more years of expected life during which progression from latent TB infection (LTBI) to active TB disease could develop. Some programs or clinicians may prioritize testing of younger non-U.S. born persons when all non-U.S. born persons are not tested. An upper age limit for testing has not been established but could be appropriate depending on individual patient TB risks, comorbidities, and life expectancy.

Foreign travel or residence

Travel or residence in countries with an elevated TB rate may increase the risk for TB exposure in certain circumstances (e.g. extended duration, likely contact with persons with infectious TB, high prevalence of TB in travel location and non-tourist travel). The duration of at least one consecutive month to trigger testing is intended to identify travel or residence most likely to involve TB exposure. TB screening tests can be falsely negative within eight weeks after exposure, so results are best obtained eight weeks after return from travel.

When to repeat a test

Re-testing should only be done in persons who previously tested negative and have new risk factors since the last assessment. Such risk factors include new close contact with an infectious TB case, new immunosuppression, and can also include foreign travel in certain circumstances.

When to repeat a risk assessment

The risk assessment should be administered at least once. Persons can be screened for new risk factors at subsequent preventive health visits.

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Tuberculosis Risk Assessment Guide - Adults

IGRA preference in BCG vaccinated persons

Because IGRA tests have increased specificity for TB infection in persons vaccinated with BCG, an IGRA is preferred over the tuberculin skin test (TST) in these persons. Most persons born outside the U.S. have been vaccinated with BCG.

Previous or inactive tuberculosis

Chest x-ray findings consistent with previous or inactive TB include fibrosis or non-calcified nodules, but do not include a solitary calcified nodule or isolated pleural thickening.

Persons with a previous chest x-ray showing findings consistent with previous or inactive TB should be tested for TB infection and evaluated for active TB disease.

A negative test for TB does not rule out active TB disease

It is important to remember that a negative IGRA or TST result does not rule out active TB disease. In fact, a negative IGRA or TST in a patient with active TB disease can be a sign of extensive disease and poor outcome.

Symptoms that should trigger evaluation for active TB disease

Patients with any of the following symptoms that are otherwise unexplained should be evaluated for active TB disease: cough for more than two to three weeks, fever, night sweats, weight loss, and hemoptysis.

How to evaluate for active TB disease

Evaluate for active TB disease with a chest x-ray, symptom screen, and – if indicated – sputum AFB smears, cultures and nucleic acid amplification testing. A negative IGRA or TST does not rule out active TB disease.

Most patients with LTBI should be treated

Persons with risk factors who test positive for TB infection should generally be treated once active TB disease has been ruled out. However, clinicians should not feel compelled to treat persons who have no risk factors but test positive for TB infection.

Emphasis on short course treatment of LTBI

Shorter regimens for treating LTBI have been shown to be as effective as 9 months of isoniazid and are more likely to be completed. Use of these shorter regimens is preferred in most patients. Drug-drug interactions and contact to drug-resistant TB are typical reasons these regimens cannot be used. Additional studies are needed to understand the safety of 3HP during pregnancy.

Shorter duration treatment regimens

Medication	Frequency	Duration
Isoniazid + rifapentine (3HP)	Weekly	12 weeks[1]
Rifampin	Daily	4 months[2]

[1] 11-12 doses must be taken in 16 weeks for treatment completion

[2] 120 doses must be completed in 6 months for treatment completion

Current recommendations concerning the administration of 3HP are available on our website.

Patient refusal of recommended LTBI treatment

Refusal should be documented. Recommendations for treatment should be made at future encounters with medical services. If treatment is later accepted, TB disease should be excluded, and a chest x-ray repeated if it has been more than six months since the initial evaluation, or more than three months if there is immunosuppression, or the prior chest x-ray was abnormal and consistent with potentially active TB disease.

Resources

Fact sheets for the LTBI treatment regimens 3HP, rifampin alone and isoniazid alone are available at: https://www.cdc.gov/tb/topic/treatment/ltbi.htm

U.S. Preventive Services Task Force Latent TB Infection Screening Recommendations are available at: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/latent-tuberculosis-infection-screening

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Tuberculosis (TB) Risk Assessment - Pediatrics

- Use this tool to identify asymptomatic **children** for TB testing.
- **Do not repeat TB testing** unless there are new risk factors since the last test.
- Do not treat for latent TB infection (LTBI) until a diagnosis of active TB disease has been excluded:
  - For children with TB symptoms or an abnormal chest x-ray consistent with active TB disease, evaluate for active TB disease with a chest x-ray, symptom screen, and – if indicated – sputum AFB smears, cultures and nucleic acid amplification testing (NAAT). A negative interferon gamma release assay or tuberculin skin test does not rule out active TB disease.

TB testing is recommended if any of the 3 boxes below are checked.

☐ **Birth, travel or residence** in a country with an elevated TB rate for at least a month

- Includes countries **other than** the United States, Canada, Australia, New Zealand, or a country in western or northern Europe.
- If resources require prioritization within this group, **prioritize** those children with at least one medical risk for progression to TB disease (see the Pennsylvania Adult TB Risk Assessment User Guide for a list).
- An interferon gamma release assay is preferred over a tuberculin skin test for non-U.S. born persons 2 years of age or older.

☐ **Immunosuppression,** current or planned

Examples include HIV infection, organ transplant recipient or treatment with a TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent to a prednisone dose of 15 mg/day for one month or longer), or other immunosuppressive medication.

☐ **Close contact** to someone with infectious TB disease during lifetime

If TB test is positive, rule out active TB disease before diagnosing LTBI.

☐ **No risk factors identified;** TB testing is not indicated at this time

Provider: _____ **Patient Name:** _____

Assessment Date: _____ **Date of Birth:** _____

For more information about using this tool see the Pennsylvania Pediatric TB Risk Assessment User Guide on our website. Adapted for local use from the California Tuberculosis Risk Assessment tools at www.ctca.org.

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Pediatric Tuberculosis (TB) Risk Assessment Guide

Special considerations for young children

Children less than 5 years of age exposed to an infectious case of TB should receive TB testing and a full medical evaluation. An IGRA may be used in children 2 years of age and older. Regardless of the IGRA or TST result, a chest x-ray should be done to rule out active TB disease.

Children less than 5 years of age exposed to an infectious case of TB typically receive window prophylaxis treatment to prevent an early yet undetectable TB infection from rapidly developing into TB disease. Children less than 2 years of age are significantly more likely than adolescents or adults to progress to active TB disease after infection and to develop life-threatening TB disease such as TB meningitis or disseminated TB.

Clinicians evaluating children for latent TB infection (LTBI) or active TB disease are strongly encouraged to contact the TB Program at 717-787-6267 to request a medical consultation with the state pediatric TB consultant.

Avoid testing children at low risk

Routine testing of children without risk factors is not recommended and may result in unnecessary evaluations and treatment because of falsely positive test results.

Mandated testing

Certain populations may be mandated for testing by statute, regulation, or policy. This risk assessment does not supersede any mandated testing for students, residents in congregate settings and others. Testing can also be considered in children with frequent exposure to adults at high risk of TB infection, such as those with extensive foreign travel in areas with high TB rates.

Patients with LTBI should be treated

Children with risk factors who test positive for TB infection should be treated once active TB disease has been ruled out with a physical exam, chest x-ray and – if indicated – sputum smears, cultures and nucleic acid amplification testing (NAAT). However, clinicians should not feel compelled to treat children who have no risk factors but test positive for TB infection.

When to repeat a risk assessment and testing

Risk assessments should be completed for new pediatric patients, children thought to have new potential exposures to TB since the last assessment, and during routine pediatric well-child visits. Repeat risk assessments should be based on the activities and risk factors specific to the child. Children who volunteer or work in health care settings might require annual testing and should be considered separately.

Retesting should only be done in children who previously tested negative and have new risk factors since the last assessment (unless they were less than 6 months of age at the time of testing). In general, new risk factors would include new close contact with an infectious TB case, new immunosuppression, a close family member with a newly positive TB test result, or even foreign travel (see “Foreign Travel or Residence”).

Immunosuppression

The exact level of immunosuppression that predisposes to increased risk for TB progression is unknown. The threshold of steroid dose and duration used in the Pediatric TB Risk Assessment are based on data in adults and in accordance with recommendations by the Advisory Committee on Immunization Practices (ACIP) for live vaccines in children receiving immunosuppression.

Foreign travel or residence

Travel or residence in countries with an elevated TB rate may increase the risk for TB exposure in certain circumstances (e.g., extended duration, likely contact with persons with infectious TB, high prevalence of TB in travel location, non-tourist travel). The duration of at least one consecutive month to trigger testing is intended to identify travel or residence most likely to involve TB exposure. TB screening tests can be falsely negative within eight weeks after exposure, so results are best obtained 8 eight weeks after a child’s return.

IGRA preference in non-U.S. born children 2 years of age or older

Because IGRAs have increased specificity for TB infection in children vaccinated with BCG, an IGRA is preferred over the tuberculin skin test (TST) for non-U.S. born children 2 years of age and older. IGRAs can be used in children less than 2 years of age, but there is an overall lack of data in this age group, which complicates the interpretation of test results. In BCG vaccinated immunocompetent children with a positive TST, it may be appropriate to confirm a positive TST with an IGRA. If an IGRA is not done the TST result should be considered the definitive result.

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Pediatric Tuberculosis Risk Assessment Guide

A negative test for TB does not rule out active TB disease

It is important to remember that a negative IGRA or TST result does not rule out active TB disease. A negative IGRA or TST in a patient with active TB disease can be a sign of extensive disease. Any suspicion for active TB disease or extensive exposure to TB should prompt an evaluation for active TB disease, including physical exam, symptom review, and two-view chest x-ray.

Emphasis on short course treatment of LTBI

Shorter regimens for treating LTBI have been shown to be as effective as 9 months of isoniazid and are more likely to be completed. Use of these shorter regimens is preferred in most patients, although the 12-week regimen is not recommended for children less than 2 years of age or children on antiretroviral medications. Drug-drug interactions and contact to drug-resistant TB are other contra-indications for shorter regimens. Additional studies are needed to understand the safety of 3HP in pregnancy.

Shorter duration treatment regimens

Medication	Frequency	Duration
Isoniazid + rifapentine (3HP)	Weekly	12 weeks[1]
Rifampin	Daily	4 months[2]

[1] 11-12 doses must be taken in 16 weeks for treatment completion

[2] 120 doses must be completed in 6 months for treatment completion

Current recommendations concerning the administration of 3HP are available at www.health.pa.gov on the tuberculosis program page for health care providers.

Refusal of recommended LTBI treatment

Refusal should be documented. Recommendations for treatment should be made at future encounters with medical services. If treatment is later accepted, TB disease should be excluded, and a chest x-ray repeated if it has been more than six months from the initial evaluation for children 5 years of age and older and three months for children less than 5 years of age.

Symptoms that should trigger evaluation for active TB disease

Patients with any of the following symptoms that are otherwise unexplained should be evaluated for active TB disease: cough for more than two to three weeks, fever, night sweats, weight loss, lymphadenopathy, hemoptysis or excessive fatigue.

Resources

Fact sheets for the LTBI regimens 3HP, rifampin alone and isoniazid alone are available at: https://www.cdc.gov/tb/topic/treatment/ltbi.htm

Information about the American Academy of Pediatrics recommendation to use an IGRA to test children 2 years of age and older is available at:

https://redbook.solutions.aap.org/chapter.aspx?sectionid=189640207&bookid=2205

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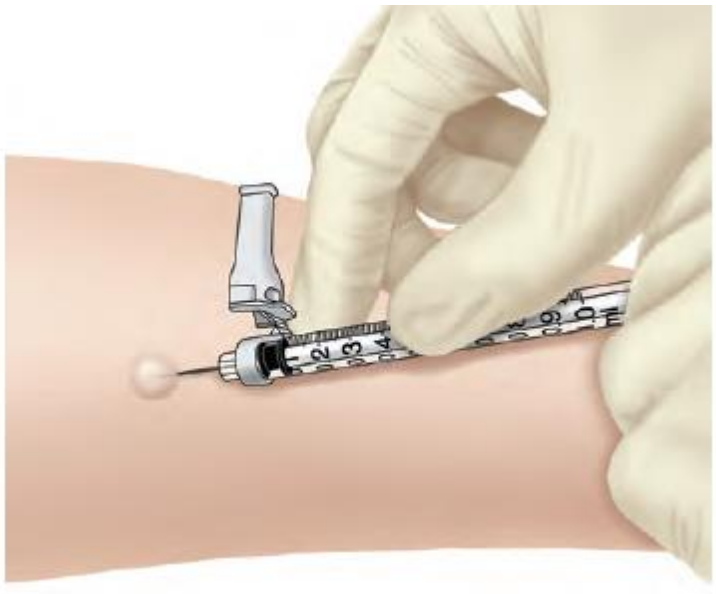
CHAPTER 11, APPENDIX B: ADMINISTERING, READING AND INTERPRETING THE TST

ADMINISTERING THE TST

The TST is performed by intradermal injection of 0.1 ml of purified protein derivative (PPD) containing 5 tuberculin units into the volar surface of the forearm. The injection should be made with a disposable 27-guage tuberculin syringe, intradermally (just below the surface of the skin), with the needle bevel facing upward. This should produce a discrete, pale elevation of the skin (a wheal), 6 mm to 10 mm in diameter (see Figure 3). Institutional infection control guidelines (e.g., the use of gloves) should be followed.

Figure 3: Administering the TST



READING THE TST

The reaction to the TST should be read by a healthcare worker trained to read TST results 48 to 72 hours after the test was placed. Reactions to PPD usually begin 5 to 6 hours after injection, reach a maximum at 48 to 72 hours, and subside over a period of a few days. Positive reactions, however, often persist for up to a week or longer. Never ask a patient to read his or her own skin test.

The TST is read by palpating the site of the injection to find an area of induration (firm swelling). The diameter of the induration should be measured ACROSS the forearm (see Figures 4.1 and 4.2). Induration should always be measured and recorded in millimeters. If no induration is found, “0 mm” should be recorded.

Figure 4.1: Reading the TST Correctly

This is correct – only the induration is being measured**.**

The correct example below measures 10 mm.

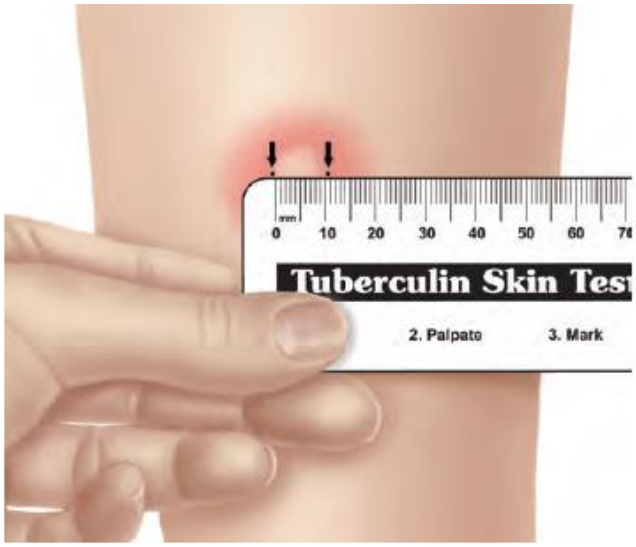
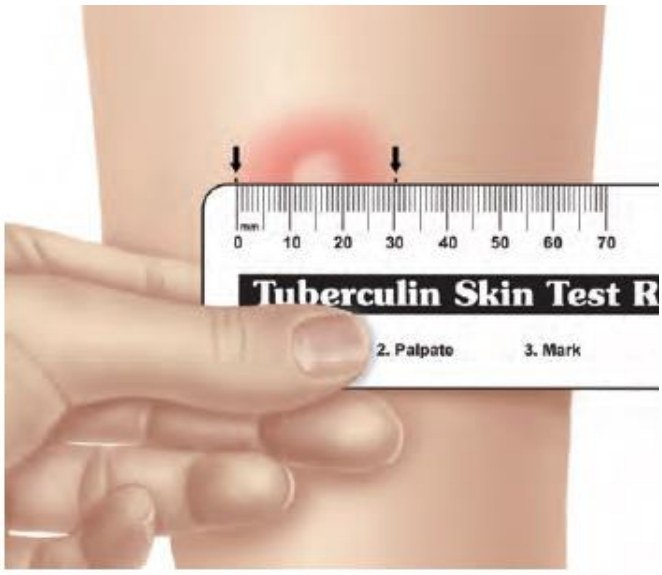


Figure 4.2: Reading the TST Incorrectly

This is incorrect – the erythema is being measured.

The incorrect example below measures 30 mm.



INTERPRETING TST REACTIONS

The interpretation of TST reactions depends on the measurement (in millimeters) of induration and the person's risk of acquiring latent TB infection or the risk of progression to TB disease if infected (see Table 2).

Table 2: Interpreting the TST Reaction

		
5 or more millimeters	**10 or more millimeters**	**15 or more millimeters**
An induration of **5 or more millimeters** is considered positive for • HIV-infected persons • Recent contacts of persons with infectious TB • People who have fibrotic changes on a chest radiograph • Patients with organ transplants and other immunosuppressed patients (including patients taking a prolonged course of oral or intravenous corticosteroids or TNF-*α* antagonists)	An induration of **10 or more millimeters** is considered positive for • People who have come to the United States within the last 5 years from areas of the world where TB is common (for example, Asia, Africa, Eastern Europe, Russia, or Latin America) • Injection drug users • Mycobacteriology lab workers • People who live or work in high-risk congregate settings • People with certain medical conditions that place them at high risk for TB (silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions) • Children younger than 5 years of age • Infants, children, and adolescents exposed to adults in high-risk categories	An induration of **15 or more millimeters** is considered positive for • People with no known risk factors for TB

TST FALSE-POSITIVE AND FALSE-NEGATIVE REACTIONS

Several factors can lead to false-positive or false-negative reactions with the TST skin test as listed below.

Table 3: False-Positive and False-Negative Reactions to the TST

Type of Reaction	Possible Cause	People at Risk
False-positive	Nontuberculous mycobacteria (NTM)	People infected with NTM
	BCG vaccination	People vaccinated with BCG
	Administering of incorrect antigen	Any person being tested
	Incorrect interpretation of TST result	Any person being tested
False-negative	Anergy	HIV-infected people, other people with weakened immune systems, severe TB disease, and some viral illness (e.g., measles, mumps, and chicken pox) or bacterial infection (e.g., typhoid, etc.)
	Recent TB infection	People infected with *M. tuberculosis* within the past 8 weeks
	Concurrent viral infection	People injected with a live-virus vaccination
	Concurrent bacterial infection	People with typhoid fever, brucellosis, typhus, leprosy, pertussis
	Concurrent fungal infection	People with fungal infection
	Chronic renal failure	People with renal failure
	Low protein states	People with severe protein depletion or afibrinogenemia
	Diseases affecting lymphoid organs	People with Hodgkin's disease, lymphoma, chronic leukemia, sarcoidosis
	Immunosuppressive drugs	People taking medical steroids, TNF-alpha blockers or comparable drugs
	Very young or elderly persons	Newborns or elderly patients with immature or waning immunity
	Stress	People who have had surgery, burns, mental illness, graft-versus-host reactions
	Incorrect storage or handling of antigen, administering the TST, or results that are **not** measured or interpreted properly	Any person being tested

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CHAPTER 11, APPENDIX C: GUIDELINES RE: DIAGNOSIS OF TB IN ADULTS AND CHILDREN

In December 2016, a taskforce supported by the American Thoracic Society (ATS), Infectious Diseases Society of America (IDSA), and the CDC – with participation by Fellows of the American Academy of Pediatrics (AAP) – issued updated clinical practice guidelines for the diagnosis of tuberculosis in adults and children.

Overall, the ATS/IDSA/CDC guidelines are based on the likelihood of infection with *Mycobacterium tuberculosis (Mtb)* and the likelihood of progression to TB disease as illustrated in Figure 1, below.

Figure 1: Paradigm for Evaluation of Those with TB Infection Based on Risk of Infection, Risk of Progression to Tuberculosis, and Benefit of Therapy

Risk of Infection ↑

Groups with Increased Likelihood of Infection with *Mtb*	Benefit of Therapy	TB Infection Testing Strategy	
Household contact or recent exposure to an active case	Yes	**Likely** to be infected **Low** to **intermediate** risk of progression (TST ≥ 10mM)	**Likely** to be infected **High** risk of progression (TST ≥ 5mM)
Mycobacteriology laboratory personnel	Not demonstrated		
Immigrants from high-burden countries (>20 cases per 100,000)	Not demonstrated		
Residents and employees of high-risk congregate settings	Yes		
None	Not demonstrated	**Unlikely** to be infected (TST ≥ 15mM)	

Risk of Developing TB if Infected →

Low	Intermediate (RR 1.3 - 3)	High (RR 3 - 10)
No Risk factors	Clinical predisposition: Diabetes Chronic renal failure Intravenous drug use	Children less than age 5 years HIV infection Immunosuppressive therapy Abnormal CXR consistent with prior TB Silicosis
Benefit of Therapy		
Not demonstrated		Yes

Note: In developing a diagnostic approach for the evaluation of those with suspected TB infection, (the taskforce) recommends the physician weigh the likelihood of infection, the likelihood of progression to tuberculosis if infected, and the benefit of therapy (Horsburg and Rubin, Clinical practice: Latent tuberculosis infection in the United States. N Engl J Med 2011; 364: 1441-8). Recommendations were formulated for each of the 3 groups illustrated above. These groups are concordant with current recommendations for the interpretation of the tuberculin skin test (American Thoracic Society; Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep 2000; 49:1-51).

The guidelines also provide testing strategies using either the IGRA blood test or the TST.

In June 2018 – eighteen months after the ATS/IDSA/CDC guidelines were published – the 31st edition of the American Academy of Pediatrics Red Book was issued. The updated Red Book included the following recommendations for testing infants or children:

- For children 2 years of age or older, either an interferon gamma-release assay (IGRA) blood test or a TST can be used. An IGRA is preferred for children who:
  - have had the Bacille Calmette-Guérin (BCG) vaccine (to avoid a false-positive TST result caused by a previous BCG vaccination), and/or
  - are unlikely to return for a TST to be read.
- For children younger than 2 years of age the tuberculin skin test (TST) is the preferred test for the detection of *M. tuberculosis* infection.
- A chest X-ray (CXR) should be done to rule out active TB, regardless of the TST/IGRA result.
- A negative TST or IGRA TB test does not rule out a diagnosis of TB.

Figure 2 on the following page reflects both the 2016 ATS/IDSA/CDC guidelines and the 2018 Red Book recommendations for testing children.

Figure 2: Summary of Recommendations for Testing for TB Infection

Group	Testing Strategy	
	ATS/IDSA/CDC 2016 Guidelines	**AAP 2018 Red Book**
Likely to be infected **High risk** of progression (TST ≥ 5mM)	**Adults** **Acceptable:** IGRA or TST **Children <5 years of age**[1] **Preferred:** TST **Acceptable:** IGRA or TST **Children 5 years of age and older**[1] **Preferred:** IGRA **Acceptable:** IGRA or TST Consider testing with an IGRA and a TST where a positive result from either test would be considered **positive**[2]	**Children <2 years of age**[3] **Preferred:** TST **Acceptable:** IGRA or TST **Children 2 years of age and older**[1] **Preferred:** IGRA (in BCG vaccinated children) **Acceptable:** IGRA or TST
Likely to be infected **Low** to **intermediate** risk of progression (TST ≥ 10mM)	**Preferred:** IGRA where available **Acceptable:** IGRA or TST	
Unlikely to be infected (TST > 15mM)	**Testing for TB infection is not recommended** **If necessary:** **Preferred:** IGRA where available **Acceptable:** IGRA or TST **For serial testing:** **Acceptable:** IGRA or TST Consider dual testing where a positive result from either test would be considered **negative**[4]	

[1] In the 2016 testing guidelines issued by the ATS, IDSA, and the CDC, the TST was listed as the preferred test for children ≤ 5 years of age. In the American Academy of Pediatricians (AAP) Red Book published in June 2018, however, the AAP listed the TST as the preferred test for children < 2 years of age. The above chart reflects the updated AAP recommendation.

[2] Performing a second diagnostic test when the initial test is negative is a strategy to increase sensitivity. This may reduce specificity, but the taskforce decided that this is an acceptable trade-off in situations in which the consequences of missing a diagnosis of TB infection (i.e., not treating individuals who may benefit from therapy) exceed the consequences of inappropriate (i.e., hepatotoxicity).

[3] In the 2016 testing guidelines issued by the ATS, IDSA, and the CDC, the TST was listed as the preferred test for children ≤ 5 years of age. In the American Academy of Pediatricians (AAP) Red Book published in June 2018, however, the AAP listed the TST as the preferred test for children < 2 years of age. The above chart reflects the updated AAP recommendation.

[4] Performing a confirmatory test after an initial positive result is based upon both the evidence that false-positive results are common among individuals not likely to be infected with *Mycobacterium tuberculosis* (*Mtb*) and the committee's presumption that performing a second test on those patients whose initial test was positive will help identify false-positive results.

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Chapter 12: Laboratory Services

INTRODUCTION

PURPOSE

Use this chapter to get contact information for laboratories, determine which tests are available and the tests' turnaround times and identify the appropriate laboratory to perform specific tests.

The diagnosis of TB, management of patients with the disease, and public health TB control services rely on accurate laboratory tests. Laboratory services are an essential component of effective TB control, providing key information to clinicians (for patient care) and public health agencies (for control services).

POLICY

Public health laboratories should ensure that clinicians and public health agencies within their jurisdictions have ready access to reliable laboratory tests for diagnosis and treatment of TB.

Effective TB control requires timely, complete, and accurate communication among the laboratory system, TB Program, and healthcare provider.

Reporting requirements:

Healthcare practitioners and healthcare facilities must report within five days any suspected or confirmed active TB disease from all sites after being identified by symptoms, appearance, or diagnosis. A person in charge of a clinical laboratory in which a laboratory test of a specimen derived from a human body yields results significant from a public health standpoint shall promptly report the findings no later than the next work day after the close of business on the day on which the test was completed. This includes: positive AFB smears, cultures, nucleic acid amplification tests and results of drug susceptibility testing.

LABORATORY CONTACT INFORMATION

To locate and contact a laboratory, refer to **Table 1: Laboratory Contact Information**. For the list of the tests performed at each laboratory, refer to **Table 2: Available Laboratory Tests**.

TABLE 1: LABORATORY CONTACT INFORMATION

Roles and Responsibilities	Contact Information
State Laboratory Full-service Mycobacteriology laboratory. Provides nucleic acid amplification by PCR, culture,	PA Department of Health Bureau of Laboratories (BOL) 110 Pickering Way Exton, PA 19341-9798

Roles and Responsibilities	Contact Information
identification and drug susceptibility testing of *M. tuberculosis* on clinical specimens submitted from PA state and county public health centers and reference isolates from PA hospital and commercial laboratories. Serves as a consultant for questions involving mycobacterium laboratory testing and liaison between clinical laboratory and public health staff. Sends *M*. *tuberculosis* isolates for genotyping to regional laboratory in Michigan.	Tel: 610-280-3464 Fax: 610-450-1932 www.health.pa.gov/labs
Private Laboratories The National Jewish Medical and Research Center (NJMRC) in Denver Colorado offers therapeutic drug monitoring (TDM) for drugs used to treat tuberculosis. Contact the TB Program to request the specimen submission forms. In cases where arrangements for therapeutic drug monitoring have been made with a local hospital lab, submit an Authorization Request form to the TB program manager for pre-approval.	National Jewish Medical and Research Center 1400 Jackson Street Denver, Colorado 80206 Tel: (303) 398-1422 www.nationaljewish.org/programs/directory/tb/
Centers for Disease Control and Prevention The pathology laboratory offers pathology diagnostic for mycobacteria in formalin-fixed tissues samples	Centers for Disease Control and Prevention 1600 Clifton Road NE MS; H18-SB Atlanta, GA 30329-4027 Tel: 404-639-3132 Fax: 404-639-3043 Pathology@cdc.gov – prior approval is needed.

AVAILABLE LABORATORY TESTS

TABLE 2: AVAILABLE LABORATORY TESTS

Test	Laboratory	Turnaround Time
Diagnosis		
IGRA	PA Department of Health Bureau of Laboratories and most local clinical laboratories	Within 24 to 72 hours from receipt in laboratory
Acid-fast (AFB) bacilli smear	PA Department of Health Bureau of Laboratories	Within 24 hours from receipt in laboratory
Culture	PA Department of Health Bureau of Laboratories	Mycobacterial growth detection by culture within 14 days from date of specimen collection Identification of cultured mycobacteria within 21 days from date of specimen collection

Test	Laboratory	Turnaround Time
Drug susceptibility	PA Department of Health Bureau of Laboratories	Within 30 days from date of specimen collection
Molecular Detection of Drug Resistance	CDC – Request is made through PA Department of Health Bureau of Laboratories	Within 24 to 72 hours from receipt in laboratory
Nucleic acid amplification (NAA) test See Molecular Testing Guidelines	PA Department of Health Bureau of Laboratories	Within 2 days from date of specimen collection
Pathology	CDC Request is made through the PA Department of Health Bureau of Laboratories	2-3 weeks
Treatment Monitoring		
Hepatic enzymes or up to 8 clinical, multichannel chem panel (that includes aspartate aminotransferase [AST], alanine aminotransferase [ALT], lactate dehydrogenase [LDH], total and direct bilirubin, alkaline phosphatase, uric acid, and calcium)	Available at most local clinical laboratories	Usually available the same day
Uric acid	Available at most local clinical laboratories	Usually available the same day
Complete blood count (CBC) and platelets	Available at most local clinical laboratories	Usually available the same day
Kidney function	Available at most local clinical laboratories	Usually available the same day
Epidemiologic Monitoring		
Genotyping and Whole Genome Sequencing	PA Department of Health Bureau of Laboratories Testing is referred to the CDC's regional genotyping laboratory. (Referral is automatic.)	2-3 weeks from the receipt of the isolate

INTERFERON GAMMA RELEASE ASSAY

The BOL performs IGRA testing for TB clinics that have the capacity to perform the required blood collection/incubation. IGRAs are also offered at private labs throughout the state.

CHEST RADIOGRAPHS

Availability and Cost	Chest x-rays are available for all TB suspects and diagnosed cases that **do not** have health insurance, (private or public), via the State Health Centers and County/Municipal Health Department referral. If the patient has health insurance, it should be noted on the Authorization for Outpatient Services unless the patient declines. The Health Department is the payer of last resort. Chest x-rays other than

	PA, AP and lateral, must be pre-approved by the TB Program prior to the patient going to the provider for services. See the Authorization policy for more information.

For more information on available laboratory services in Pennsylvania, contact the BOL at 610-280-3464.

SPECIMEN COLLECTION

Sputum is phlegm from deep in the lungs. The important characteristics needed in sputum specimens are freshness and actual sputum, rather than saliva. An early morning specimen is best, so when collecting a set of three sputum specimens, at least one of them should be an early morning specimen.

To isolate mycobacteria from clinical materials successfully, handle specimens carefully after collection. For optimal results, collect specimens in clean, sterile containers and keep them in conditions that inhibit the growth of contaminating organisms, since most specimens will contain bacteria other than mycobacteria.

Refer to Table 3 to review the methods used to collect various specimens and the type of specimens obtained for pulmonary TB.

During procedures in which aerosols may be produced, use appropriate respiratory protection and environmental controls. For more information, refer to the CDC's "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

TABLE 3: SPECIMEN COLLECTION METHODS AND TYPES FOR PULMONARY TB

Pulmonary Tuberculosis Collection Method	Specimen Type
Spontaneous sputum collection occurs when the patient can cough up sputum without extra assistance.	5–10 ml of sputum from deep in the lung
Induced sputum collection should be considered if a patient needs assistance in bringing up sputum.*	5–10 ml of sputum from deep in the lung
Gastric aspirates can be submitted for the diagnosis of pulmonary tuberculosis (TB) in young children who cannot produce sputum.	15 ml of gastric contents Consult laboratory for special collection and handling process Must be neutralized with sodium bicarbonate.
Bronchoscopy can be used in the following situations: • If a patient cannot produce sputum by the above three methods; • If a patient has a substantial risk of drug-resistant TB and has initial routine studies that are negative;	Bronchial washings Bronchoalveolar lavage Transbronchial biopsy

Pulmonary Tuberculosis Collection Method	Specimen Type
• In a patient in whom there is suspicion of endobronchial TB; or • If a variety of clinical specimens for the diagnosis of pulmonary TB or other possible diseases need to be obtained.	
* It is important to specify if the sputum is induced or not, because induced sputum is "more watery" and appears to be just saliva. Some laboratories may throw out induced sputum and report it as an inadequate specimen.	

TABLE 4: SPECIMEN COLLECTION METHODS AND TYPES FOR EXTRAPULMONARY TUBERCULOSIS

Extrapulmonary Tuberculosis Collection Method	Specimen Type	
Extrapulmonary specimen collection from tissue and other body fluids can be submitted for the diagnosis of extrapulmonary tuberculosis.	Examples of tissues (biopsy)* Lymph node Pleural Bone/joint Kidney Peritoneal Pericardial	Examples of fluids Pleural Cerebrospinal Blood Urine Synovial Peritoneal Pericardial

Sputum Collection Kits

Sputum Collection Instructions

- Collection kit will include:
  - Plastic collection tube
  - Biohazard bag with absorbent sheet
  - Lab slip with clear plastic bag
  - Cold pack – Place the cold pack into freezer until shipping
  - Foam insert
  - Pre-addressed postage-paid outer mailer box
- The public health nurse will help you fill out the lab slip and put the return address on the mailer.
- Write the date of the collection on the lab slip and tube.
- Sputum comes from the lungs, after a deep cough. When you first wake up in the morning, cough up the sputum before drinking, eating or smoking.
- Cough directly into the tube. DO NOT get the sputum on the outside of the tube. If necessary, wash the outside of the tube.
- Replace the cap on the plastic tube. Fasten the cap securely. Place the tube into the biohazard bag containing the absorbent pad. Seal and refrigerate the specimen bag until shipping.

Shipping Directions

- Place the cold ice pack into the foam one side of the foam insert.
- Place the specimen bag(s) containing the specimen into the other half of the foam. Up to three samples can be shipped in the same box.
- Place the foam box into the pre-addressed postage paid cardboard box mailer.
- Place the lab slip(s) one per each sputum tube into clear plastic bag.
- Place the lab slip bag on the outside of the foam and inside of the mailer.
- Use the courier service with pre-addressed label

For more information, please refer to the Sputum Collection Diagram.

Sputum collection kits and shipping materials can be ordered on the PA DOH BOL Supply Order Form.

QUICK COURIER 800-355-1004
TB/SPUTUM
SHIPPING DIRECTIONS
Effective March 14, 2012

1. Package the specimen appropriately.
2. Address package:

   PA Department of Health
   Bureau of Laboratories 110 Pickering Way
   Exton, PA 19341

3. Call Quick Courier at **800-355-1004** to request pickup of a "***TB Pickup Account #PA-BOLTB"*** package for next day delivery to the **Laboratory**.
4. A dispatcher will pick up the specimen from the public health center and deliver it to the State Laboratory the next business day. Calls to Quick Courier must be made by **12 noon** for delivery the next business day.

TB / SPUTUM ONLY

Please Note: Do not ship TB/Sputum Specimens out on Fridays, weekends, day before a holiday or holidays,

If specimen will not arrive at the Bureau of Laboratories/State Public Laboratory within 24-48 hours of collection, REFRIGERATE specimen and ship the next business day.

For additional resource information:

Bureau of Laboratories Directory of Services, submission form and guidelines are located at www.health.state.pa\labs

1. Click on the link
2. Select “Clinical Microbiology”
3. Select Bacteriology
4. Select Tuberculosis
5. Use PA State Laboratory Specimen Submission Form H840.336.
6. Please complete all the sections including the date of birth.

It is especially important to **specify if the sputum is induced or not,** because an induced sputum generally is “more watery” and appears to be just saliva. Some private laboratories may throw out the specimen and report it as an “inadequate specimen.”

1. Indicate type(s) of testing requested.
2. Make sure the specimen and laboratory requisition are packaged into appropriate shipping containers, per laboratory instructions.
3. If possible, send the specimen on the day it is collected. If this is not possible, refrigerate the specimen until it is sent on the next day.
4. Do not keep specimens to send all three on the same day.

Make every effort to submit specimens to the laboratory within 24 hours of collection. Normal flora can overgrow any mycobacteria in the specimen and make it unusable. If specimens cannot be submitted within 24 hours, keep in mind that most laboratories will not run a specimen more than five days old. Know how long it takes the specimen to get to the laboratory from the time it leaves your hands and submit specimens accordingly.

HOW TO DIRECT A PATIENT TO PERFORM SPONTANEOUS SPUTUM COLLECTION AT HOME

If a patient will be collecting sputum specimens at home, provide the following guidance:

- Put a mark at the 5 ml level on the sputum tubes (if not already marked) to show the patient the minimum amount of sputum needed. (Most laboratories consider 5 to 10 ml an adequate amount.)
- Review with the patient how to collect sputum.
- Make arrangements for a healthcare worker to pick up the specimen or for the patient, a family member, or a friend to drop off the specimen.

Click here to see a pictorial explanation of the proper method for collecting sputum.

INDUCED SPUTUM COLLECTION AT A HEALTHCARE FACILITY

If the patient cannot produce sputum spontaneously, arrange for induced sputum to be collected at a facility. Facilities where sputum can be collected include the respiratory therapy department of a local hospital, TB clinic, or laboratory. Facilities should have appropriate respiratory protection, environmental controls, and policies and procedures.

HOW TO COLLECT GASTRIC ASPIRATES

This information is provided for guidance to private healthcare professionals.

The following are basic guidelines for collecting gastric aspirates:

- Collect the specimen after the patient has fasted for 8 to 10 hours and, preferably, while the patient is still in bed.
- Collect a specimen daily for three days.

For additional information on how to collect a gastric aspirate and prepare the specimen for transport, see the guide and Francis J. Curry National Tuberculosis Center's online video *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure, please copy and paste this link in your browser:* http://www.currytbcenter.ucsf.edu/catalogue/epub/index.cfm?tableName=GAP

BRONCHOSCOPY OR COLLECTION OF EXTRAPULMONARY SPECIMENS

If TB staff are consulting with physicians before the specimens are collected, the physician should be reminded to send part of the specimen (not in formalin) to the microbiology laboratory for AFB smear and culture, in addition to any other tests or pathology examinations the physician plans to obtain. (Note: if a specimen is placed in formalin, then a pathology test must be requested via the BOL; refer to Table 2 in this chapter.) In addition, a post-bronchoscopy sputum specimen should be sent for AFB smear and culture.

- **Bronchoscopy:** Refer the patient to a local specialist.
- **Extrapulmonary specimens:** These specimens will be collected by the physician performing the diagnostic work-up.
- DOH is responsible for the testing of TB specimens only. Routine bacteriology culture and susceptibility testing must be performed at clinical laboratory.

SPECIMEN SHIPMENT

There are three main categories of transportation methods: medical couriers, ground transportation, and air transportation. Category B Infectious Substances (raw diagnostic specimens, such as sputum, blood, or tissue) can be mailed through the US Postal Service (USPS), shipped by private carrier (e.g., Federal Express, Airborne Express, etc.), or

transported by a medical courier. Tuberculosis mycobacterium cultures (or culture isolates suspected of being mycobacteria) are Category A Infectious Substances and can be transported only by a medical courier or shipped by private carrier as dangerous goods. Category A Infectious Substances cannot be mailed through the US Postal Service. Each category requires different packaging requirements to provide increased levels of protection against leaks and contamination.

For more information, contact TB lab supervisor, PA State Laboratory at 610-280-3464.

Ship to: PA Department of Health
Bureau of Laboratories
Division of Clinical Microbiology-TB Lab
110 Pickering Way
Exton, PA 19341

- Please call the Bureau of Laboratories at 610-280-3464 (option #3) and inform us of the expected time of arrival.
- Previously processed respiratory specimens may be used for testing within 3 days of processing.
- Specimens can be processed the same day **if received by 10:00 a.m. and prior notice is given.**
- The positive smear, PCR and resistant antimicrobial susceptibly results will be phoned and faxed to the submitter. All results will be messaged to PA-NEDSS.

REFERENCES

RESOURCES FOR LABORATORY SERVICES

- Detailed descriptions of recommended laboratory tests; recommendations for their correct use; and methods for collecting, handling, and transporting specimens have been published.
- For more information on laboratory testing for tuberculosis (TB), see the following:
- ATS, CDC, IDSA. “Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America” (*MMWR* 2005;54[No. RR-12]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5412.pdf.
- ATS,CDC, IDSA Clinical Practice Guidelines: *Diagnosis of Tuberculosis in Adults and Children Clinical Infectious Diseases*, Volume 64, Issue 2, 15 January 2017, Available at: https://academic.oup.com/cid/article/64/2/e1/2629583

- CDC. Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* infection – MMWR US 2010 Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm
- CDC. Updated Guidelines for the Use of Nucleic Acid Amplication Tests in the Diagnosis of Tuberculosis. MMWR January 16, 2019. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm
- National Committee for Clinical Laboratory Standards. *Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard* [Document no. M24-A2] (Wayne, PA; March 2011).

RESOURCES FOR SPECIMEN COLLECTION AND SHIPMENT

- CDC. "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.
- CDC. *Public Health Mycobacteriology: A Guide for the Level III Laboratory* (Atlanta, GA; 1985).
- Francis J. Curry National Tuberculosis Center. *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure* (Francis J. Curry National Tuberculosis Center Web site). Available at: https://www.currytbcenter.ucsf.edu/products/pediatric-tuberculosis-guide-gastric-aspirate-procedure
- For information about the tests done by the National Jewish Medical and Research Center and how to submit specimens for testing, visit https://www.nationaljewish.org/for-professionals/diagnostic-testing/adx/diagnostic-testing.
- US Department of Transportation. Hazardous Materials: Revision to standards for infectious substances. Part III 49 CFR Part 171. Federal Register (August 14, 2002).
- USPS. *Mailing Standards of the United States Postal Service: Domestic Mail Manual* (USPS Web site). *Available* at: http://pe.usps.com/.

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Chapter 13: TB Surveillance in Pennsylvania

INTRODUCTION

PURPOSE

This chapter includes information about:

- The importance of surveillance in TB prevention and control,
- When to report suspected and confirmed cases of TB,
- The role of genotyping in TB surveillance, and
- PA-NEDSS

BACKGROUND

In public health, surveillance refers to the ongoing systematic collection, analysis, interpretation and reporting of data about a health-related event. In the U.S., the National Electronic Disease Surveillance System (NEDSS) facilitates the transfer of public health surveillance data from the healthcare system to public health departments.

In Pennsylvania, TB surveillance data is entered in and reported to the Centers for Disease Control and Prevention (CDC) from Pennsylvania's version of the National Electronic Disease Surveillance System (PA-NEDSS). The data elements collected in PA-NEDSS are based on the Report of a Verified Case of TB (RVCT) form developed by the CDC.

Currently, data about the diagnosis and treatment of latent TB infection (LTBI) is reportable to the CDC for just two groups – contacts to active cases of TB and immigrants and refugees with a B2 medical classification.

It is the responsibility of private healthcare providers to report suspected or confirmed cases of active TB disease in accordance with 28 Pa Code § 27.21a. Public health staff shall process electronic reports and enter TB case data in PA-NEDSS on a timely basis. Many laboratories also report TB diagnostic data directly into PA-NEDSS.

State TB program personnel are responsible for reviewing PA-NEDSS case data for accuracy and completeness, patient de-duplication, merging investigations, managing out-of-state reports, updating the questionnaires as needed, counting cases that meet the criteria for TB disease and closing counted TB cases once all available data has been entered and transmitted to CDC.

Every Sunday night (or per request) information entered in PA-NEDSS on any new or revised counted TB case since the previous Sunday is automatically downloaded to the CDC.

TB surveillance data is used on local, state and national levels to:

- Determine TB patterns and trends;
- Identify potential tuberculosis (TB) outbreaks, recent transmission of TB, multi-drug resistance, and deaths;
- Identify high-risk populations and settings;
- Establish priorities for prevention and control activities; and
- Strategically plan the use of limited human and financial resources.

Surveillance data is also used to evaluate whether quality standards are being met, determine the effectiveness of health programs, and measure progress toward TB elimination.

LAWS AND REGULATIONS

Pennsylvania laws and regulations related to TB reporting are included in 28 Pa. Code § 27.21a, § 27.22, and §27.4, which can be viewed at https://www.pacode.com/secure/data/028/chapter27/subchapBtoc.html.

CASE DEFINITIONS

In the fourth quarter of each year, the CDC issues its summary of *Reported Tuberculosis Cases in the United States* for the previous calendar year. The appendices to that report include "Tuberculosis Case Definition for Public Health Surveillance" (Appendix A) and "Recommendations for Reporting and Counting Tuberculosis Cases" (Appendix B). Both are helpful resources for public health personnel involved in reporting and/or counting tuberculosis cases.

Clinical Case Definition

Appendix A of the CDC annual report of TB cases defines a clinical case of TB as a case that meets **ALL** the following criteria:

- A positive tuberculin skin test (TST) result or a positive interferon gamma release assay for *M. tuberculosis;*
- Other signs and symptoms compatible with TB (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease);
- Treatment with two or more anti -TB medications; and
- A completed diagnostic evaluation.

Laboratory Criteria for Diagnosis

Appendix A of the CDC annual report defines the laboratory criteria for diagnosis as any one of the following:

- Isolation of *M. tuberculosis* complex from a clinical specimen;[1]
- Demonstration of *M. tuberculosis* complex from a clinical specimen by nucleic acid amplification test (NAAT)[2]; or
- Demonstration of an acid-fast bacilli in a clinical specimen when a culture has not been obtained, cannot be obtained or is falsely negative or contaminated.

A confirmed case of TB is a case that meets the clinical case definition or is laboratory confirmed.

Within the two types of case definitions, cases are further classified by morbidity verification. Morbidity verifications identify the criteria used to determine that the definition of a confirmed case of TB is met. Morbidity verifications for a clinical case of TB are clinical case definition or provider certified/diagnosed at clinic. Morbidity verifications that meet the laboratory criteria for diagnosis are: positive culture, positive nucleic acid amplification, and positive smear.

REPORTING TUBERCULOSIS

The CDC recommends immediate reporting of a suspected or confirmed case of TB to the jurisdictional health agency.

In Pennsylvania, 28 Pa Code §27.21a(b)(2) requires that suspected or confirmed cases of active TB disease (all sites) must be reported within five work days after being identified by symptoms, appearance or diagnosis. Reports may be submitted electronically via the PA-NEDSS or by calling the local state health center (SHC) or county or municipal health department (CMHD).

For laboratories, 28 Pa Code §27.22 requires that a person who is in charge of a clinical laboratory in which a laboratory test of a specimen derived from a human body yields results significant from a public health standpoint shall promptly report the findings no later than the next work day after the close of business on the day on which the test was completed. This includes confirmation of positive smears or cultures and results of drug susceptibility testing.

TB is suspected in a patient who 1) has had recent contact with a person known to have active TB or 2) who has signs and symptoms of active TB (such as a persistent cough that lasts for two or more weeks) and is currently undergoing a medical evaluation for TB.

For more information about reporting TB, see **TABLE 1: REPORTING CONFIRMED OR SUSPECTED CASES OF TB**.

TABLE 1: REPORTING CONFIRMED OR SUSPECTED CASES OF TB

What Condition/ Test Result	Who Reports	When to Report	How to Report
Confirmed or suspected cases of TB disease. Confirmation by laboratory tests is not required. This includes pulmonary and extra-pulmonary cases.	• TB clinicians • Other healthcare providers • Hospitals • Other similar private or public institutions • Anyone providing treatment to the confirmed or suspected case **Note:** The attending TB clinician or other healthcare provider must report even if the laboratory is also reporting the test results.	**Suspected or confirmed active cases (all sites) must be reported within 5 work days after being identified by symptoms, appearance or diagnosis.**	• Information can be called in or faxed to the local SHC or CMHD. • An on-line report can be made at www.nedss.state.pa.us
Sputum smears positive for acid-fast bacilli (AFB) Cultures positive for Mycobacterium TB complex* Nucleic acid amplification tests/DNA probes positive for Mycobacterium tuberculosis (Mtb) complex	All laboratories that perform TB testing In-state laboratories that send specimens for out-of-state testing **Note:** The laboratory must report even if the attending TB clinician or other healthcare provider is also reporting.	**Promptly, no later than the next work day after the close of business on the day the test was completed.**	• Test results can be reported via an electronic lab report (ELR) submitted to PA-NEDSS. • An on-line report can be manually entered at www.nedss.state.pa.us

PA-NEDSS

The Pennsylvania National Electronic Data Surveillance System (PA-NEDSS) is a web-based application that allows for the secure communication of laboratory results, clinical data, and the diagnosis and treatment of reportable health conditions between laboratories, hospitals, private medical practices and public health departments. Tuberculosis is specified in Pennsylvania Code Title 28, Chapter 27 as one of several reportable diseases in the state. Information documented in PA-NEDSS is used by the Pennsylvania Department of Health (DOH) to routinely submit reportable public health data to the CDC.

PA-NEDSS is accessible 24 hours a day, 7 days a week via: https://www.nedss.state.pa.us. Access is limited to authorized users.

All confirmed and suspected cases of TB must have a PA-NEDSS investigation initiated. The data elements collected in PA-NEDSS are based on the Report of a Verified Case of TB (RVCT) form developed by the CDC and constitute the basis for substantiating a case of TB. A PA-NEDSS investigation should also be initiated for all cases of LTBI diagnosed or treated in a SHC or CMHD.

For information on how to initiate a TB investigation and the information required for a TB investigation in PA-NEDSS, please refer to the "Tuberculosis Reference Guide". The "Tuberculosis Reference Guide" can be located under "Training Materials" on the PA-NEDSS home screen after log in.

MANAGING NON-ELECTRONIC REPORTS IN PA-NEDSS

All laboratory reports for suspected and confirmed cases of TB must be entered in PA-NEDSS.

- Health care professionals and laboratories who don't report directly into PA-NEDSS can use the laboratory report form to provide test results.
- Public health staff must enter into PA-NEDSS any hard copy reports not submitted electronically by a provider or laboratory and retain a copy in the patient's chart.
- For tests performed at the BOL, results will be reported directly into PA-NEDSS and via fax to the submitting entity or health care professional.

GENOTYPING

In August 2017, the CDC announced the establishment of the National Tuberculosis Molecular Surveillance Center (NTMSC) at the Michigan Department of Health and Human Services, which has done CDC-sponsored genotyping since the early 1990's. The NTMSC is part of the CDC's Antibiotic Resistance Laboratory Network and began parallel testing of all *Mycobacterium tuberculosis* isolates with both conventional genotyping and whole genome sequencing (WGS) in 2018. WGS examines significantly more of the TB genome than conventional genotyping. In 2021, after three years of parallel testing, WGS will become the standard method for analyzing patterns of transmission with the added benefit of the identification of recent transmission.

All U.S. TB programs can use the NTMSC at no cost to patients, healthcare providers, or health departments, but the isolates to be tested must be submitted via the state's public health laboratory. Therefore, an isolate for each case of culture positive TB in Pennsylvania should be sent to the Bureau of Laboratories (BOL) in Lionville (Exton). The BOL will then submit the isolates to the MDHHS for genotyping.

Genotyping provides valuable information about the pathogenesis, epidemiology, and transmission of *Mycobacterium TB (Mtb).* As a result, it is a key tool for TB programs in the early detection and control of TB outbreaks, the discovery of unsuspected relationships between cases, and the identification of incorrect TB diagnoses based on false-positive test results.

> **Note:** One of the National TB Program Indicators Project (NTIP) objectives for 2025 is to increase the proportion of TB patients with a positive culture result who have a MTBC (*Mycobacterium tuberculosis* complex) genotyping result reported.

Genotyping identifies specific strains of *Mtb* based on an analysis of deoxyribonucleic acid (DNA). As mycobacteria reproduce, their DNA is typically reproduced without alteration from generation to generation. Over time, however, spontaneous mutations in DNA occur at a low frequency, ultimately resulting in the diversity of *Mtb* strains that we see today.

The diversity of TB strains and specificity of genotyping methods provide a means to:

- Determine whether TB cases with matching genotypes are part of the same transmission chain;
- Differentiate between **reactivation** – where a patient previously treated for and cured of TB has a subsequent episode of TB disease caused by the **same strain** of *M. tuberculosis* as the first episode – and **reinfection** – where a subsequent episode of TB disease is caused by a **different strain** of M. tuberculosis; and
- Identify false positive *M. tuberculosis* cultures. It's estimated that about 2% of *M. tuberculosis* cultures are false positives, usually due to mislabeling of the isolate or cross-contamination.

When two or more *M. tuberculosis* isolates match by genotype they are referred to as a "genotype cluster". A "cluster" refers to the possibility that the cases *may* be transmission related and triggers an investigation to determine whether the patients share overlapping timeframes (i.e., dates and times) or physical locations (e.g., worksite, method of transportation, social gatherings) where TB transmission may have occurred. If not, then it's unlikely the patients are both part of the same transmission chain but may share an unidentified index case. Refer to Appendix A of this chapter for more information about cluster investigations.

Genotyping can also identify strains of *M. Bovis* associated with Bacille Calmette-Guerin (BCG), an attenuated live virus used 1) to vaccinate young children against TB meningitis or disseminated TB in countries with a high incidence of TB or 2) as a form of immunotherapy to treat bladder cancer. Such cases are often reported as Bovis BCG or attenuated Bovis, identified by a spoligotype (a poly-morphism in the repeat units of DNA used to identify *Mtb* complex strains) ending in "600" and a MIRU (a rapid genotyping method using mycobacterial interspersed repetitive units) with "x, y, or z" as the second character.

TB OUTBREAK

In Module 9 of the Self-Study Modules on Tuberculosis, the CDC states that a "TB outbreak is generally defined as a situation where there are more TB cases than expected within a geographic area or population during a particular time period, and there is evidence of recent transmission of *M. tuberculosis* among those cases". The time period generally refers to a situation where TB transmission occurred within the previous 2-year period, implying that patients who are part of an outbreak were exposed to an infectious case of TB in the recent past, not several years ago and then progressing over time from LTBI to TB disease.

Because an outbreak indicates that there is ongoing – and possibly extensive – transmission of TB, a TB outbreak should always be considered a public health emergency.

A potential outbreak is detected through the following activities:

- Observations from public health staff and others in the community
- TB contact investigations
- TB case surveillance
- TB genotyping

During these activities, public health staff should be alert for signs of more TB cases than expected and evidence of recent transmission among those cases.

For more information about TB outbreaks, refer to Module 9 of the CDC Self-Study Modules on Tuberculosis at: https://www.cdc.gov/tb/education/ssmodules/pdfs/Module9.pdf.

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[1] Use of rapid identification techniques for *M. tuberculosis*, such as DNA probes and mycolic acid high-pressure liquid chromatography performed on a culture from a clinical specimen, are acceptable under this criterion.

[2] For clinical purposes, a NAAT must be accompanied by a culture for mycobacteria species. A culture isolate of *M. tuberculosis* complex is required for complete drug susceptibility testing and for genotyping. For surveillance purposes, CDC will accept results from NAATs approved by the U.S. Food and Drug Administration (FDA) and used according to the approved product labeling on the package insert, or a test produced and validated in accordance with applicable FDA and Clinical Laboratory Improvement Amendments (CLIA) regulations.

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CHAPTER 13, APPENDIX A: CLUSTER INVESTIGATIONS

A TB cluster is two or more cases of TB with matching genotypes in a specific geographic area over a particular period of time. In some cases, a TB cluster can cross several jurisdictions (cities or counties) and still be in relatively close proximity to qualify as a cluster.

The purpose of a cluster investigation is to determine epidemiological linkages between the cases to prevent further transmission of TB. If the linkages between the cases are known, a cluster investigation is not necessary.

Cluster investigations are initiated when one of the following occurs:

- The TB Program receives a cluster alert notification from the CDC's TB Genotyping Information Management System (TB GIMS)
- The local jurisdiction or TB Program becomes aware of two or more cases with matching genotypes or PCR type and linkages are unknown

If a jurisdiction becomes aware of two or more cases with matching genotypes, the jurisdiction should alert the TB program manager who will initiate the cluster investigation. The jurisdiction should provide the PA-NEDSS investigation numbers and any known epidemiological links. The TB program manager will initiate the following when notified of a cluster with unknown linkages:

1. Review genotyping results in TB GIMS to include running the national distribution report.
2. Complete a cluster investigation chart to include the following information from each PA-NEDSS investigation:

    Patient initials
    NEDSS investigation number
    Accession number
    County of residence
    Street name
    Town/city
    Age at investigation
    Gender
    Date of diagnosis
    Date of US entry
    Country of birth
    Risk factors
    Occupation
    Reason evaluated
    Symptom onset/infectious start date

Diagnostic test results
Co-morbidities
Health-care providers
Other pertinent information as available

3. Look for evidence of laboratory contamination and discuss with the PA Department of Health Bureau of Laboratories (BOL) if warranted.
4. Review investigations for any common contacts or locations.
5. Schedule a conference call to discuss the cases. Cluster investigation team members should include the assigned community/public health nurse and nurse supervisor, TB program manager, TB surveillance coordinator, TB medical consultant and BOL staff if appropriate.
6. Conduct the conference call as soon as possible, but no later than two weeks after receiving notification of a cluster. Participants on the call should:
    - Briefly review each case and look for commonalities;
    - Determine if additional patient interviews need to be conducted; and
    - Identify next steps.

    The TB program manager will document next steps, identify outcomes and disseminate to the call participants.
7. Participants will conduct follow-up activities as warranted and report outcomes back to the TB program manager.
8. Participants should document actions in PA-NEDSS investigation notes as it relates to each patient.
9. The TB program manager will update the cluster chart with new information, next steps and outcomes, and disseminate updates as the investigation progresses.
10. The TB program manager will conclude the cluster investigation by sending a final summary email regarding the outcome of the cluster investigation.

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Chapter 14: Nontuberculosis Mycobacteria

INTRODUCTION

Nontuberculous mycobacteria (NTM) occur naturally in the environment and are related to the bacteria that cause tuberculosis (TB) and leprosy. The highest concentrations of NTM bacteria are found in soil and water, including both natural and treated water sources.

To date, more than 180 species of NTM have been identified. The number of identified species continues to increase due to improved culturing techniques in the mycobacteriology lab and more precise differentiation between individual NTM species. The top three most frequently reported NTM isolates in the U.S. are *M. avium* complex (MAC), *M. kansasii*, and *M. abscessus.* MAC organisms are the most common disease-causing NTM species.

Most people exposed to NTM do not become sick, but persons who are immunocompromised or have existing lung disease are at increased risk for developing NTM disease. Persons with third stage human immunodeficiency virus (HIV) infection – known as acquired immune deficiency syndrome, or AIDS – are known to be at increased risk of NTM disease. However, now the prevalence of NTM disease appears to be increasing among people without AIDS and NTM infections are being seen in new settings with new clinical manifestations.

The diagnosis of NTM may be challenging because the tuberculin skin test (TST) cannot distinguish between TB and NTM. Interferon gamma release assay (IGRA) tests have greater specificity than a TST and are unaffected by most NTM bacteria but positive IGRA results have been documented in cases of infection with three specific types of NTM bacteria – *M. kansasii*, *M. szulgai*, and *M. marinum*. Some symptoms associated with TB and NTM are also commonly seen with other respiratory conditions including bronchiectasis, bronchitis, pneumonia and chronic obstructive pulmonary disease (COPD). Though rare, patients can be infected with both TB and NTM and a specimen culture – which differentiates between TB and NTM at the species level – takes approximately 8 weeks. Once diagnosed, NTM treatment is typically managed by a pulmonologist or infectious disease specialist and requires several antibiotics and a minimum of 12 months of treatment.

Like TB, NTM infections can occur throughout the body but the most common sites are the lungs, lymph nodes, and skin or soft tissues. In addition to pulmonary disease, NTM may cause disseminated disease, lymphadenitis, and skin and soft tissue infections. Disseminated disease is most frequently seen in severely immunocompromised patients.

Since NTM disease has not been shown to be transmissible, and current communicable disease reporting laws are limited to *M. tuberculosis* or *M. tuberculosis* complex, NTM pulmonary disease is not reportable to the Pennsylvania Department of Health.

PATHOGENESIS

Unlike TB, the precise mode of NTM transmission to humans has not been confirmed, but it is highly likely the bacteria are ingested or inhaled. No evidence of animal-to-human or human-to-human NTM transmission has been reported in the literature.

Persons who are immunocompromised due to a medical condition (e.g. HIV) or immuno-suppressive treatment (e.g., TNF-alpha inhibitors for rheumatoid arthritis) or who have preexisting lung disease or damage (e.g., bronchiectasis, COPD, or asthma) are at increased risk for developing NTM lung disease.

In persons with HIV infection:

- MAC is the most common NTM organism causing pulmonary disease.
- Disseminated NTM infections may develop when CD4 T-lymphocyte levels fall below 50µl.

It should be emphasized that most persons with NTM pulmonary disease are not HIV infected.

NTM pulmonary disease may present with clinical manifestations and a radiographic appearance like those for TB disease.

DIAGNOSIS OF NTM DISEASE

Diagnosis of NTM disease is often delayed because current TB screening tests can't differentiate between TB and NTM, some symptoms for both diseases are also common to other respiratory conditions and a specimen culture – which differentiates between TB and NTM – takes approximately 8 weeks.

- Both prior Bacille Calmette-Guerin vaccination and NTM infection can yield a positive result with the tuberculin skin test (TST) when screening for TB. The package inserts for QuantiFERON (QFT) and T-Spot indicate both tests are unaffected by most NTM bacteria, but positive IGRA results have been documented in cases of infection with *M. kansasii*, *M. szulgai*, and *M. marinum*.
- One or more symptoms of TB and NTM disease – a persistent cough, fatigue, night sweats, weight loss, fever and less frequently shortness of breath and coughing up blood – are also seen with other respiratory conditions including bronchiectasis, bronchitis, pneumonia and chronic obstructive pulmonary disease (COPD).

For more information about the diagnosis of NTM disease, refer to the 2007 ATS/IDSA guidelines titled "Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases".

A single sputum culture positive for NTM, especially one with a small number of organisms, is generally not enough to support a diagnosis of NTM lung disease. Clinical, radiographic and microbiologic criteria are equally important and all must be met to diagnose NTM lung disease.

Any patient being treated as a pulmonary TB suspect, but **not** responding well to treatment, may be suspected of having TB and NTM co-infection or NTM lung disease alone, which can only be confirmed or ruled-out by a specimen culture.

RISK FACTORS FOR PULMONARY NONTUBERCULOUS MYCOBACTERIAL DISEASE

Various host defense dynamics and immune defects are associated with NTM. Disseminated NTM is a manifestation of either an acquired or a genetic immunologic defect. Susceptibility to pulmonary NTM disease is poorly understood but associations include:

1. Genetic syndromes with specific mutations in interferon-y and interleukin-2
2. Slender body type in post-menopausal women with features including thoracic scoliosis, pectus excavatum, and mitral valve prolapse
3. HIV
4. Chronic obstructive pulmonary disease (COPD), bronchiectasis, and cystic fibrosis
5. Prior pulmonary TB

TREATMENT

The Pennsylvania Department of Health does not provide treatment for NTM infection. However, in those instances where patients are co-infected with TB disease and NTM, it is necessary to treat both conditions to ensure the successful treatment of TB.

When a patient is co-infected with TB and NTM, the public health nurse and/or TB clinician should refer the patient to a pulmonologist or infectious disease specialist for the treatment of NTM.

The treatment of NTM differs somewhat from the treatment of TB. The choice of the drug treatment regimen is optimally based on the identified NTM species, in vitro susceptibility testing, and clinical presentation. Drug regimens used in the treatment of pulmonary NTM disease may include a macrolide (e.g., clarithromycin or azithromycin) as well as first- and second-line anti-TB medications.

Table 1 lists examples of drug regimen options for the treatment of the most common NTM species. It's important to know the common treatments for NTM disease in the event he or she is coordinating care for patients coinfected with TB and NTM. For more detailed information about the treatment of *M. avium complex*, *M. kansasii* and *M. abscessus*, see the section of the 2007 ATS/IDSA guidelines titled "NTM Species: Clinical Aspects and Treatment Guidelines".

TABLE 1: DRUG TREATMENT OPTIONS FOR NTM LUNG DISEASE

NTM Species	Treatment Guidelines for Pulmonary Disease
M. avium complex (MAC)	Treat with a macrolide such as clarithromycin or azithromycin, with ethambutol and a rifamycin. An injectable aminoglycoside such as streptomycin or Amikacin may be added in severe, previously treated, or cavitary disease. Macrolide-resistant disease requires extensive drug treatment, and consultation should be sought with an expert experienced in MAC therapy.
M. kansasii	For rifampin susceptible isolates, treat daily with rifampin, isoniazid, pyridoxine and ethambutol. Rifampin-resistant disease should include a three-drug regimen to which the organism is susceptible.
M. abscessus	Consultation with experts is strongly recommended. Combination of surgical resection of focal disease combined with multidrug therapy (macrolide and one or more parental agent such as Amikacin, cefoxitin, or imipenem, in addition to oral agents) may increase the chance of cure.

All patients receiving pulmonary NTM treatment should have close clinical monitoring with frequent sputum examinations for mycobacterial culture throughout treatment.

- *M. avium complex* pulmonary disease treatment should be continued until sputum cultures are consecutively negative for 12 months while on treatment. Since sputum conversion usually requires 3 to 6 months of treatment, the typical patient with MAC will be treated for 15 to 18 months. Patients on MAC treatment are likely to respond best the first time they are treated; for that reason, it is very important that patients receive the recommended multidrug therapy the first time they are treated for MAC.
- *M. kansasii* pulmonary disease treatment should also be continued until sputum cultures are consecutively negative for 12 months while on treatment.
- Least responsive to treatment is disease due to *M. abscessus*, a rapidly growing NTM species that is resistant to the standard antituberculosis drugs. Currently the only predictably curative treatment of *M. abscessus* lung disease is surgical resection of the involved lung tissue combined with multidrug chemotherapy.

NURSING IMPLICATIONS

The community health nurse (CHN) can play a major role in the recognition of pulmonary NTM disease. It's common for patients suspected of having TB to begin treatment before the final culture results are available. However, if the patient is not responding to treatment, that may suggest that the patient has either NTM disease alone or TB and NTM disease.

For patients co-infected with TB and NTM, the CHN may play an important role in encouraging compliance with the NTM treatment regimen. The lengthy regimen can be difficult, and poor compliance can lead to treatment failure.

No evidence of animal-to-human or human-to-human NTM transmission has been reported, and pulmonary NTM disease without TB does not pose a public health threat. Therefore, contact investigations are not needed for cases of NTM pulmonary disease and public health legal interventions such as health orders do not need to be considered.

If the final culture report returns with the identification of NTM instead of TB, the public health nurse's responsibility for managing the patient's treatment ends, but it's strongly recommended that the community health nurse and/or the TB clinician refer the patient to the pulmonologist or infectious disease physician who will oversee the treatment of NTM disease.

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Chapter 15: B1 And B2 Electronic Disease Notifications (EDNs)

BACKGROUND

Each year, approximately 450,000 permanent immigrants and 75,000 refugees legally enter the United States. Before leaving for the United States, these individuals are required to undergo medical examinations by overseas panel physicians following guidelines provided to the U.S. Department of State by the Centers for Disease Control and Prevention (CDC). The CDC is part of the U.S. Department of Health and Human Services (HHS), and the Secretary of HHS has the "statutory responsibility for preventing the introduction, transmission, and spread of communicable diseases into the United States".[1]

The purpose of the overseas medical examination is to identify whether the immigrant or refugee has a medical condition that would prevent him or her from entering the United States (Class A), or a medical condition that is admissible but that might require extensive medical treatment or follow-up (Class B). Class A conditions include, but are not limited to, a communicable disease of public health significance, such as active infectious tuberculosis (TB). Class B conditions include inactive, non-infectious pulmonary TB or extrapulmonary TB (B1) and latent TB infection (B2). Medical follow-up is recommended for individuals with a B1 or B2 condition upon their arrival in the U.S.

Newly arriving immigrants and refugees with Class A and Class B medical conditions are required to provide a copy of their panel medical exam documents to U.S. Customs and Border Protection (CBP) agents. CBP personnel then submit the documents to the CDC quarantine station with jurisdiction for the specific U.S. port of entry. Within 24 to 48 hours, the quarantine station sends the forms to the CDC Electronic Disease Notification (EDN) system data entry center in Atlanta, Georgia. Once the information is recorded in the EDN system, notifications of B1 or B2 arrivals are sent electronically to the applicable state health department, which forwards the information to the appropriate local jurisdiction. In Pennsylvania, the local jurisdiction is a Pennsylvania Department of Health (PADOH) state health center (SHC) or a county or municipal health department.

The local jurisdiction is responsible for contacting the newly arrived immigrant or refugee, scheduling an appointment for the individual to come into the TB clinic, and evaluating the individual for latent TB infection or active TB. All information pertinent to the U.S. evaluation, diagnosis and – where applicable – treatment of each immigrant or refugee is documented by

[1] Centers for Disease Control and Prevention. Disease surveillance among newly arriving refugees and immigrants – electronic disease notification system, United States, 2009. MMWR 2013;62(No. SS-7):1-20

the local jurisdiction on the EDN Worksheet and submitted to the PADOH TB Program central office for data entry in the EDN system.

POLICY

SHCs and county or municipal health departments must complete timely TB evaluations of newly arrived immigrants and refugees in order to diagnose and treat TB or active TB disease, thereby preventing new cases and the spread of active disease. The timely completion of TB evaluations is a condition of the program funding provided by the CDC, and CDC grantees are expected to strive to meet or exceed the four objectives for the evaluation and care of immigrants and refugees as specified in the National Tuberculosis Indicators Project (NTIP),[2] as follows:

- **Examination initiation:** The local jurisdiction should initiate a medical examination within 30 days of notification for immigrants and refugees with abnormal chest radiographs (X-rays) read overseas as consistent with TB.
- **Examination completion:** The local jurisdiction should complete a medical examination within 90 days of notification for immigrants and refugees with abnormal chest X-rays read overseas as consistent with TB.
- **Treatment initiation:** For immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB who are diagnosed with latent TB infection or have radiographic findings consistent with prior pulmonary TB (ATS/CDC Class 4) on the basis of examination in the U.S., for whom treatment was recommended, increase the proportion who start treatment.
- **Treatment completion:** For immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB who are diagnosed with latent TB infection or have radiographic findings consistent with prior pulmonary TB (ATS/CDC Class 4) on the basis of examination in the U.S., and who have started on treatment, increase the proportion who complete treatment.

EDN PROCEDURES

Initiation Procedures

The TB Program Central Office clerk typist 3 (CT3) will complete the following:

1. Receive EDN email.
2. Log into EDN system.
3. Click on alien list.
4. For each new alien:
    a. Click on alien number.
    b. Click on generate follow-up worksheet.
    c. Click on print to print just page one of the worksheet.

[2] To find the NTIP targets currently in effect, search the internet for 'CDC TB NTIP targets.'

d. Repeat for each new alien.
e. Log out of the EDN system when all new worksheets have been printed.

5. Log into PA-NEDSS.
6. Open an investigation for each new alien following the PA-NEDSS Investigation Initiation for EDNs procedures. (For Philadelphia, assign the investigation to the CDC Public Health Advisor or designee.)
7. Record the NEDSS investigation number on the worksheet.
8. Enter the EDN information to include the PA-NEDSS investigation number in the PA TB Program's EDN spreadsheet located on the N: drive.
9. Send the standard notification email containing the information specific to each alien to the EDN clinic level user(s) for the alien's jurisdiction, ensuring the instructions for accessing and completing worksheets are attached:

   > The following alien number is available for downloading on the EDN website:
   >
   > 000-000-000, NEDSS #0000000, DOB 01/01/1900
   >
   > Consistent with the National TB Indicators Project (NTIP) Objectives and Performance Targets, our goal is to increase the proportion of immigrants (with abnormal chest X-rays read overseas as consistent with TB) who complete a medical examination within 90 days of this notification.
   >
   > EDN follow-up worksheets should be completed and returned to the TB Program central office within three months of this notification. Do not wait for completion of treatment to return the worksheet.
   >
   > - If the individual has not completed treatment within three months of this notification, answer questions and E1a, E1c, E2, E3 and E4 on the worksheet, leave question E5 blank, and return the worksheet. Retain a copy of the worksheet to be updated upon completion of treatment.
   > - Once the individual completes treatment, answer questions E5a and, if applicable, E5b. If the response to E5a is no or unknown, and the reason is included as one of the responses listed for E5b, then there is no need to write-in a response to "specify reason therapy stopped" under E6. Return the final worksheet to the TB Program central office.
   >
   > Download instructions are attached. If you have any questions, please contact me.

   Copy the public health program administrator (PHPA) or the public health program assistant administrator (PHPAA) on the email notification.

10. Shred all worksheets.

EDN Email Reminder Notifications

The TB Program PHPA or the PHPAA should send reminder notifications via email to the local jurisdiction 30, 60, 90 and 120 days after the notification that an immigrant or refugee in need of a TB evaluation has entered the U.S. Reminder email notifications only need to be sent until the follow-up worksheet for each immigrant or refugee is received.

- For immigrants and refugees in the jurisdiction of a SHC, send the reminder to 1) the clinic level user who received the initial notification from the TB Program clerk typist, and 2) the community health nurse administrator (CHNA) for that jurisdiction.
- For immigrants and refugees in the jurisdiction of a county/municipal health department, send the reminder to the clinic level user who received the initial notification from the TB Program clerk typist.

The standard text for EDN email reminder notifications can be found in Appendix A of this document.

Completing the EDN Worksheet

Within the first week after receiving notification that an immigrant or refugee in need of a TB evaluation has entered the local jurisdiction, the community health nurse (CHN) assigned by the SHC or the public health nurse (PHN) assigned by the county or municipal health department will begin efforts to contact the patient to schedule an appointment for a medical evaluation in the TB clinic. For refugees, the nurse should reach out to the appropriate refugee resettlement agency for their assistance in locating the patient.

At a minimum, the following attempts should be made to contact an immigrant or refugee for evaluation: three telephone calls (at least one per week), one letter to be sent after first failed telephone call, and one home visit. If the individual is not home, leave a general letter addressed to the individual in a sealed envelope asking the individual to contact the health department). All attempts to reach the individual should be recorded in the investigation notes section of the NEDSS record.

At the completion of the medical evaluation, or when it has been determined that the evaluation cannot be completed because the patient could not be found, was lost to follow-up, refused evaluation, moved to another state within the U.S. or moved outside the U.S., the assigned nurse should complete Sections C (U.S. Evaluation), D (Evaluation Disposition in U.S.) and questions E1 through E4 (U.S. Treatment for TB Disease or latent TB infection) of the EDN follow-up worksheet following the guidance provided in Appendix B of this document. Once completed, SHC staff should submit the EDN follow-up worksheet via the TB Program Resource Account (TB_Program_Central_Office@pa.gov); county and municipal health departments should submit the worksheet via encrypted email to the TB Program Resource Account or via fax to 717-772-4309.

For patients who started treatment following completion of the U.S. medical evaluation, the completed EDN follow-up worksheet should be submitted to the TB Program Central Office on two occasions – first after completing the U.S. medical evaluation and again after the patient either completes the full course of treatment or stops taking the anti-TB medications.

If an immigrant or refugee moves out of state **after** the TB evaluation is initiated but before it is completed, SHC and county or municipal staff should complete as much of Section C of the EDN worksheet as possible, answer questions D1a, D1b, D2a, D2b, D2c and D3, and return the EDN worksheet to the PHPA or the PHPAA. For these cases, SHC and county or municipal staff should also complete an Interjurisdictional Notification (IJN) form and fax it to the TB Program central office at 717-772-4309.

If an immigrant or refugee moves out of state **before** the TB evaluation is initiated, SHC and county or municipal staff should answer questions D2a and D2c and return the EDN worksheet to the PHPA or the PHPAA. It is **not** necessary to complete an IJN form in cases where the patient moves out of state before the TB evaluation is initiated.

Upon return of the EDN worksheet to the TB Program central office, SHC and county or municipal staff must update the corresponding investigation in PA-NEDSS (Pennsylvania's version of the National Electronic Disease Surveillance System). If no further contact with the patient is needed, the NEDSS investigation can be closed at this time.

Completed Worksheet Processing Procedures

1. Upon receipt of a completed EDN follow-up worksheet (via mail or email in the resource account), the CT3 will enter the worksheet return date in the PA TB Program's EDN spreadsheet.
   (The CT3 will check the resource account daily and print any EDN worksheets located in the account.)
2. The CT3 will provide the completed worksheets for county/municipal health departments and/or SHCs to the public health program administrator (PHPA) or the public health program assistant administrator (PHPAA) as assigned.

The PHPAA, PHPA, and/or TB program manager will complete the following steps:

3. The PHPAA, PHPA, and/or TB program manager will review the worksheets for accuracy.
4. If there are errors on the form, the need for corrections will be communicated to the assigned CHN or PHN along with a date for revisions to be completed and submitted to the TB Program.
5. Upon receipt of the revised form or if the form was completed correctly upon initial submission, the form will be provided to the CT3 for data entry.

The CT3 will:

6. Log into the CDC EDN system.

7. Click on alien search and enter the alien number. (If the worksheet is older than one year from the alien's date of entry, the arrival date will also need to be entered.) Click on search.
8. Click on the alien number from the table generated by the search.
9. Click on worksheet data entry.
10. Enter all the worksheet data.
    a. Click save if additional data will be entered at a future date e.g., when the patient completes or stops treatment (questions E5a, E5b, or E6).
    b. Click submit once the final disposition (e.g., not located, lost to follow-up, completed or stopped treatment, etc.) has been determined and all data have been entered in the EDN system.
        i. Once an EDN worksheet is submitted in the EDN system, you will not be able to re-open the file to make changes or enter new information. In cases where a previously submitted EDN worksheet needs to be re-opened, contact the EDN Help Desk at edn@cdc.gov and request a "worksheet reset".
        ii. Any submitted worksheets that are re-opened will be auto-populated into the 2019 EDN worksheet format, and data for any of the new fields (e.g., E4 – Initial LTBI regimen) will need to be entered.
11. For worksheets that are "saved" in step 10a:
    a. The CT3 will:
        i. Open the PA TB Program's EDN spreadsheet, go to the alien number and enter "tickler" in the "Disposition" column
        ii. File the worksheet in an EDN "tickler" file for the PHPA or PHPAA
    b. The PHPA or PHPAA will:
        i. Retain the worksheet in a tickler file until treatment is due to be completed and a worksheet with the treatment completion information is submitted.
        ii. Review the tickler file once a month to identify patients likely to have completed treatment by the current date and follow up with the CHN or PHN.
        iii. Upon receipt of the updated worksheet, the PHPA or PHPAA will provide the completed worksheet to the CT3.
    c. The CT3 will then:
        i. Enter the new data in the CDC EDN system
        ii. If all data has now been entered and the final disposition determined, click "submit" and exit the CDC EDN system
        iii. Open the PA TB Program's EDN spreadsheet, go to the alien number, click "submitted" and enter the final disposition in the "Disposition" column
        iv. File the paper copy of the completed EDN worksheet by jurisdiction
12. For worksheets that are "submitted" in step 10b:
    a. The CT3 will:

i. Open the PA TB Program's EDN spreadsheet, go to the alien number, click "submitted" and enter the final disposition in the "Disposition" column
Ii. File the paper copy of the completed EDN worksheet by jurisdiction

13. Retain the EDN worksheet files for seven years.

The TB program manager will:

14. Run a report during the first week in May and November in the EDN system to analyze worksheets that have not been submitted. The PHPAA, PHPA, and/or TB program manager will follow up with the assigned CHNs or PHNs regarding the status of worksheets not submitted and provide a due date for the submission. Should the worksheets not be submitted by the due date, a supervisor will be notified of the missed due date.

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CHAPTER 15, APPENDIX A: FREQUENTLY ASKED QUESTIONS

Q. Do the tests performed during the overseas panel examination need to be repeated in the US?

A. It is at the discretion of the TB clinician to determine what tests are needed to evaluate the patient.

Any immigrant or refugee with any EDN classification, having an abnormal CXR overseas and negative smear and culture, should have a repeat CXR in US and an IGRA. However, if the IGRA was positive overseas, there is no need to repeat it in the US. If the US CXR is abnormal, obtain three sputa specimens for smear, culture and a NAAT and an IGRA if one was not performed.

Q. Should children with a B2 classification and a positive tuberculin skin test (TST) overseas have a repeat TB test in the U.S.?

A. Yes, children should be retested for TB in the U.S. An IGRA is preferred for children 2 years of age and older, while a TST is recommended for children less than two years of age.

Q. An adult with a B2 classification had an IGRA overseas. Does the test need to be repeated in the U.S.?

A. As of October 1, 2018, all immigrants and refugees undergoing a panel exam overseas are to be tested for TB with an IGRA. CDC DTBE does not have enough data to comment on any discordance between overseas and U.S. IGRA results. Therefore, any decision to re-do the IGRA in the U.S. is at the TB clinician's discretion.

Q. Is a U.S. CXR recommended for <u>all</u> immigrants and refugees whose overseas TST or IGRA was negative?

A. If the overseas CXR was normal and the U.S. IGRA or TST is negative, there is no need to repeat the CXR.

However, any abnormal overseas CXR needs to be re-evaluated by repeating the CXR and administering an IGRA in the U.S. This is true regardless of whether the overseas CXR was 'abnormal – not suggestive of TB' and/or the overseas smears and cultures were negative.

Q. If an immigrant or refugee has an overseas CXR read as 'abnormal, not suggestive of TB' should the CXR be repeated in the U.S.?

A. Yes. Any abnormal overseas CXR needs to be re-evaluated by repeating the CXR and administering an IGRA in the U.S. This is true regardless of whether the overseas CXR was 'abnormal – not suggestive of TB' and/or the overseas smears and cultures were negative.

Q. What U.S. testing is recommended for an immigrant or refugee whose overseas CXR was abnormal but whose pre-immigration smears and cultures were negative?

A. Any abnormal overseas CXR needs to be re-evaluated by repeating the CXR and administering an IGRA in the U.S. This is true regardless of whether the overseas CXR was 'abnormal – not suggestive of TB' and/or the overseas smears and cultures were negative.

If the U.S. CXR is also abnormal, three repeat sputa specimens should be obtained for smear and culture with at least one specimen tested with a nucleic acid amplification test (NAAT) to rule out active TB disease.

If the U.S. CXR is normal and the U.S. IGRA is positive, the patient should be offered treatment for LTBI. Treatment should be strongly recommended if the patient is from a high TB incidence country.

If the U.S. CXR is normal and the U.S. IGRA is negative, no further testing is needed.

Q. What follow-up should be done for an immigrant or refugee whose U.S. CXR is abnormal but the U.S. IGRA is negative?

A. In this case the answer depends on whether the patient is symptomatic, what specifically the U.S. CXR showed and the clinician's judgment.

An asymptomatic patient with a negative CXR and IGRA or TST can still have early TB disease, so depending on what the CXR shows the physician may want to order a CT scan of the chest and/or sputa to be collected for smear, culture and possibly a NAAT.

If the patient is symptomatic, however, sputa should be collected for smear, culture and possibly a NAAT.

Q. A recent immigrant to our jurisdiction has a B2 classification and was enrolled in PTOPS. What is PTOPS? Does participation in PTOPS affect the U.S. EDN evaluation?

A. The Preventing TB Overseas Pilot Study, or PTOPS, is a CDC-funded pilot study at an overseas panel site in Vietnam. In the study, immigrants bound for the U.S. are tested for TB and, if diagnosed with LTBI, offered the INH + Rifapentine (3HP) regimen to start in Vietnam and complete prior to immigration or shortly after arriving in the U.S.

For PTOPS participants who completed treatment with 3HP, document that they did so on the EDN form and send the completed EDN form to the TB program.

Physicians or nurses who have other questions about EDN evaluations are encouraged to call the PA TB program at 717-787-6267.

CHAPTER 15, APPENDIX B: EDN EMAIL REMINDER NOTIFICATIONS

30-Day Reminder – Initiation of Medical Evaluation for Immigrants and Refugees

Approximately 30 days ago, notification was received that the immigrants and refugees listed below entered into the United States. CDC advises that for immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB, a medical examination should be initiated within 30 days of notification.

If you have not already attempted contact, please do so now to ensure this requirement is met.

If the medical evaluation has already been done, please complete the EDN follow-up worksheet and submit it to the TB Program. SHC staff should submit via the TB Program Resource Account (TB_Program_Central_Office@pa.gov); county/municipal health departments should submit via encrypted email to the TB Program Resource Account or via fax to 717-772-4309.

Please do not hesitate to contact me with any questions.

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

60-Day Reminder – Medical Evaluation for Immigrants and Refugees

Approximately 60 days ago, notification was received that the immigrants and refugees listed below entered into the United States. The CDC advises that for immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB, a medical examination should be initiated within 30 days of notification and completed within 90 days of notification.

At this point, a medical evaluation should be in process. If the medical evaluation has not yet been initiated, please do so now to ensure this requirement is met.

If the medical evaluation has already been done, please complete the EDN follow-up worksheet and submit it to the TB program. SHC staff should submit via the TB Program Resource Account (TB_Program_Central_Office@pa.gov); county/municipal health departments should submit via encrypted email to the TB Program Resource Account or via fax to 717-772-4309.

If you have any questions, please do not hesitate to contact me.

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

90-Day Reminder – Completion of Medical Evaluation for Immigrants and Refugees

Approximately 90 days ago, notification was received that the immigrants and refugees listed below entered into the United States. CDC advises that for immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB, a medical examination should be initiated within 30 days of notification and completed within 90 days of notification.

At this point, a medical evaluation should be completed. If the medical evaluation has not yet been initiated, please do so now. While it is not ideal for the evaluation to be completed beyond 90 days, it is better than not having a completed evaluation.

If the medical evaluation has already been done, please complete the EDN follow-up worksheet and submit it to the TB Program. SHC staff should submit via the TB Program Resource Account (TB_Program_Central_Office@pa.gov); county/municipal health departments should submit via encrypted email to the TB Program Resource Account or via fax to 717-772-4309.

If you have any questions, please do not hesitate to contact me.

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

120-Day Reminder – EDN Follow-Up Worksheets Overdue

Approximately 120 days ago, notification was received that the immigrants and refugees listed below entered into the United States. CDC advises that for immigrants and refugees with abnormal chest x-rays read overseas as consistent with TB, a medical examination should be initiated within 30 days of notification and completed within 90 days of notification.

At this point, a medical evaluation should have been completed and the EDN follow-up worksheet submitted to the TB Program.

If the medical evaluation has not yet been initiated, please do so now. While it is not ideal for the evaluation to be completed beyond 90 days, it is better than not having a finished evaluation.

If the medical evaluation has already been done, please complete the EDN follow-up worksheet and submit it to the TB Program. SHC staff should submit via the TB Program Resource Account (TB_Program_Central_Office@pa.gov); county/municipal health departments should submit via encrypted email to the TB Program Resource Account or via fax to 717-772-4309.

If you have any questions, please do not hesitate to contact me.

Date of notification, Alien #, DOB, NEDSS #

Date of notification, Alien #, DOB, NEDSS #

CHAPTER 15, APPENDIX C: INSTRUCTIONS FOR COMPLETING THE EDN FOLLOW-UP WORKSHEET

General Instructions

- Write legibly.
- Send only the EDN follow-up worksheet to the central office staff.
- Do not send the Alien Information Chart or medical information. If needed, the central office staff can access that information via the EDN system.
- Do not send progress notes. A NEDSS investigation is initiated for each EDN received. Information in the progress note should be recorded in the investigation notes section of the patient's NEDSS investigation.
- Please submit your EDN follow-up worksheets to the TB central office staff as follows:
    - State health centers – via the TB Resource Account TB_Program_Central_Office@pa.gov
    - County or municipal health departments – via fax to the TB Program at 717-772-4309 or via U.S. mail to the:

      Pennsylvania Department of Health
      TB Program
      Bureau of Communicable Disease, Division of TB/STD
      Health and Welfare Building, Room 1013
      625 Forster St.
      Harrisburg, PA 17120

- If you have questions about how to complete the EDN worksheet, call the TB Program central office at 717-787-6267 and ask to speak with the PHPA or the PHPAA.

Question-Specific Guidance for Completing the EDN Follow-Up Worksheet

- Sections A (Demographics) and B (Jurisdictional Information) of the EDN follow-up worksheet are prepopulated by the EDN system.
- Sections C (U.S. Evaluation), D (U.S. Evaluation Disposition), E (U.S. Treatment for TB Disease or Latent TB Infection), F (Evaluation Site Information), G (Treatment Site Information) and H (Comments) of the worksheet are completed by medical personnel at the state health center or county or municipal health department with jurisdiction for the geographic area where the patient lives. The completed EDN follow-up worksheet is then submitted to the TB central office, where it is reviewed for completeness and the data entered into the EDN system.

- Question-specific guidance for completing the EDN follow-up worksheet is provided in the chart that begins below.

Question Number	Question	Comment(s)
C1.	Date of first U.S. test or provider/clinic visit?	1. To answer C1, enter the earliest of the following: a. The date a TST skin test was administered, blood was drawn for an IGRA, or a chest x-ray (CXR) was done in the U.S., or b. The date the patient was first seen and evaluated for a TB condition by a medical provider in the U.S. 2. If no diagnostic tests were completed and the patient was not seen in the U.S. by a medical provider, then leave C1 blank. TIP: If C1 is blank, the EDN system will only accept "Did not initiate evaluation" in response to question D2a.
C2a.	Was a TST administered in the U.S.?	If "Yes," also answer questions C2b, C2c, C2d and C2e.
C2e.	History of previous positive TST?	Check "Yes", "No" or "Unknown" based on information from the DS forms or the patient's verbal history.
C3a.	Was an IGRA performed in the U.S.?	If "Yes," also answer questions C3b, C3c, C3d and C3e.
C3e.	History of previous positive IGRA test?	Check "Yes", "No" or "Unknown" based on information from the DS forms or the patient's verbal history.
C4.	Pre-immigration CXR available?	If "Yes," also answer question C5. **TIP:** Answer "Yes" to C4 only if you have the pre-immigration CXR film or disc. If there is no CXR film or disc, answer "No". If a CXR film is available, but lacks documentation of patient's name and birthdate, then answer "Unknown". **TIP:** The CDC's Division of Global Migration and Quarantine plans to gradually implement a new process where the overseas panel physician will upload a patient's CXR to a system that will make this information available in the EDN file. Over time, this should significantly increase the percentage of arriving immigrants and refugees with a pre-immigration CXR that can readily be viewed by the U.S. physician.
C5.	U.S. interpretation of pre-immigration CXR	If the U.S. interpretation of the pre-immigration CXR is "Abnormal," then you must also check the appropriate sub-category, either:

Question Number	Question	Comment(s)
		1. "Suggestive of TB," or 2. "Non-TB condition." Check "Unknown" if no CXR film or disc is available. **Tip:** The U.S. interpretation must be based on a review of the CXR film or disc, not the notes documented on Form DS-3030.
C6a.	U.S. domestic CXR done?	If "Yes," enter the date (mm/dd/yy) of the U.S. CXR in response to C6b.
C7.	Interpretation of U.S. CXR	Similar to C5, if "Abnormal" is checked here, then you must also check the appropriate sub-category.
C8.	Comparison of the U.S. and pre-immigration CXRs	**TIP:** The EDN System requires a response to this question. 1. If C4 and C6a are both "Yes," answer C8 by checking "Stable," "Improving" or "Worsening" as appropriate. 2. If the response to C4, C6a or both is "No," then the response to C8 is "Unknown."
C9a.	Completed treatment pre-immigration?	If the patient completed treatment pre-immigration for either TB disease or latent TB infection check "Yes" and answer questions C9b, C9c, C9d, C9e and C9f. **TIP:** Panel physician refers to the physician who did the pre-immigration exam overseas.
C9b.	If treated for TB disease, was treatment completed…	If the response is "treatment completed after panel physician diagnosis (as documented on the DS 3030)", then check the appropriate sub-category: 1. At designated DOT site 2. At non-designated DOT site 3. Other, specify **TIP:** Designated DOT site refers to a site that meets U.S. requirements for providing DOT as defined by the CDC's Division of Global Migration and Quarantine (DGMQ). The site can be either a panel physician's clinic or the local national TB program. Non-designated means the DOT site has not been designated by the DGMQ as meeting U.S. requirements. The DGMQ has little or no confidence in the quality or quantity of treatment provided at a non-designated DOT site.

Question Number	Question	Comment(s)
C10a.	Arrived in the U.S. on treatment?	If "Yes," then you must also: 1. Answer C10b by checking either "TB disease" or "LTBI" as appropriate; and 2. Enter the start date of treatment in C10c (or check the box if the start date is unknown).
C11a.	Pre-immigration treatment concerns?	**TIP:** The EDN System requires a response to this question. 1. If C9a and C10a are both answered "No," then check "No" in response to C11a. 2. If C11a is "Yes," select the appropriate sub-category: a. "Treatment duration too short"; b. "Incorrect treatment regimen"; c. "Inadequate information provided"; d. "Lack of adequate diagnostics"; e. "Unknown DOT/adherence status"; or f. "Other (please specify)."
C12.	U.S. Microscopy/Bacteriology	Answer "Yes" or "No" in response to the question "Sputa collected in the U.S." **TIP:** This question pertains only to sputa collected in the U.S. and covers all results regardless of the specimen collection method – including sputum induction, bronchoscopy and bronchial lavage.
D1a.	Evaluation disposition date in the U.S.	To answer D1a, enter the date when the U.S. evaluation disposition recorded in D2a was made. **TIP:** The EDN System requires a response to D1a whether the patient was seen in the U.S by a health care provider or not.
D1b.	State/jurisdiction of evaluation disposition in U.S.	Enter the name of the Pennsylvania state health center or county or municipal health department that determined the evaluation disposition.
D2a.	Evaluation disposition in U.S.	There are three main options for answering D2a: 1. Completed evaluation; 2. Initiated evaluation/not completed; or 3. Did not initiate evaluation. Check "Initiated evaluation/not completed" if the patient completed a diagnostic test or was seen in the U.S. by a medical provider but was lost to follow-up, moved to another jurisdiction or died before the U.S. evaluation was completed.

Question Number	Question	Comment(s)
		Check “Did not initiate evaluation” if no diagnostic tests were completed and the patient was not seen in the U.S. by a medical provider.
		Next, answer the appropriate follow-up questions: • If “Completed Evaluation” is checked, answer D2b: – Was treatment recommended? Check “Yes” or “No.” – If “Yes,” check either “LTBI” or “Active TB.” • If “Initiated evaluation/not completed” or “Did not initiate evaluation” is checked, answer D2c by checking all of the following that apply: – Not located – Lost to follow-up – Refused evaluation – Unknown – Moved with U.S., transferred to (specify state or local jurisdiction) – Moved outside U.S. – Died – Other (specify)
D3.	Diagnosis	1. **Class 0** and **Class 1** have been combined on the revised EDN form. Check **Class 0** if the patient has no evidence of latent TB infection and no history of exposure to active TB (Class 0), or if the patient has no evidence of latent TB infection but does have a history of exposure to active TB (Class 1). 2. Check **Class 2** for a diagnosis of latent TB infection, no disease 3. Check **Class 3** for TB disease and indicate whether the TB site is pulmonary, extra-pulmonary or both. 4. Check **Class 4** when the patient has a history of TB disease, was treated for active TB, and has no current signs or symptoms of active TB.
D4.	If Diagnosed with TB Disease in D3	To answer D4, enter a zero (0) followed by the patient’s NEDSS investigation number in the space provided for the RVCT number. TBLISS (the TB Latent Infection Surveillance System) is not currently used in PA.
E.	U.S. Treatment for TB Disease or Latent TB Infection	**TIP:** Complete Section E only if treatment for LTBI or active TB is recommended in D2b.

Question Number	Question	Comment(s)
E1.	U.S. Treatment Initiated	1. If E1a is "No," answer E1b by checking all sub-options that apply (patient declined against medical advice, died, currently on treatment, contraindication for treatment, was lost to follow-up, etc.). 2. If E1a is "Yes,": a. Answer E1c by checking either "Treated for TB Disease" or "Treated for LTBI", b. Enter the treatment start date in E2; and c. Enter the name of the state or local jurisdiction where treatment occurred in E3.
E4.	LTBI Regimen	If the answer to E1c is "Treated for LTBI" specify the initial LTBI regimen by checking the prescribed regimen, e.g., isoniazid 9 months, isoniazid/rifapentine 3 months, rifampin 4 months, isoniazid/rifampin/ethambutol/pyrazinamide [RIPE], Unknown, or other (specify). **TIP:** RIPE is listed as a LTBI regimen because some patients suspected of having TB disease are started on RIPE treatment and later determined to have latent TB infection, not TB disease. By the time the final diagnosis is made, some patients have completed enough RIPE therapy to be considered adequately treated for latent TB infection.
AT THIS POINT, SEND THE EDN WORKSHEET TO THE CENTRAL OFFICE STAFF AND KEEP A COPY FOR YOUR FILES.		
E5.	U.S. Treatment Completed	1. For E5a, check: a. "Yes" when the patient completes the full course of treatment and enter the date of the last dose in E6. b. "No" if the patient started but did not complete treatment. i. Next, answer E5b by checking all the reasons why the patient did not complete therapy; and ii. Enter the date the last known dose was taken in E6. c. "Unknown" if contact with the patient is lost and enter the date the last known dose was taken in E6. 2. Resend the EDN worksheet to the central office staff so they can complete entering the data into the EDN system. **TIP:** If known, enter the actual date the patient stopped taking therapy in response to E6. If the actual date isn't

Question Number	Question	Comment(s)
		known, enter your best estimate based on the information available (e.g., date of last clinic visit). **TIP:** If the response to E5a is no or unknown, and the reason is included as one of the responses listed for E5b, then there is no need to write-in a response to "reason therapy stopped" under E6.
F.	Evaluation Site Information	Enter the health care provider's name, the clinic name and the clinic phone number.
G.	Treatment Site Information	If different from Section F, enter the health care provider's name, the clinic name and the clinic phone number. Otherwise, check the box "Same as evaluation site information".
H.	Comments	Add any comments relevant to the case.

pennsylvania
DEPARTMENT OF HEALTH

Chapter 16: TB Patients Lost to Follow-Up

BACKGROUND

Patients with active TB disease who do not complete treatment are at increased risk of relapsing and/or developing resistance to one or more of the drugs commonly used to treat TB. Patients treated for pulmonary TB and deemed non-infectious at the time they were lost to follow-up pose a public health risk if they relapse. Patients with extra-pulmonary TB who were lost to follow-up may also pose a public health risk if they relapse and their TB disease spreads to the lungs or airway.

PURPOSE

The purpose of the policy is to establish a systematic approach to the prompt reporting of any patient with active TB disease who is lost to follow-up.

PROCEDURES

1. The public health nurse (PHN), community health nurse (CHN) or outreach worker will notify their supervisor immediately when a patient with active TB disease misses any appointment for directly observed therapy (DOT).
2. When notified about a third consecutive missed appointment, the Nurse Supervisor will report the missed doses to the state TB program manager and document the notification in the patient's NEDSS investigation within 24 hours.
3. The PHN, CHN or outreach worker will take the following steps to locate the patient within the first 48 hours after the second missed dose. All actions should be documented in the patient chart and the NEDSS investigation.
   a) Call the patient at his or her last known phone number.
   b) Following your local procedure, send a letter via certified mail to the patient's last known residence.
   c) Visit the patient's home or other place of residence. If the patient isn't there, ask other family members, residents or neighbors where the patient may be located.
   d) If the patient is employed and it is appropriate to do so, contact the employer for any information about the patient's whereabouts.
   e) Check other locations frequented by the patient, such as bars, shelters, places of worship, food banks, etc.
   f) Check with the local post office, welfare office, social security office and morgue.
   g) Once the above actions have been completed – and within five working days of the patient's third missed dose – a conference call should be scheduled among the PHN or CHN, the nurse supervisor, TB clinic physician (based upon availability), state TB

medical consultant and state TB program manager to discuss whether all avenues to locate the patient have been exhausted, additional steps to locate the patient need to be taken, or the case can be closed.

4. If the patient is located, identify and address any barriers to the patient continuing treatment, such housing instability or being homeless, lack of transportation, food insecurity, or other physical or mental health issues.
   a) If appropriate, request Reimold funds to address barriers to treatment such as a lack of housing, nutrition, or transportation.
5. If the patient left the jurisdiction and their new location is known, the PHN or CHN will forward that information as follows:
   a) Movement between jurisdictions within Pennsylvania can be reported directly to the state health center or county or municipal health department with responsibility for the patient's new location.
   b) Movement outside the state of Pennsylvania must be reported using an Interjurisdictional Notification form. (See Interjurisdictional Transfer Procedures for instructions.)
   c) If the patient has left the United States and their overseas location is known, contact the Migrant Clinicians Network for their help arranging continued treatment of the patient. (See Interjurisdictional Transfer Procedures for instructions.)

If the patient is not located, document in PA-NEDSS as well as the patient chart and submit the investigation in PA-NEDSS to "Waiting for Central Office Review" for closure.

Chapter 17: Reimold Trust Fund

BACKGROUND

The Reimold Fund was established to assist patients with latent TB infection (LTBI), active TB disease and presumptive TB disease. The Reimold Fund may be used to 1) keep a patient isolated if they do not have a place to stay, 2) purchase food needed for proper nutrition, and 3) secure transportation to medical appointments. Often, TB patients are unable to work during the infectious period, and this puts a strain on the patient and the family. All efforts should be made by the community health nurse (CHN) to connect patients with social services such as the food bank, county assistance office, human service agencies, Low Income Home Energy Assistance Program (LIHEAP), etc. Reimold funds may be used to pay utility bills or purchase clothing that cannot be funded through other community or government assistance programs. The Reimold Fund may also be utilized to purchase items that can motivate patients to be compliant with treatment.

POLICY

The Reimold Fund may be utilized by the state health centers (SHCs) as well as county and municipal health departments (CMHDs).

The Reimold Fund is to be used when enablers and incentives, such as meals, food coupons and local transportation, are necessary to assure patients complete their treatment or when patients are unable to meet their basic needs like housing, utilities and food.

The requests for funds are processed by the district offices. The TB Program considers special requests to spend more than the allocated amounts. Regardless of the amount of the request, the Request for Use of Reimold Fund Form must be completed and maintained on file. The completed form is required to be submitted with the request for an expenditure adjustment. Approval from the TB Program is not required unless expenditures for a specific patient exceed $300 in a fiscal year. Requests that exceed $300 in a fiscal year for a patient must be pre-approved by the TB Program office.

The fund may be used for:

- patients on LTBI treatment;
- patients who have presumptive active TB disease; and/or
- patients who have active TB disease.

PROCEDURES

1. Complete a Reimold Fund Request form

- For SHCs - a Department of Health community health nurse supervisor (CHNS) will complete and sign the SHC Reimold Fund Request form.

  For CMHDs – a CMHD designee will complete and sign the CMHD Reimold Fund Request form.

- The completed request form shall be submitted as soon as possible in advance of the needed service.
- All sections, except the "TB Program Central Office Only" box, must be completed.
- The form shall be completed as follows:
  - Each request shall be for only one patient.
  - The request shall be specific for:
    - the item or service requested,
    - the cost of the item or service,
    - length of time the service will be needed, and
    - justification for the expenditure for the item or service.

      *Cost of the transportation, subsistence and hotel rooms shall not exceed the current reimbursable allowances as specified in the Commonwealth of Pennsylvania directives.
- For SHCs – obtain the signature of the community health nurse administrator (CHNA).

  For CMHDs – obtain an authorized signature.
- For SHCs - if the request exceeds $300 for the state fiscal year for the patient, the district office shall submit the request to the TB Program Central Office via the resource account (TB_Program_Central_Office@pa.gov) for approval. Approval from the TB Program will be emailed to the submitter.

  Example 1: In January 2015, a Reimold request is processed in the amount of $200 for a patient for groceries. Approval from the TB Program is not required, as the request is less than $300.

  Example 2: In February 2015, a Reimold request is processed in the amount of $200 for a patient for transportation. This is the patient's first Reimold request. Approval from the TB Program is not required, as the request is less than $300. In March of 2015, a Reimold request is completed for the same patient in the amount of $150 for groceries. Approval from the TB Program is required because the amount of this request and the previous request in the same fiscal year exceeds $300.

  Example 3: In January of 2015, a Reimold request is processed in the amount of $400 for rent. Approval from the TB Program is required.

  Example 4: In June of 2015, a Reimold request is processed for a patient in the amount of $200 for groceries. TB Program approval is not requested, as the request is less than $300. In July of 2015, a Reimold request is completed for the same patient in the amount of $250. Approval from the TB Program is not required. While the total amount for the patient exceeds $300, July is the start of a new fiscal year,

so the amount does not exceed $300 in the same fiscal year; therefore, approval is not required.

For CMHDs – all requests from CMHDs shall be submitted to the TB Program Central Office via the resource account (TB_Program_Central_Office@pa.gov) for approval.

Approval from the TB Program will be emailed to the CHNA for signature and distribution to appropriate staff for purchasing/processing of requested resources.

2. For approved requests, prepare a general invoice for each patient receiving service.
   - If only one vendor provided a service, a single invoice will suffice.
   - If multiple services were provided to one patient (or family), but by different vendors, a general invoice must be prepared for each service provided for the patient (family).
   - A receipt must be obtained for the item/service purchased.
   - If paying rent, a copy of the lease or a written statement from the landlord stating the amount of the rent must be obtained.
   - **Under no circumstances will cash be given directly to the patient.**
3. The CHN will document (in the plan of care in the patient's record) the type of inducement/enabler given to the patient and the cost of the item.
4. Staff in the district office will work with the CMHD for the purchase of the Reimold-funded item or service.
5. Staff in the district office will maintain a record of all disbursements.
6. Bureau of Community Health Systems (BCHS) will submit a request for an expenditure adjustment (EA) to the TB Program via the resource account (TB_Program_Central_Office@pa.gov).
7. Upon approval, submit the EA, EA backup documentation, and TB Program approval to the Budget Office to process the EA.

EXAMPLES OF ITEMS/SERVICES THAT MAY BE REQUESTED

- Automotive-related items
- Clothing
- Food
- Household items
- Housing
- Personal care items
- Pharmacy items
- Seasonal items (particularly for children)
- Toys and books
- Transportation
- Utilities

HELPFUL HINTS

- Utilize the most current Reimold Fund Request form.

- Complete the form in its entirety.
- Be specific with the justification. To say that the patient has TB is not adequate justification. Here are some sample justifications:
    - Patient is infectious and without a place to live during the infectious period.
    - Patient is unable to work and has applied for food stamps but has not yet been approved and is not currently receiving adequate nutrition.
    - Patient has been sporadic in being present for directly observed therapy (DOT); a gift card for McDonalds will be used as an incentive.
    - Patient does not have transportation and is therefore not willing to take the 12-week LTBI regimen which requires DOT. Reimold funds would be used to buy bus tokens to attend DOT.
- Record all previous Reimold-funded purchases in the bottom table.
- Review amounts of previous and current requests for accuracy.
- If you have questions regarding how to complete the Reimold Fund Request form, contact the TB Program Central Office at 717-787-6267.

COMMONWEALTH OF PENNSYLVANIA
DEPARTMENT OF HEALTH
TUBERCULOSIS CONTROL PROGRAM
REQUEST FOR USE OF REIMOLD FUND

COUNTY/MUNICIPAL HEALTH DEPARTMENT CLINIC/REQUESTOR INFORMATION

Clinic name/county: _____

Return form to (Staff name and email address): _____

PATIENT INFORMATION

NEDSS investigation #_____

Complete the table below by providing the requested information. (Please request no more than 2 months worth of services at one time. Submit completed form to the TB Program Manager via the TB resource account TB_Program_Central_Office@pa.gov.)

Current Reimold requests for this patient in table below:

Date of request	Item or service requested/time period	Justification/statement of need	Amount per service/ per request

Previous Reimold requests for this patient in table below:

Date of request	Item or service requested/time period	Justification/statement of need	Amount previously requested

I hereby certify that this patient is registered in a state, county or municipal health department tuberculosis clinic and qualifies for use of expenditures from the Reimold Fund.

Amount of current request: $0.00

_____ _____
County/municipal health department designee signature Date

Amount approved: $_____

_____ _____
Tuberculosis controller signature* Date

_____ _____
DNA signature Date

*When requests total more than $300.00 per patient, approval from the Tuberculosis Control Officer and the Comptroller is required.

TB Program Central Office staff USE Only: Patient name _____

Email approval from comptroller was received (check if **yes**) ☐

Chapter 18: Do Not Board List

BACKGROUND[1]

In 2007, the U.S. Department of Health and Human Services (HHS), the Centers for Disease Control and Prevention (CDC), and the Department of Homeland Security (DHS) implemented a public health Do Not Board (DNB) list. Use of the list is limited to those communicable diseases that would pose a public health threat if the infected traveler were to be permitted to board a flight. Because infectious tuberculosis (TB) is spread from person to person via the air, individuals with infectious TB pose a public health risk to fellow travelers if they fly on commercial aircraft.

To qualify for placement on the DNB list, individuals must meet the first criteria listed below **and** any one of the other three criteria (#2-4):

1. The individual is known or reasonably believed to be infectious or reasonably believed to have been exposed to a communicable disease that would be a public health threat if the individual were to be permitted to board a commercial aircraft or travel in a manner that would expose the public.
2. The individual is not aware of his or her diagnosis, has been advised regarding the diagnosis and is non-compliant with public health requests, or is unable to be located.
3. The individual is at risk of traveling on a commercial flight or of traveling internationally by any means.
4. The individual's placement on the DNB list is necessary to effectively respond to outbreaks of communicable disease or other conditions of public health concern.

Airlines have been instructed not to issue a boarding pass to an individual on the DNB list for any domestic or international commercial flight arriving in or departing from the United States. To remove an individual from the DNB list, HHS and CDC require a written statement from the treating physician or public health authority that the individual is no longer infectious.

POLICY

To reduce the risk of TB transmission, any TB patient meeting criteria #1 **and** #2, #3 or #4 above must not be permitted to board a commercial flight or travel internationally by any means of transportation. Public health personnel who learn of such a patient should take immediate

[1] Source: Criteria for requesting federal travel restrictions for public health purposes, including for viral hemorrhagic fevers; Federal Register; Vol. 80, No. 59; pgs. 16400-16402

steps, as outlined in the following section, to discuss the case with the proper state and federal public health agencies and determine whether to add the patient to the DNB list.

PROCEDURES

1. Upon identification of a patient who is believed to meet the criteria for the DNB list and is a flight risk, health department staff from the local jurisdiction will notify the TB Program Central Office immediately by calling 717-787-6267 during normal business hours (Monday - Friday, 7:30 a.m. to 4:30 p.m.).

   After normal business hours or on weekends, health department staff from the local jurisdiction should call the Division of Global Migration and Quarantine (DGMQ) at the Philadelphia Quarantine Station – located in Terminal A of the Philadelphia International Airport – at 215-365-6401. Someone is on call at that number 24 hours a day, 365 days a year.

2. Health department staff from the local jurisdiction should ensure the patient's NEDSS investigation is updated with all pertinent information, including:

   a. Laboratory results (smear, culture, nucleic acid amplification test [NAAT], drug susceptibilities);

   b. Chest radiograph results;

   c. Treatment regimen;

   d. Investigation note indicating patient's level of compliance; and

   e. Investigation note including all known flight information. For each flight segment, provide the travel date, departure airport, departure time, airline, flight number, scheduled flight duration and destination airport if known.

3. TB Program Central Office staff will contact DGMQ to arrange a conference call to discuss the case and agree on the action(s) to be taken. Call participants should include staff from:

   a. State health center or county/municipal health department managing the investigation;

   b. TB Program Central Office; and

   c. DGMQ.

4. After the conference call, the TB program manager or public health program administrator will record action steps identified in NEDSS under investigation notes.

   Health department staff from the local jurisdiction will implement action steps as discussed.

   If the patient is placed on the DNB list, he or she can be removed from the DNB list when no longer infectious. This is accomplished by providing DGMQ with a written statement from the treating physician or public health authority attesting that the individual is no

longer infectious. For a patient to be permitted to board a commercial flight, the criteria listed in the chart on the following page must be met:

Condition	Criteria
AFB smear positive or chest x-ray with cavity	• Treatment with an appropriate drug regimen for more than two weeks; and • Three negative smear results
MDR or XDR TB	• Treatment for more than four weeks; • Currently on appropriate treatment; • Three negative smear results; and • Two or more negative culture results after more than two weeks of treatment with no subsequent positive cultures

Questions regarding this process should be directed to the TB Program Central Office staff at 717-787-6267.

Chapter 19: Cohort Review

BACKGROUND

Cohort review is a systematic review of the clinical and case management of tuberculosis (TB) patients and their contacts. A "cohort" is a group of TB cases counted over a specific period. In Pennsylvania, the state TB program conducts at least one cohort review annually. Cohort reviews may be held in person or virtually. County and municipal health departments (CMHDs) can participate in the state TB program cohort review and/or organize and conduct their own cohort review.

The cohort review process serves as a method for evaluating the strengths and weaknesses of the program, increases accountability related to outcomes, and assists in identifying areas where public health staff need additional training and education. It is important to note that cohort review is a mandated activity per the Centers for Disease Control and Prevention (CDC) Cooperative Agreement.

Ideally, all cases in the cohort are reviewed but it is equally appropriate to present a subset of cases based on pre-defined criteria such as sputum smear or culture positive (i.e., infectious) cases, cases with challenging medical and/or case management issues, and cases that offer learning opportunities distinct from textbook cases of TB.

At the end of each cohort review, the TB program issues a written summary of the meeting to include:

- Cohort findings,
- Strengths and weaknesses,
- Suggestions for improvement, and
- Educational points.

The summary is based on information available at the time of cohort review and is distributed to public health nurses in the state Bureau of Community Health Systems (BCHS) and the CMHDs.

OVERVIEW OF THE COHORT REVIEW PROCESS

During cohort review, the care, case management and outcomes of individual TB cases are reviewed by a group that typically includes:

- State TB program staff;
- State TB medical consultant(s) and local TB clinic physicians;
- Public health nurses and supervisors; and

- Public health laboratory staff.

SELECTION OF CASES FOR REVIEW

Two months prior to a scheduled cohort review, the TB program manager will ask BCHS and CMHD nurse supervisors to submit TB cases for presentation along with a brief explanation for why the case is of educational value to all participants. The TB program manager and surveillance coordinator will collaborate on reviewing the cases submitted, add any other cases based on their review of surveillance data, and determine the final list of cases to be presented. The selected cases will cover a variety of challenges including, but not limited to, diagnosis, treatment, identifying and managing side effects/adverse events, case management, contact investigation and interjurisdictional collaboration.

ROLES OF THE COHORT REVIEW PARTICIPANTS

TB program staff plan and implement the review, develop and update the cohort review form, make the final selection of the cases to be presented, review completed cohort review forms for accuracy and completeness, provide programmatic feedback during case reviews and write and issue a written summary of the results following the completion of cohort review.

For each case selected for presentation, it is expected that the BCHS or CMHD nurse or case manager responsible for the care of the patient shall complete the cohort review form for the case, present the case, follow-up on any missing or inaccurate case information, update or correct the case record in PA-NEDSS as needed and share feedback from the medical consultants and/or TB program staff with the clinic staff who could not attend. If the nurse who cared for the patient is no longer providing TB care in the jurisdiction, it is recommended that the nurse supervisor present the case.

The state TB medical consultants provide clinical feedback on the cases presented and provide education when the specifics of a case provide a “teachable moment”. The consultants provide feedback and education constructively and without judgement to reinforce a culture of learning and continuous improvement.

CASE INFORMATION TO BE PRESENTED

A TB Program Cohort Review Presentation Guide Form must be completed by the BCHS or CMHD nurse or case manager responsible for the care of the patient whose case is to be presented. Completed forms must be submitted to the TB program at least two weeks before cohort review. TB program staff review each form for accuracy and completeness and give feedback about any errors to be corrected or omissions to be addressed.

The following information is typically included in each case presentation:

- Patient demographics, e.g., age, sex, birth country, and date of U.S. arrival (if applicable)

- Diagnosis (pulmonary or extra-pulmonary), site of TB disease, co-morbidities, symptomatic or asymptomatic, and status of HIV testing
- TB test information, including interferon gamma-release assay (IGRA) or tuberculin skin test, chest x-ray (CXR) or computer assisted tomography (CT), specimen smear and culture results, nucleic acid amplification test (NAAT), sputum conversion (if applicable) and drug susceptibility test (DST) results
- Treatment information including the initial regimen, treatment start date, treatment stop date (and the reason why) or the date treatment is likely to be completed, method of administration (i.e., directly observed therapy), and whether the patient was privately managed
- For cases of pulmonary, laryngeal and pleural TB, the number of contacts identified, evaluated, and tested as well as their diagnosis, treatment status and challenges related to contact evaluation and treatment
- Any care or case management challenges or obstacles and how they were addressed

ADMINISTRATIVE PROCEDURES

The state TB program completes the following steps to prepare for and conduct the annual regional cohort reviews.

In preparation for cohort review, the TB program manager:

- Sets the cohort review date(s) based on the availability of the state TB medical consultant(s) and, if cohort review is to be held in-person, the availability of an appropriate meeting space.
- Sends a “Save the Date” email for each cohort review session to the state TB medical consultant(s), Bureau of Community Health Systems (BCHS) staff, state TB clinicians, state laboratory staff, TB program staff, and CMHD TB nurses, nurse supervisors and TB clinicians.
- Makes the final selection of cases to be presented at cohort. Case selection is based on pre-defined criteria such as sputum smear or culture positive (i.e., infectious) cases, cases with challenging medical and/or case management issues, and cases that offer learning opportunities distinct from textbook cases of TB.
- Sends a notification email to BCHS and CMHD nurse supervisors to include the final list of the cases to be presented, the date(s) and time(s) for cohort review, the Cohort Review Presentation Guide Form, the instructions for completing the form, the due date for submission of completed cohort forms and any other pertinent information.
- Schedules a teleconference to review cohort review procedures with new attendees (on an as needed basis).

If cohort review is to be held in-person, the TB program manager also:

- Sends the completed case list to the BCHS Assistant Director for identification of staff attending cohort review.
- Obtains necessary approval from the Bureau of Communicable Diseases (BCD) Director to send a formal request to the BCHS Director requesting approval for the identified

nurses to attend cohort review. The formal request includes a list of the cases to be presented and the presenter for each case, the date(s), time(s) and location(s) for cohort review, the Cohort Review Presentation Guide Form and the due date for submission of completed cohort forms and any other pertinent information.

The day of cohort review:

- TB Program staff confirm who is in attendance and that each attendee has signed and returned a confidentiality form.
  - For virtual cohort reviews, TB program staff monitor who has accepted the cohort review meeting notice and joined the meeting and confirmed that each attendee has signed the confidentiality form and emailed it to the TB resource account.
  - For cohort reviews held in-person, TB program staff ensure that each participant 1) lists their name, email address, and organization name on the sign-in sheet and 2) reads, signs, and returns the confidentiality form.
- The TB program manager opens the cohort review by welcoming the participants, reviewing the purpose of cohort review, covering the ground rules, and briefly demonstrating how to present a case using the information from the case review form.
- One or both TB medical consultants adds their perspective that cohort review is not judgmental or punitive, but a forum for the constructive discussion of what is being done well and where there are opportunities for improvement, as well as an opportunity for impromptu education in response to specific case challenges and obstacles.
- Once all cases have been presented, the TB program manager summarizes the cohort findings, results, and recommended actions for improvement.
- The TB program manager then asks the state TB medical consultants for their perspective on the cohort findings, results, and recommended actions for improvement.

After cohort review:

- TB program staff write and issue a summary of the cohort findings, results, and recommended actions for improvement.
- As needed, TB program staff follow-up with the responsible BCHS or CMHD nurses to resolve any discrepancies in PA-NEDSS for the cases presented.
- A condensed version of the cohort review summary is also submitted as part of the TB Program's annual update to the Cooperative Agreement with the CDC.

CMHD COHORT REVIEWS

CMHDs have the option to participate in the TB program cohort review and/or to organize and conduct their own cohort review. If a CMHD elects to hold its own cohort review, CMHD staff must:

- Conduct at least one cohort review per year;
- Send to TB program staff a completed cohort review form for each case counted during the defined cohort period;

- Notify TB program staff 60 days in advance of the cohort review date so that TB program staff can participate; and
- Submit a report to TB program staff summarizing the results of the cohort review.

The Philadelphia TB program has a separate cooperative agreement with the CDC and conducts their own cohort review with the understanding that state TB program staff must be able to attend.

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Chapter 20: Window Prophylaxis for TB-Exposed Children

BACKGROUND

The goal of window prophylaxis is to prevent an early yet undetectable TB infection from rapidly developing into TB disease in vulnerable patients.

The timeframe between exposure to someone with infectious tuberculosis (TB) disease and when *Mycobacteria TB* can be detected by TB tests is typically a 'window' of 8 to 10 weeks, and the treatment of presumptive latent TB infection (LTBI) during this period is typically referred to as window prophylaxis.

The American Thoracic Society (ATS), the Centers for Disease Control and Prevention (CDC)[1] and the American Academy of Pediatrics (AAP)[2] all recommend window prophylaxis for children younger than 5 years of age who are contacts to a person with infectious TB – even if the child's initial TB test is negative – once a diagnosis of TB disease is eliminated.

Window prophylaxis is especially important for children less than 2 years of age because they are significantly more likely than adolescents or adults to:

- Progress to active TB after infection; and
- Develop life-threatening TB disease (e.g., TB meningitis or disseminated TB).

TB clinicians may also prescribe window prophylaxis for children 5 years of age or older, adolescents, or adults of any age who are immunocompromised or, for other medical reasons, are at increased risk of progression from LTBI to TB disease[1].

Clinicians evaluating children for LTBI or active TB disease are strongly encouraged to contact the TB Program at 717-787-6267 to request a medical consultation with the state pediatric TB consultant.

IDENTIFICATION

Children who are candidates for window prophylaxis are most often identified during contact investigations. When public health staff conduct a contact investigation for a patient with infectious TB, be sure to ask whether they live with, care for or interact with children on a regular basis. If interviewing the patient in his or her home, be aware of the surroundings and

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[1] CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis. MMWR 2005;54(No. RR-15):1-37

[2] American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018: pp. 829 - 53

look for any evidence of a child in the household, e.g., toys or stuffed animals, a tricycle, children's clothing, a high-chair or booster seat, etc.

TESTING

Infants or children identified as contacts to an infectious case of TB should be tested promptly.

- For children younger than 2 years of age the tuberculin skin test (TST) is the preferred test for the detection of *M. tuberculosis* infection[2].
- For children 2 years of age or older, either a TST or an interferon gamma-release assay (IGRA) blood test can be used[2]. An IGRA is preferred for children who:
  - Have had the Bacille Calmette-Guérin (BCG) vaccine (to avoid a false-positive TST result caused by a previous BCG vaccination), and/or
  - Are unlikely to return for a TST to be read.
- A chest X-ray (CXR) should be done to rule out active TB, regardless of the TST/IGRA result.
- A negative TST or IGRA TB test does not rule out a diagnosis of TB.

TREATMENT

All children younger than 5 years of age who were exposed to a case of infectious TB should receive a full diagnostic medical evaluation, including a CXR. After the evaluation, proceed as follows unless otherwise directed by the TB clinician:

- For children with an initial TST result greater than or equal to 5 mm of induration or a positive IGRA:
  - If TB disease is ruled out by the diagnostic medical evaluation, start and complete a full course of treatment for LTBI.
- For children with an initial TST result of less than 5 mm of induration or a negative IGRA:
  - If it has been less than eight weeks since the child's last exposure to TB, start the child on window prophylaxis once TB disease has been ruled out. Administer a second TST or IGRA 8 to 10 weeks after the child's last exposure to TB. If the second test is negative, window prophylaxis treatment can be discontinued. If the second test is positive, the child should be re-evaluated, including a repeat CXR to rule out TB disease, and treated accordingly for LTBI or TB disease.
  - If the initial TST or IGRA was a) administered eight or more weeks since the child's last exposure to the patient with infectious TB and b) the TST result was less than 5 mm of induration or the IGRA was negative, then no further evaluation or treatment is needed.
- In Pennsylvania, the standard of care is for children younger than 5 years of age to receive window prophylaxis via directly observed therapy (DOT). DOT administration of window prophylaxis is recommended for children between the ages of 5 and 15 years. If field resources are limited, the decision whether to provide DOT should be made on a case by case basis with the TB clinician and the nurse supervisor.

TIPS FOR GIVING TB MEDICATIONS TO CHILDREN

Given a lack of pediatric dosage forms for most anti-TB drugs, it can be very challenging to administer medication daily to a child over many months. Here are some tips:

- Explain to the parent(s) that the treatment is necessary to reduce the risk of the child developing more serious forms of TB such as TB meningitis.
  - Let the parent(s) know that if the second TST or IGRA is also negative, then the medication can likely be stopped. However, if the second test is positive, the infant or child has already started treatment by being given window prophylaxis.
- Engage the parent(s) in preparing the medication and giving it to the child.
- Be calm, honest and soothing – but firm – with the child.
- Praise the child for taking the medication.
- Consider creating a pleasant routine around taking the medicine using distractions (a hand puppet or a spinner with lights) or small food rewards (such as gummy worms).
- Crush the tablet(s) using a pill crusher, mix in a little warm water to create a slurry, and stir the slurry into a small amount of juice, yogurt, mashed banana, baby food or pudding to help mask the flavor of the pills.
  - If isoniazid (INH) is being combined with food or a beverage for dosing in children, be aware that INH absorption decreases when combined with glucose or lactose and should be mixed with low-glucose food or beverages such as sugar-free pudding[3].
- For infants, consider administering the medication when the baby is hungry.
  - Put a small amount of the medication slurry in the tip of the bottle nipple when feeding an infant warm breast milk or formula. Do this repeatedly during the feeding until all the slurry mixture has been administered.

Be sure that the child consumes all the food or beverage in which the medication has been mixed.

RESOURCES

For more detailed information about the evaluation of contacts, including children less than 5 years of age, see the 2005 CDC “Guidelines for the Investigation of Contacts of Persons with Tuberculosis,” which can be found at https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm.

For updated recommendations from the American Academy of Pediatrics about testing children 2 years of age or older with an IGRA blood test, providing window prophylaxis to children less than 5 years of age, and treatment of children 5 years of age and older with the once-weekly 12-dose regimen of isoniazid and rifapentine (3HP), see the Tuberculosis chapter of the 2018 Red

[3] ATS, CDC, IDSA. Treatment of drug-susceptible tuberculosis. *Clinical Infectious Diseases*, Volume 63, Issue 7, 1 October 2016, Pages e147–e195

Book[2]. The 3HP regimen should not be used in children younger than 2 years of age due to the lack of pharmacokinetic data or an established dose in this age group.

If you have questions about any of this information or want to request a medical consultation by the state pediatric TB consultant, call the Pennsylvania TB Program at 717-787-6267.

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Chapter 21: Testing for HIV/TB Coinfection

BACKGROUND

Human immunodeficiency virus (HIV) infection is the most important known risk factor for progression from latent tuberculosis infection (LTBI) to TB disease. Individuals who test positive for LTBI and HIV infection, and remain untreated for both conditions, have a 7 to 10 percent chance ***per year*** of progressing from LTBI to TB disease. As illustrated below, that is significantly higher than the lifetime risk of progression of about 10% for persons with untreated LTBI and no other risk factors.

Risk of Developing TB Disease

Risk Factor	Risk of Developing TB	Description
TB infection and no risk factors	About 10% over a lifetime	For people with TB infection, **no risk factors**, and no treatment, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime.
TB infection and diabetes	About 30% over a lifetime	For people with TB infection and **diabetes**, and with no treatment, the risk is three times as high, or about 30% over a lifetime.
TB infection and HIV infection	About 7% to 10% PER YEAR	For people with TB infection and **untreated HIV infection** and with no LTBI treatment, the risk is about 7% to 10% PER YEAR, a very high risk over a lifetime.

Visual: CDC Core Curriculum on Tuberculosis, Chap. 2, Figure 2.5

In individuals who have TB disease and are HIV positive, each condition makes the other worse. The Centers for Disease Control and Prevention (CDC) considers a diagnosis of TB disease for someone who is HIV positive as evidence that he or she now has advanced to the third stage of HIV infection known as acquired immunodeficiency syndrome (AIDS)[1].

Today, of the people with TB disease who know their HIV status, about 5% are living with HIV.

THIRD PARTY GUIDELINES

In 2006, the CDC issued new recommendations for HIV testing[2] designed to increase the early diagnosis of HIV infection by recommending that HIV screening be a routine part of medical care. The recommendations included the following:

[1] Source https://www.cdc.gov/hiv/library/factsheets/coinfections/index.html#HIV-and-TB
[2] Source https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

- In all health-care settings, screening for HIV infection should be performed routinely for all patients aged 13--64 years.
- All patients initiating treatment for TB should be screened routinely for HIV infection.
- HIV screening should be voluntary and undertaken only with the patient's knowledge and understanding that HIV testing is planned.
- Patients should be informed orally or in writing that HIV testing will be performed unless they decline (opt-out screening).

Concerning HIV testing in TB clinics, the CDC recommends the following:

- All patients in TB clinics should be tested for HIV, including patients with TB disease or LTBI; persons suspected of having TB because they exhibit the signs and symptoms of TB; and persons identified as contacts to a case of infectious TB disease[3].
- All people newly diagnosed with HIV infection should be tested for TB as soon as possible, even if they have no signs or symptoms of TB disease. People living with HIV and at ongoing risk for TB exposure should be tested annually. The risk for exposure to TB is the same for everyone – being in contact with someone who has an infectious case of TB disease[4].

PENNSYLVANIA STATE LAW

The state laws governing issues of HIV testing, consent, confidentiality, and counseling are:

- The Confidentiality of HIV-Related Information Act of Nov. 29, 1990, P.L. 585, No. 148, as amended by
- The Confidentiality of HIV-Related Information Act – Legislative Intent, Consent to HIV-Related Tests and Counseling Act of Jul. 7, 2011, P.L. 274, No. 59

The full text of Act 148 as amended by Act 59 can be found at https://www.legis.state.pa.us/cfdocs/legis/li/uconsCheck.cfm?yr=1990&sessInd=0&act=148.

OFFERING THE HIV TEST

Consistent with the CDC's 2006 guidelines and the Act 59 Amendment, health care providers in Pennsylvania are expected to provide routine, opt-out HIV testing to their patients.

How the provider offers the test makes a significant difference in patient acceptance. Here are some tips for framing the message:

- Normalize it! Introduce the HIV test as you would any other blood test.
- Emphasize that the HIV test is considered routine for everyone and is not being recommended due to a perceived risk or suspicion of disease.

[3] https://www.cdc.gov/tb/publications/factsheets/testing/HIVscreening.pdf
[4] https://www.cdc.gov/hiv/library/factsheets/hiv-and-tb.html

- Explain to patients diagnosed with or being treated for TB that it's especially important to know their HIV status since it can affect their prognosis and treatment plan.

HIV TESTING PROCEDURES

County and Municipal Health Departments

County and municipal health departments (CMHDs) must comply with the provisions for HIV testing specified in the current contracts with the Pennsylvania HIV and Tuberculosis programs.

CMHDs and state health centers are advised to follow applicable laws, regulations and local procedures concerning HIV testing.

TRAUMA-INFORMED CARE

Despite significant advances in HIV treatment, a positive HIV test result remains a life-altering diagnosis for most patients. Also, many individuals have endured one or more forms of trauma, including a history of – or being witness to – physical or sexual abuse; being part of a minority or marginalized group; social stigma; food and housing instability; addiction; depression or other mental health issues.

Health care providers are encouraged to follow the principles of trauma-informed care (as described in the following chart) when informing patients that they are HIV positive or have progressed to AIDS.

Chart by the Institute on Trauma and Trauma-Informed Care (2015)

Chapter 22: Culturally Competent Care

BACKGROUND

The U.S. Census Bureau projects that over the next few decades the U.S. population will grow at a slower pace, age considerably and become more racially and ethnically diverse[1]. By 2030, net international migration to the U.S. is projected to overtake natural increase (defined as births minus deaths) as the primary driver of U.S. population growth. By 2045, just over 50% of the U.S. population will be Hispanic, black, Asian or multi-racial.

The increasing diversity of the U.S. population challenges health care systems and individual health care providers to provide culturally competent services – especially considering that racial and ethnic diversity among U.S. physicians lags that of the country, with about 70% of primary care physicians identifying as white, though the percentage varies by primary care specialty (i.e. general, family, internal or pediatric medicine)[2].

The goal of culturally competent health care is to provide health care services that meet the social, cultural and linguistic needs of patients. Cultural competence can improve health outcomes and quality of care while also reducing health disparities among racial and ethnic groups[3].

As the cultural diversity of residents in Pennsylvania has increased over the past several decades, so too has the need to understand and practice culturally competent care. This document provides guidance for health care practices and individual health care providers implementing the principles of culturally competent care with their TB and other patients.

CULTURAL COMPETENCE AND TUBERCULOSIS (TB)

Cultural competence is highly relevant to the provision of TB care and services. In 2018, 70 percent of newly diagnosed cases of TB in Pennsylvania were in non-U.S. born individuals. When seeking help to diagnose and treat their illness, non-U.S. born patients often face barriers to medical care including misconceptions and stigma about TB, fear of isolation, loss of community, concerns about immigration status, instability in securing food, housing and transportation. Add in differences in the experience of illness across cultures and any one or more of these factors can challenge effective communication between physician and patient.

KEY TERMS IN CULTURALLY COMPETENT CARE

There are important distinctions among the definitions for several key terms in cross-cultural care as defined below.

Culture is the characteristics and knowledge of a group of people, including language, ethnicity, religion, values, customs, social habits, food, music and arts.

Cultural bias is the tendency to interpret the actions and beliefs of someone from another culture through the lens of the observer's own culture.

Cultural Competency is the knowledge and interpersonal skills that enable health care providers to understand, appreciate and work with individuals from other cultures. It involves an awareness and acceptance of cultural differences, self-awareness, knowledge of the patient's culture and the use of observation, listening and problem-solving skills.

Cultural Knowledge is the familiarization with cultural characteristics, history, values, belief systems and behaviors of the members of another cultural group.

Cultural Awareness is developing sensitivity to and understanding of another ethnic group. This usually involves internal changes in a person's attitudes and values.

Cultural Sensitivity involves recognizing that differences and similarities exist between cultures – without assigning values to those differences.

Diversity among and between groups of people exists on two levels. Individual characteristics that cannot be changed, such as age, race and ethnicity, are examples of primary diversity. Characteristics that can be influenced and can change over a person's lifetime, such as geographic location, marital status, religious beliefs, occupation and economic status are examples of secondary diversity.

COMMON STRATEGIES IN PROVIDING CULTURALLY COMPETENT CARE

While the benefits of cultural competency are well-documented, it's equally important that health systems and medical facilities commit to providing culturally competent care. Common strategies for implementing culturally competent care include the following[4]:

1. **Training** – Training is essential to providing health care providers with the self-awareness, knowledge and interpersonal skills necessary to embrace and deliver culturally competent care to individuals from cultures other than their own. See the Resources section on page 22-6 of this chapter for training resources.
2. **Cultural Exposure** – While it's not feasible to learn about all cultures in detail, prioritize learning about and experiencing the cultures of patient groups represented in your practice.
3. **Interpreter Services** – For patients who do not speak or are not fluent in English, provide interpreter services in the language most comfortable to the patient. Determine whether interpreter services will be needed before meeting with the patient and schedule an interpreter accordingly. Use a professional, qualified interpreter. Some patients may prefer to be accompanied by a friend or relative, but avoid using friends or family as interpreters unless no other option is available.
4. **Mirror the Community** – As appropriate, hire physicians, nurses, outreach workers and office staff that mirror the racial and ethnic makeup of the community served. Because they speak the language and understand the cultural beliefs of community members,

they naturally create a more welcoming environment that can foster better communication.

5. **Include Family and/or Community Members** – A core principle in U.S. medicine is the protection of patient confidentiality, so adult patients are commonly seen alone. However, some cultures – and other groups such as the disabled or the elderly – may prefer or need a family member or close friend to be present during the physician visit.
6. **Work with Community Leaders** – Building relationships with community leaders in business, places of worship, or non-traditional medicine can lead to a better understanding of community beliefs, social structure and traditions. Seek out instances where traditional beliefs overlap current medical practices and use those synergies to build credibility with patients and engage them in their care plan.
7. **Provide Culturally Competent Patient Education** – Wherever possible, provide patient education materials in the primary language of the patient.
8. **Make Accommodations** – If there are enough clinical resources, offer day and evening clinic hours to better meet the needs of your patients. For patients without transportation, consider offering free tokens or tickets for public transportation. For health departments and large medical facilities, work with your local municipal or county transportation authority to see whether a public transportation stop can be added at or near your facility.

GUIDANCE FOR HEALTH CARE PERSONNEL

The following tips about the practice of culturally competent care are based on a presentation by Dr. Laszlo Madaras, a TB clinician who has extensive experience practicing medicine in the U.S. and overseas.

The CONFHER Model

The CONFHER[5] model was designed as a tool to help clinicians apply cross-cultural concepts to patient care. The name of the model is an acronym, with each letter standing for a specific concept as follows:

Communication
: Is the patient comfortable speaking English and can understand common health terms such as pain or fever? If not, use a professional medical interpreter.

Orientation
: Does the patient identify with a specific group? Where were they born? How long have they lived in the U.S.?

Nutrition
: What are the patient's preferred foods? Are there any food taboos in their culture?

Family Relationships
: How is family defined and who is in the family? Who makes the decisions in the family? Is it important for family to be present when someone is sick?

Health and Health Beliefs

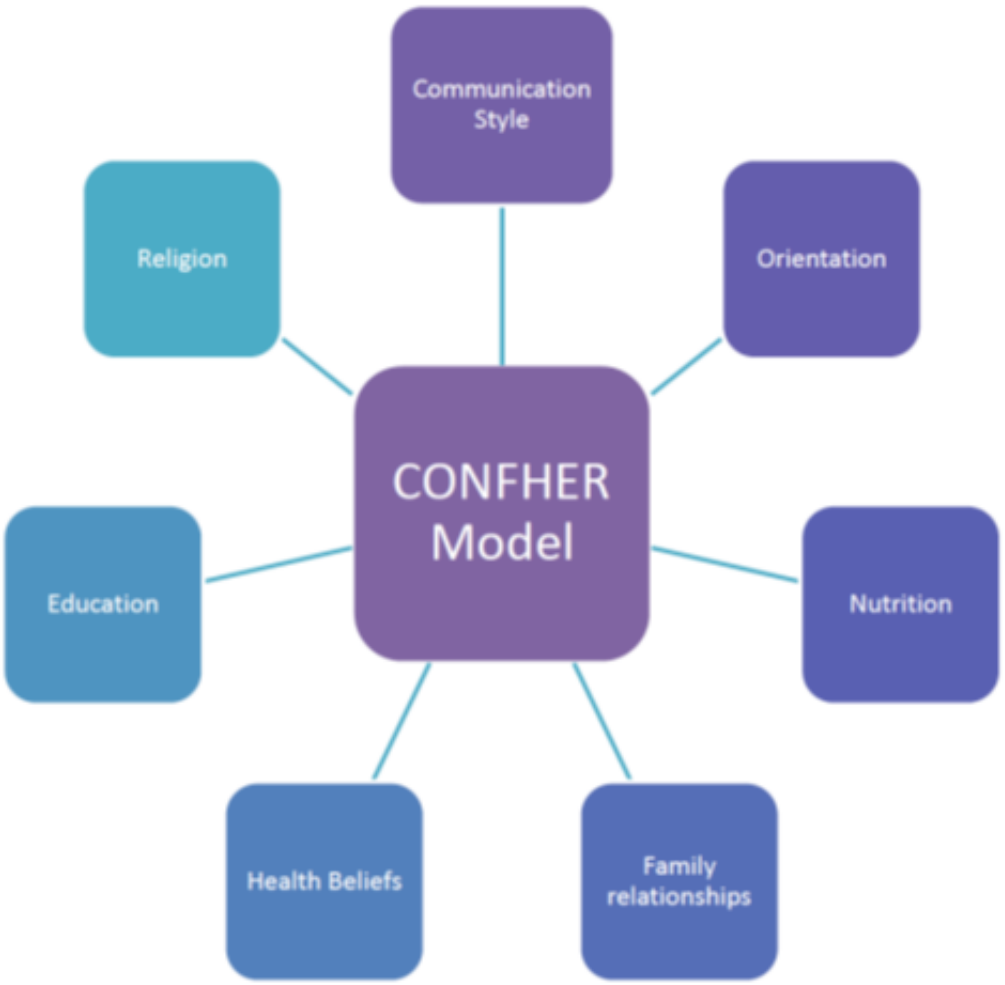
Some cultures believe illness is caused not by germs, but by evil spirits or something being out of balance.

Education

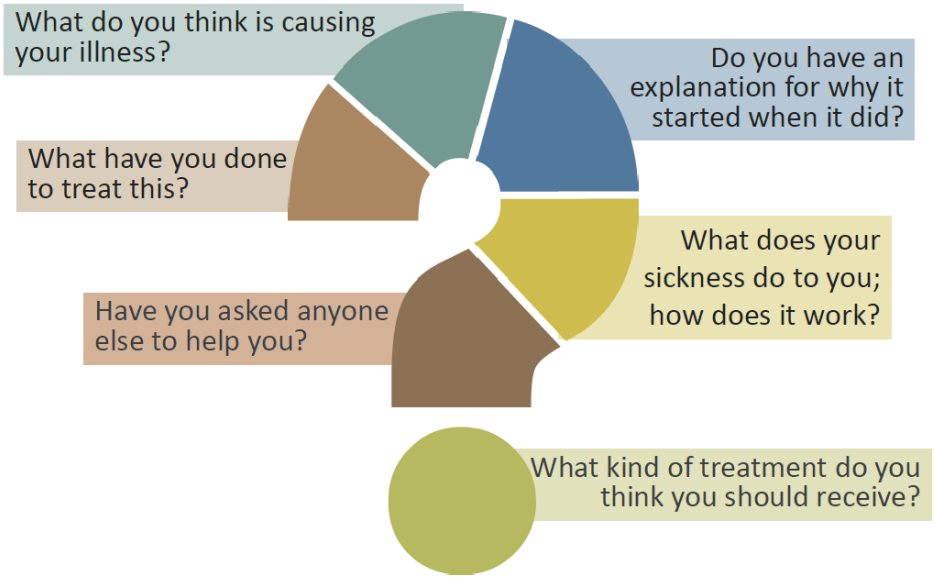
What is the person's educational level? Occupation?

Religion

Does the individual have any religious beliefs or restrictions that have an impact on healthcare and illness?



Here are some questions that health care personnel might ask a patient when using the CONFHER model as a guide:



Before meeting with a patient, try to determine whether they are comfortable speaking in English. If not, arrange for a professional medical interpreter who speaks the patient's primary language to be available in person or via phone. Avoid asking a family member or friend to interpret unless no other option is available.

Cross-Cultural Communication

- **DO** speak directly to the patient, even if using an interpreter.
- **DO** avoid using medical jargon.
- **DO** pay attention to nonverbal behavioral cues by the patient.
- **DO** encourage questions.
- **DO** respect the patient's privacy and modesty.
- **Don't** use family members – especially children – to interpret.
- **Don't** ignore cultural differences e.g., some cultures view looking at someone directly as a sign of aggression.
- **Don't** rely on brochures to communicate – they can reinforce your conversation but should not replace it.
- **Don't** shout – not being comfortable speaking English doesn't mean the person is hard of hearing.

Behavioral Cues

Be aware of the following behavioral cues when talking with a patient:

- If a patient shows signs of impatience or annoyance during your conversation, that may indicate intercultural misunderstanding.
- If a patient asks *you* personal questions, that may indicate a cultural need to establish trust and reassurance.
- Hesitation by the patient when talking with you may mean you've hit a cultural wall.
- Try to treat the patient the way he or she wants to be treated – not the way you like to be treated.
- If patients repeat your instructions exactly, it's possible they are repeating your words without understanding them. Rephrase your instructions and ask the patient to restate in his or her own words.

It's not possible for anyone to be familiar with all cultures or with all aspects of any one culture. However, by striving to be open-minded, non-judgmental and genuinely interested in understanding the patient's cultural background and context, physicians can engender the trust and cooperation of patients from different cultures, ultimately resulting in a better health outcome for the patient.

If you have questions about culturally competent care, contact the TB Program at 717-787-6267.

RESOURCES

- The U.S. Department of Health & Human Services, Office of Minority Health offers on-line, case-based courses about culturally competent care. Both courses provide up to 9 hours of CME or CE credit upon completion.
  - For physicians at https://thinkculturalhealth.hhs.gov/education/physicians
  - For nurses at https://thinkculturalhealth.hhs.gov/education/nurses

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[1] United States Census Bureau (Rev. Sept. 6, 2018). 2030 Marks Important Demographic Milestones for U.S. Population. Available at https://www.census.gov/newsroom/press-releases/2018/cb18-41-population-projections.html

[2] Xierali IM, Nivet MA. The Racial and Ethnic Composition and Distribution of Primary Care Physicians. *J Health Care Poor Underserved*. 2018;29(1):556–570. doi:10.1353/hpu.2018.0036

[3] McCourt School of Public Policy, Georgetown University. (2004) Cultural Competence in Health Care: Is it Important for People with Chronic Conditions? Available at https://hpi.georgetown.edu/cultural/

[4] Brach C , Fraserirector I. Can Cultural Competency Reduce Racial and Ethnic Health Disparities? A Review and Conceptual Model. *Med Care Res Rev.* 2000; 57(Suppl 1): 181-217

[5] Reference: Fong, C. M (1985). Ethnicity and nursing practice. Topics in Clinical Nursing, 7(3), 1-10.

pennsylvania
DEPARTMENT OF HEALTH

Chapter 23: Interjurisdictional Transfers

BACKGROUND

The movement of tuberculosis (TB) patients from one jurisdiction to another is a unique challenge to public health providers and requires that health departments share information promptly in order to maximize the likelihood of continuity of care. The Interjurisdictional TB Notification (IJN) will assist Pennsylvania health departments to facilitate and standardize communication to enhance continuity and completeness of care. It should also improve outcome evaluation of verified cases.

POLICY

The Pennsylvania Department of Health's (PADOH) TB program is responsible for the coordination of IJNs when a patient moves in or out of the commonwealth. Local state health centers (SHCs) and county/municipal health departments (CMHDs) should notify the PADOH TB program central office when a patient plans or moves to another jurisdiction outside of Pennsylvania. The local SHCs and CMHDs within the state are responsible to notify other local SHCs or CMHDs if a patient moves to their jurisdiction. An IJN is not required if a patient is transferring to another jurisdiction within the state of Pennsylvania.

PROCEDURES

I. TB cases transferring within Pennsylvania and the United States

A. TB cases transferring into Pennsylvania:

The TB program's clerk typist III will:

1. Receive the IJN via fax from a state health department.
2. Stamp the date received on the IJN.
3. Provide the IJN to the TB surveillance coordinator.

The TB surveillance coordinator will:

1. Review the information on the IJN for completeness, including:
   a. referring jurisdiction (city, county, state and date sent); and
   b. contact person, phone and fax.
2. Open a new investigation in NEDSS for the following case statuses with all pertinent information from the IJD TB notification:
   a. Verified case;
   b. Suspect case;
   c. Close contact; and

d. Latent TB infection (LTBI).

3. Fax copy to respective jurisdiction.
4. Enter pertinent data into the interjurisdictional database.
5. File IJN in respective general office file folders (verified case/close contact/LTBI). Create new folders each year.

B. TB cases transferring out of Pennsylvania

1. SHC or CMHD staff will complete the IJN and submit it to the TB program central office as follows:

   State health centers – via the TB Resource Account at TB_Program_Central_Office@pa.gov

   County or municipal health departments – via fax to the TB program at 717-772-4309

The clerk typist III will:

1. Receive the IJN via fax or in the TB Resource Account.
2. Stamp the date received on the IJN.
3. Provide the IJN to the TB surveillance coordinator.

The TB surveillance coordinator will:

1. Review the IJN to ensure all information is in PA-NEDSS.
2. Fax IJN to respective state health department TB control program in new state jurisdiction.
3. Enter data on IJN into the interjurisdictional database.
4. File IJN in respective general office file folders (Verified case/Close contact/LTBI). Create new folders each year.
5. For IJNs associated with an electronic disease notification (EDN), review the EDN follow-up worksheet – ensuring that it includes a notation of the patient's new address – and provide a copy to the clerk typist III.

The clerk typist III will:

1. Enter the follow-up worksheet data into the EDN system to include processing the change in address.

C. TB cases transferring to another county within Pennsylvania

SHC or CMHD staff will:

1. Contact new jurisdiction with all pertinent patient information.
2. Ensure patient information is updated and transfer to new jurisdiction in PA-NEDSS.

II. International TB notifications

A. If a patient moves outside of the United States, an international TB notification should be coordinated (with the patient's consent) with one of the services listed

below. Referrals must be noted in the patient's PA-NEDSS investigation indicating that a referral was sent.

TB Net, part of the Migrant Clinicians Network
Phone: 800-825-8205 or 512-327-2017
Medical and confidential fax: 512-327-6140
Website: https://www.migrantclinician.org/services/network/tbnet.html

CureTB, a collaboration between the CDC's Division of Global Migration and Quarantine (DGMQ) and the San Diego County TB Control Program
Phone: 619-542-4013
Fax: 404-471-8905
Email: CureTB@CDC.gov
Website: https://www.cdc.gov/usmexicohealth/curetb.html

Additional information about interjurisdictional transfers outside the U.S. can be found on the CDC website at https://www.cdc.gov/tb/programs/international/default.htm.

B. In cases where patient consent cannot be obtained and there is a public health risk due to active TB disease, the following procedures should be followed:

SHC or CMHD staff will:

1. Complete the international TB notification form.
2. Submit to TB central office.

TB surveillance coordinator will:

1. Review international TB form for completeness and appropriateness of referral.
2. If determined to be appropriate, forward the international notification form to the appropriate international jurisdiction.
3. Contact the Division of Global Migration and Quarantine (DHMQ) at the Philadelphia airport in cases where a flight investigation or Do Not Board procedures may need to be initiated.

III. IJN Definitions, Forms, and Instructions for Initiation and Completion

A. Definitions

Referring jurisdiction: The jurisdiction that initiates the interjurisdictional TB notification. For most verified active TB disease and suspect cases, the referring jurisdiction will be the same as the reporting jurisdiction.

Reporting jurisdiction: The jurisdiction that reports a verified active TB disease patient to the Centers for Disease Control and Prevention (CDC) and, therefore, counts the case in their jurisdiction.

Receiving jurisdiction: The jurisdiction that receives the interjurisdictional TB notification.

RVCT: The Report of Verified Case of TB is the national form used to report a verified case to the CDC.

Follow-up 2 (F/U 2): The Follow-up 2 is the national form used to report outcomes of verified cases to the CDC.

B. Forms

Interjurisdictional TB Notification: Provides a standard array of information to be transmitted to new jurisdictions for active TB disease and suspect cases, contacts, persons with LTBI and source case findings. A copy of the Interjurisdictional TB Notification form can be obtained by going to the following webpage: http://www.tbcontrollers.org/docs/resources/IJN_Form_May2015.

Interjurisdictional TB Notification Follow-up: Provides a standard array of follow-up information to be transmitted back to referring jurisdictions. A copy of the Interjurisdictional TB Notification Follow-up form can be obtained by going to the following webpage: http://www.tbcontrollers.org/docs/resources/IJN_FollowUpForm_November2014.

International TB Notification: Provides a standard array of information to be transmitted to a new jurisdiction for active TB cases. A copy of the IJN form can be obtained by going to the following CDC webpage: https://www.cdc.gov/tb/programs/international/internat_proces.htm.

Note: The IJN form should be initiated by the SHC or the CMHD and sent to the TB program central office. Interjurisdictional paperwork should be sent to the TB program prior to sending any paperwork to the patient's new jurisdiction. The TB program will then forward the IJD to the out-of-state jurisdiction.

C. The following situations are when an IJN should be initiated:

1. For active TB disease and suspect cases who move out of the state.
2. When active TB disease and suspect case patients will be moving out of the state for 30 days or more. Notification may be initiated for patients with shorter planned stays or less than 30 days of treatment remaining at the time of their move, at the discretion of the referring jurisdiction. (For example, if a patient must continue DOT after he/she moves, a notification should be initiated.)
3. For close contacts to AFB smear positive or smear negative active TB disease pulmonary cases. If there are multiple contacts to the same case, they should have individual TB notifications sent.
4. For documented TB infection (LTBI convertors) who have initiated treatment and who will be moving out of the state for 30 days or more. The results and dates of the last negative skin test and the first positive skin test must be entered into the Contact/LTBI section of the IJN to provide information on when the skin test conversion occurred.

5. For latent TB infection (LTBI reactors) who have initiated treatment and who will be moving out of the area for 30 days or more. For LTBI patients, include specific risk factors for disease progression to assist receiving jurisdictions in prioritizing follow-up.
6. For investigation of close associates to an active TB disease index case when that index case has a clinical presentation consistent with recently acquired disease (e.g., children who are <3 years of age). Notifications should not routinely be sent to perform source case finding for a child with LTBI.

D. The following situations are when initiation of an IJN is optional or not required.
1. Notification is optional for contacts, LTBI and source case findings.
2. Notifications should not be sent for contacts, LTBI and source case findings unless reasonable locating information, usually consisting of at least a street address or phone number, is available.
3. An IJN is not required if a patient moves to another jurisdiction in Pennsylvania.
4. An IJN is not required for B1/B2 patients who have not been evaluated or seen in a SHC or CMHD.

E. Instructions for completing the IJN form

Indicate when key information is unknown or pending; do not just leave the section blank.

1. Referring jurisdiction information: Complete all information to provide specific contact information for the receiving jurisdiction.
2. Referral category: Specify the type of patient referral. For verified cases, supply the RVCT number and the state that reported the case to the CDC. This will allow the receiving jurisdiction to ensure the follow-up form is sent to the reporting jurisdiction. Attach the RVCT form whenever possible. For classified immigrants, attach pertinent overseas forms when available.
3. Patient information: Complete all information. If some elements are unknown, indicate this in the space provided. The emergency contact should be a relative or associate who is likely to have locating information about the referred patient.
4. Clinical information: When some or all of the laboratory information is pending at the time of referral, the referring jurisdiction should indicate this and update the information when available. To ensure rapid transfer of information, updates should be accomplished by faxing an updated notification form or by calling the receiving jurisdiction. The tuberculin skin test (TST) information in this section should be used for cases/suspects only. Attach copies of laboratory and X-ray information whenever possible. The “Other” section should include additional types of tests including computerized tomography (CT) scans and nucleic acid amplification tests (NAAT) – attach copies of the reports whenever possible.

5. Contact/LTBI information: This section should be used for contacts, convertors and reactors. The TB skin test #1 and #2 should be completed for all convertor referrals and for other referrals when appropriate. For contact referrals, exposure information should be completed to enhance appropriate investigation by the receiving jurisdiction.
6. Medications: Complete as indicated. Supply adherence information that may be of importance to the receiving jurisdiction for appropriate patient management.
7. Follow-up: All active TB disease and suspect case referrals require an IJN follow-up form to be sent by the receiving jurisdiction. For other referral categories, the referring area should indicate if the follow-up form is requested. Note that the ultimate decision to provide follow-up for contacts and patients with LTBI is at the discretion of the receiving jurisdiction.

F. Initiation of the IJN follow-up form

The IJN follow-up form should be initiated by the SHC or the CMHD and sent to the TB program central office. The TB program will forward the follow-up form to the proper jurisdiction.

The situations when an IJN follow-up form should be initiated are:

1. An interjurisdictional TB notification follow-up form should be used to communicate back to the referring jurisdiction when final disposition of the patient is known.
2. Thirty-day status: At 30 days after notification was received, a status report should be sent to the referring jurisdiction. In instances when the patient is not located within 30 days, “lost” will be considered to represent the final disposition. If the patient is subsequently located, an update should be sent to the referring jurisdiction using the follow-up form.
3. Interim status: This may be sent if an interim update in status is appropriate.
4. Final status: This is when a final status is known.

G. Instructions for completing the IJN TB follow-up form

1. Date Notification Received: Receiving jurisdiction should indicate the date the IJN referral was received.
2. Status:
    a. Thirty days: At 30 days after notification was received, a status report should be sent to the referring jurisdiction. In instances when the patient is not located within 30 days, “lost” will be considered to represent the final disposition. If the patient is subsequently located, an update should be sent to the referring jurisdiction using the follow-up form.
    b. Interim: This status should be used whenever updated information needs to be sent to the referring jurisdiction.
    c. Final: This is to be used at the time a final status is known.

3. Return follow-up form to: The receiving jurisdiction should complete this information using the contact information provided on the original IJN referral form.
4. Patient information: Complete as indicated.
5. Case: Final outcome in the receiving jurisdiction will be indicated. The follow-up form should be sent to the reporting jurisdiction. The original reporting area will be responsible for providing follow-up form results to CDC.
6. Suspect: The receiving jurisdiction will indicate whether the suspect case was active, and, if so, the method of verification. In some cases, the referring jurisdiction may still be the appropriate jurisdiction to report the case. If so, the receiving jurisdiction should also provide a final follow-up status and follow-up form to the reporting jurisdiction. This section can also be used to provide follow-up information for individuals investigated as part of a source case finding.
7. Contact: Some jurisdictions may not provide follow-up on all contact referrals and should indicate, “No follow-up performed” on the 30-day status report. If follow-up is performed, indicate the final outcome. Whenever possible, the receiving jurisdiction should attach contact follow-up information including screening dates and results, as well as treatment dates and outcome. This will assist the referring area in completing contact information required by the CDC.
8. LTBI: Some jurisdictions may not provide follow-up on all LTBI referrals and should indicate, “no follow-up performed” on the 30-day status report. If follow-up is performed and the patient is located, indicate the outcome. This section can also be used to provide follow-up information for convertors.

Chapter 24: Providing Tuberculosis (TB) Services During a Public Health Emergency

BACKGROUND

A public health emergency can be the result of an outbreak of an infectious disease, the emergence of a new pathogen, natural causes such as severe weather, accidents such as an explosion at a refinery or plant that releases toxic fumes or radiation, threats to public safety resulting in curfews or restricted access to certain geographic areas or acts of domestic terrorism.

Even when redeploying public and private healthcare resources to address a public health emergency, it remains critically important to continue providing TB services. TB is the world's deadliest infectious disease and kills about 1.5 million people worldwide every year – or more than 4,000 men, women and children per day.

As the primary provider of TB services, public health personnel evaluate patients for TB, treat patients diagnosed with TB disease or latent TB infection (LTBI), complete contact investigations for patients with infectious TB to prevent the spread of TB, assess patient response to treatment, and monitor patients for side effects and adverse reactions. During a public health emergency, public health personnel need to quickly devise and implement creative, efficient and safe ways to continue providing critical TB services – while also protecting their own health and safety.

This document provides guidance for providing TB services during a public health emergency based on recommendations from the Centers for Disease Control and Prevention[1] (CDC), the Pennsylvania (PA) TB medical consultants and the PA TB program.

PRIORITY TB SERVICES

During the COVID-19 outbreak, the CDC recommended prioritizing patient care services considering the following factors:

- The level of community transmission in the service area;
- Characteristics of the populations to be served;
- Local capacity to implement effective prevention and control activities; and
- Availability of effective interventions

[1] Specifically, the National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHHSTP) at the CDC

The first factor can be modified based on the nature of the specific public health emergency.

Table 1: CDC Recommendations for Priority TB Services Based on Levels of Community Transmission lists the recommended priority TB services in situations where the community impact of the public health emergency is none to minimal or minimal to substantial.

TABLE 1: CDC RECOMMENDATIONS FOR PRIORITY TB SERVICES BASED ON LEVELS OF COMMUNITY TRANSMISSION

CDC Recommendations for Priority TB Services	
In Communities with None to Minimal Transmission	**In Communities with Minimal to Substantial Transmission**
Services for clients for whom medical management cannot be delayed or interrupted:	
• Initial evaluation and treatment of patients with suspected or confirmed TB disease • Clinical follow-up of patients on treatment for suspected or confirmed TB disease • Directly observed therapy (DOT) of patients on treatment for suspected or confirmed TB disease • Evaluation of high-risk contacts to infectious TB patients • Treatment initiation of contacts diagnosed with TB disease or LTBI	• Initial evaluation and treatment of patients with suspected or confirmed TB disease • Clinical follow-up of patients on treatment for suspected or confirmed TB disease • Directly observed therapy (DOT) of patients on treatment for suspected or confirmed TB disease • Evaluation of high-risk contacts to infectious TB patients • Treatment initiation of contacts diagnosed with TB disease or LTBI
Services that could be continued or delayed depending on local circumstances:	
• Evaluation of low-risk contacts to infectious TB patients • Targeted TB testing • Evaluation of Class B immigrants and refugees • Administrative TB screening	

Source: Interim CDC Guidance on Handling Non-COVID-19 Public Health Activities that Require Face-to-Face Interaction with Clients in the Clinic and the Field in the Current COVID-19 Pandemic; April 8, 2020. Downloaded on June 9, 2020 at https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-covid-19-client-interaction.html

In addition to the above guidance, Dr. Edward Zuroweste, medical consultant to the TB program, recommends that individuals (including those with EDN referrals) be prioritized for TB evaluation based on their risk of progressing from LTBI to TB disease. Individuals with the highest risk of progression – especially children – should be evaluated first.

ALTERNATE METHODS OF PATIENT CONTACT

Under normal circumstances, patients are seen in-person for a range of TB services. During a public health emergency, public health personnel are encouraged to increase the use of alternate methods of patient contact.

Telehealth Visits

- Telehealth visits are an acceptable alternative to in-person visits if:
  - The TB clinician determines that the objectives of the patient visit can successfully be met through a telehealth visit. Factors to consider in making that determination include the reason for the telehealth visit, the patient's medical history and current medical issues, and the patient's ability to communicate with the TB clinician or nurse.
  - The telehealth technology is compliant with the privacy provisions of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).
- The U.S. Department of Health and Human Services (HHS) Office of Civil Rights (OCR) is responsible for enforcing HIPAA regulations. The OCR has the authority not to impose penalties on healthcare providers for HIPAA violations during a public health emergency if "patients are served on a good faith basis". For the most up-to-date status of HIPAA enforcement, refer to the health information privacy page on the HHS website at https://www.hhs.gov/hipaa/index.html.

In-person Visits

- The following patients need to be seen in-person either in TB clinic or through a house call by the TB clinician:
  - Patients with TB disease who are not responding to treatment; and
  - Any patients with TB disease or LTBI experiencing side effects or adverse reactions.
- TB clinicians may choose to visit a patient where they live in order to evaluate the individual for TB disease and/or monitor their response to treatment.
- Proper health and safety precautions should be followed by the clinician when visiting a patient, taking into account the need for personal protective equipment (PPE) and the nature of the patient's place of residence (e.g., a private residence or a congregate setting such as a nursing home or homeless shelter).

Video DOT

- To optimize personnel resources during a public health emergency, video DOT may be used with the explicit approval of the TB clinician for appropriate TB patients and LTBI patients on the once-weekly, 12-dose regimen of isoniazid plus rifapentine.
- As with telehealth visits, only those telehealth technologies compliant with HIPAA privacy protections should be used.

DELIVERY OF TB MEDICATIONS TO PATIENTS

Alternative methods of delivering TB medications to patients will likely be necessary during a public health emergency. Options include:

- Providing the patient with enough medication to self-medicate until the next scheduled in-person DOT or clinic appointment;
- Personally delivering medication directly to the patient. Based on the specific circumstances, clinic personnel or outreach workers can deliver medications using a “no-contact” delivery procedure or with appropriate PPE; and
- Implementing curbside or drive-through medication delivery at the public health facility or a nearby parking area on specified dates and times or by individual appointment.

The TB program does **not** recommend mailing medications to patients.

COLLECTION OF SPECIMEN SAMPLES

- The collection and bacteriologic testing of specimen samples is a core element of the diagnostic process. The initial clinical evaluation of a patient for TB should include specimen collection as appropriate.
- Refer to **Chapter 5: Diagnosis of LTBI and TB Disease** of the PA TB Manual for guidance on the collection and testing of specimen samples.

PATIENT RECORDS

While patient care is the priority, maintaining accurate, concise and timely patient records remains a key task during a public health emergency. During prolonged periods of long hours and multiple responsibilities, it becomes even more difficult to recall conversations and key information can be lost.

- Patient records should be maintained in accordance with local policies and procedures. If it’s not practical to document progress notes in the patient’s record during or immediately after a patient encounter, consider capturing the key points in notes organized by the PA National Electronic Disease Surveillance System (PA NEDSS) investigation number – avoiding the use of any personally identifiable information. The information can subsequently be entered in the patient’s chart or electronic health record.
- Progress notes and other pertinent information should be entered as soon as practicable in PA NEDSS or any future surveillance system used by the PA Department of Health.
- In some instances, TB Program staff may provide alternate guidance concerning entry of surveillance data in PA-NEDSS.

TB PATIENTS NEEDING HELP WITH BASIC NEEDS

Patients having difficulty meeting their basic needs for food, shelter or transportation during a public health emergency will find it even harder to successfully complete their TB treatment. Local public health jurisdictions are encouraged to submit a request for Reimold funds to assist such patients.

Refer to **Chapter 17: Reimold Trust Fund** of the PA TB Manual for guidance on how to submit a request for Reimold funds.