This Manual is dedicated to:

CHARLES DEGRAW

KAREN FUSILIER

SHIRLEY HOOPER

SHARON LINER

LOUISE MCFARLAND

ROMA OLIVERI

JUDY PLOUGH

WILLIAM “BILL” STUTSON

NYS (NANCY) WEIMER

CAROL WILLIAMS

MERETTA WILSON

for their years of service and commitment to the
Tuberculosis Control Program and citizens of Louisiana.
Manual Revisions

This Manual supersedes all previous versions

If you have any questions regarding diagnosis, treatment, screening, and contact investigations is available on request from the Office of Public Health TB Control Program’s Central Office located in New Orleans, or The Regional TB Control Programs.

<table>
<thead>
<tr>
<th>Central Office, New Orleans, 504-568-5015</th>
<th>Region 5, Lake Charles, 337-478-6020 ext. 6070</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region 1, New Orleans, 504-826-2049</td>
<td>Region 6, Alexandria, 318-487-5299</td>
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<tr>
<td>Region 2, Baton Rouge, 225-242-4917</td>
<td>Region 7, Shreveport, 318-676-5251</td>
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<tr>
<td>Region 3, Thibodaux, 985-447-0916 ext. 323</td>
<td>Region 8, Monroe, 318-361-7208</td>
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<td>Region 4, Lafayette, 337-262-5616 ext. 154</td>
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1 Outline

1.1 Goals

1.1.1 The goal of the Tuberculosis Control Program is to lower the morbidity and mortality from tuberculosis (TB) in Louisiana, and ultimately obtain eradication of the disease.

1.1.2 To reach this goal the program’s objectives are:
- To reduce the risk of becoming infected with TB for persons who are not yet infected
- To reduce the risk of progressing to active disease in persons who have become infected with TB
- To reduce the risk of severe complications and death once active disease has developed

1.2 Methods

1.2.1 The methods used to reduce these risks are:

1.2.1.1 Case finding among symptomatic persons in groups with high prevalence of TB infection or disease (e.g. high-risk contacts of a TB case), or in groups where the presence of an infectious case could provoke a major TB outbreak, e.g.:
- Persons with HIV/AIDS
- Persons with immunosuppression due to diseases or disease treatments such as cancer or chemotherapy
- Persons taking TNF-α (tumor necrosing factor-alpha) inhibitors or prolonged corticosteroids
- Persons with substance abuse disorders
- Persons with silicosis
- Persons with diabetes mellitus
- Persons with severe kidney disease
- Persons who have had organ transplants
- Persons residing in long-term care facilities
- Persons in correctional facilities
- Homeless persons
- Persons in long-term drug treatment programs

1.2.1.2 Early diagnosis, treatment, and follow-up of patients with TB disease, to stop transmission and reduce the risk of complications and death. Treatment of infectious cases, by sterilizing the main source of bacilli is the best way to reduce the risk of infection in the population.

1.2.1.3 Early detection of TB infection and preventative treatment to reduce the risk of progressing to active TB disease.

1.2.1.4 Preventative treatment of non-infected high-risk contacts to reduce risk of infection/disease.

1.2.1.5 Education of all persons with TB infection or disease and the general population.

1.3 Program Structure and Services

1.3.1 Central Office

1.3.1.1 Central Office staff are responsible for the planning and implementation of statewide TB control activities. These responsibilities include:
- Consultation to regional and local public health staff and private medical providers
- Create and implement statewide program policies and guidelines
- Statewide surveillance and reporting
- Education and training
- Program budgeting and finance
- Program monitoring and evaluation

1.3.2 Regional TB Program Managers

1.3.2.1 The nine regional program managers are responsible for the operations of the TB Control Program in each designated region. These responsibilities include:
- Ensuring compliance with program policies and procedures
- Managing and monitoring surveillance and containment activities, including the Louisiana Administrative Code 51:II.117 (Public Health - Sanitary Code)1 and quarantine regulations
- Supervision of disease intervention specialists (DIS)

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1 Louisiana Administrative Code, Title 51, Part II (LAC 51:2)
• Regional reporting, surveillance, and case management
• Serving as a liaison with the regional TB clinic, parish health units, and area health care facilities

1.3.3 Disease Intervention Specialists (DIS)

1.3.3.1 The DIS are responsible for treatment adherence and patient management. DIS responsibilities include:
• Case management
• Contact investigation
• Clinic and field directly observed therapy (DOT)
• Entering patient information into LATB, EHS, etc.
• Sputum collection
• Blood assay (IGRA) and Tuberculin skin testing

1.3.4 Regional TB Medical Clinics

• The nine regional medical clinics provide medical care and supervision to TB suspects, cases, and contacts.
• The clinics accept referrals from public and private health care providers
• Monthly nursing assessments and monitoring of patients receiving treatment for TB infection or disease are conducted at these clinics.

1.3.5 Surveillance

• Surveillance is the ongoing process of systematic collection, analysis, and interpretation of data, for the purpose of planning, implementing and evaluating public health practice.
• For more information about TB Control Program surveillance activities see Section 4. Surveillance.

1.3.6 Diagnostic Services

1.3.6.1 Diagnostic services available through the Office of Public Health, at no out-of-pocket expense to the patient include:
• Testing for TB infection or disease, which is available for TB suspects, cases, and contacts.
• Radiological testing for patients receiving TB care through the Regional Medical Clinics
• Medical evaluation and treatment provided by physicians who are specialists in the care of persons with TB infection and disease, for adult and pediatric patients

1.3.7 Laboratory Services

• Microbiological testing including smear, NAAT (nucleic acid amplification test), culture identification to determine the presence or absence of mycobacterium tuberculosis.
• Drug susceptibility testing of M.tb positive specimens
• Xpert® MTB/RIF Assay
• Testing for antibodies to Human Immunodeficiency Virus (HIV) in all adult and adolescent patients over the age of 13 years. Those 12 years of age and younger receive an HIV test when indicated as necessary.
• Blood testing for liver and kidney function as indicated by program guidelines, when drug treatment is given for TB infection or disease.

1.3.8 Pharmacy Services

• Anti-TB drugs are available throughout a treatment regimen with a written prescription from a Louisiana licensed physician at no expense to persons being treated in Louisiana.
• The Office of Public Health pharmacy fills all prescriptions for anti-TB medications for TB infection and disease. The pharmacist will not fill unusual regimens or second line drugs without approval of the TB Control Program Central Office.

2 Tuberculosis (TB)

2.1 Classifications-Definitions

2.1.1 The classification of TB is based on the broad host-parasite relationships as described by exposure history, infection, and disease. The classification system applies to adults and adolescents.

2.1.1.1 Class 0: No TB exposure, Not infected. No history of TB exposure, and no evidence of M. tuberculosis infection or disease, negative reaction to tuberculin skin test (TST) or interferon gamma release assay (IGRA)
2.1.1.2 **Class 1:** TB exposure, Not Infected. History of exposure to *M. tuberculosis*, no reaction to TST or IGRA at least 8-10 weeks after exposure.

2.1.1.3 **Class 2:** TB infection, No TB disease. Positive reaction to TST or IGRA, negative bacteriological studies (smear, NAAT, culture), no radiographic evidence of active TB disease.

2.1.1.4 **Class 3:** TB disease. Positive culture for *M. tuberculosis* - or - positive reaction to TST or IGRA, plus clinical, bacteriological, or radiographic evidence of current, active TB disease.

2.1.1.5 **Class 4:** Previous TB disease. Not clinically active, may have past medical history of TB disease, abnormal but stable radiographic findings, positive reaction to TST or IGRA, negative bacteriologic studies (smear, NAAT, culture), no clinical or radiological evidence of current active TB disease.

2.1.1.6 **Class 5:** TB Suspect. Signs and symptoms of active TB disease, but medical evaluation not complete.

2.2 Transmission and Pathogenesis

2.2.1 TB is an airborne, communicable disease caused by Mycobacterium tuberculosis. TB can affect any organ of the body. The most common source of transmission is patients with pulmonary or laryngeal TB who produce sputum that is smear positive with acid fast bacilli (AFB).

2.2.2 Infectious droplet nuclei are particles produced when a person with pulmonary or laryngeal TB coughs, sneezes, talks or sings. Small droplets (1-5 microns) may remain suspended in the air for hours after being exhaled. When inhaled, droplet nuclei may reach the alveoli starting a new infection.

2.2.3 The probability of transmission depends on four factors:
- The infectiousness of the person with TB disease, which is determined by microscopic examination of sputum samples.
- The duration of exposure to the infectious case.

- The environment in which the exposure to an infectious case occurred.
- The susceptibility of the person exposed to the infectious case.

2.2.4 Tuberculosis infection occurs if droplet nuclei are inhaled, pass down the bronchial tree, and settle in the alveoli beyond the mucociliary blanket. The bacilli are phagocytized and multiply locally. The bacilli may spread through the lymphatic channels and bloodstream. The initial lesions in the lungs and draining lymph nodes are of limited duration and heal without treatment.

2.2.5 TB infection or disease occur most often among household contacts or other high-risk contacts. There is a low risk of infection in casual or other low-risk contacts.

2.2.6 Approximately 5% of persons recently infected with tuberculosis bacilli will develop active disease within two years of infection, if not preventatively treated for infection. This risk is higher in infants and toddlers than in older adolescents and adults. Among those who do not develop disease in the first two years, 3% to 5% may develop active disease later in life.
- Of those 5% who develop disease within two years of being infected, 50% will develop disease within one month, 75% will develop disease within three months, and 90 percent will develop disease within one year.

2.2.7 Individuals with HIV and tuberculosis infection have an 8-10% annual risk of progressing to active disease.

2.2.8 The host develops delayed-type hypersensitivity, which is a cell-mediated reaction to the tubercle bacilli. This is associated with a TST or IGRA that can become positive 2 to 10 weeks after infection.
- Although no definite proof is available yet, it seems that the reaction of hypersensitivity plays little role in acquired immunity of TB in humans. Although both immunity and hypersensitivity involve a cellular type
of immune response, separate T-lymphocyte populations mediate responses.

2.2.9 Factors that prevent relatively healthy individuals from controlling the dividing bacilli are poorly understood. The immune response may be altered:
- By certain conditions, e.g. HIV, silicosis, diabetes, cancer, diseases associated with immunosuppression, malnutrition, etc.
- By treatment with corticosteroids or other immunosuppressant medications.
- During the first few years of life, during puberty and adolescence, and in the postpartum period for women.

2.2.10 In a small percentage of recently infected persons, the initial control of tubercle bacilli by the body is inadequate. There is direct progression of infection to active primary disease, with or without dissemination outside the lungs to the pleura, meninges, or other organs.

2.2.11 Tubercle bacilli may remain viable but dormant within the tissues for years. The immunocompetent response inhibits replication of tubercle bacilli. However, the immune system does not have the capacity to eliminate all tubercle bacilli. An individual’s protective response may wane over time. In some previously infected individuals there is a breakdown in resistance to the tubercle bacilli and bacilli multiply. The reasons for this breakdown are unknown. Tubercle bacilli from a remote infection may shift from a dormant state to multiply and cause disease.

2.2.12 Tuberculosis should be designated as recurrent if a patient has previously had verified tuberculosis, responded to therapy, and was discharged or lost to follow up for more than 12 months, and again has active TB disease.

2.3 Clinical Information

2.3.1 Active TB is an infectious disease that usually presents with symptoms. However, many patients, even some with extensive disease, have insidious symptoms they may not recognize or consider significant. Other patients may be truly asymptomatic. Patients who are asymptomatic or do not recognize their symptoms as symptoms of TB can only be identified through a history of exposure, an abnormal chest radiograph, confirmation of infection with a skin or blood tuberculosis test, or cultures positive for Mycobacterium tuberculosis.

2.3.2 Symptomatic patients can be characterized as having (1) generalized systemic signs and symptoms, (2) pulmonary signs and symptoms, (3) signs and symptoms related to other organs, or (4) a combination of these characteristics.

2.3.2.1 Generalized Signs and Symptoms
- Frequently patients are first aware of fatigue, anorexia, weight loss, night sweats, or low-grade fever that persists over weeks or months. Other patients present with acute febrile illness, chills, and generalized influenza like symptoms, and medical attention is not sought until the symptoms fail to resolve. Erythema nodosum may occur rarely with the acute onset of TB. At times non-specific systemic symptoms associated with fever of unknown origin may be the only manifestation of TB. This syndrome can defy intensive diagnostic evaluation at the hospital, and may be resolved only through a systematic evaluation of diagnostic studies such as repeated chest radiographs, biopsies and cultures of specimens for mycobacteria from lung, pleura, pericardium, liver, peritoneum, bone marrow, blood, or even an exploratory laparotomy.
- In children the onset of TB is usually asymptomatic and may be far advanced before fever and weight loss begin. A productive cough in children is extremely rare; obtaining gastric aspirates via gastric washing to support the diagnosis should be considered.
• Miliary TB, also referred to as disseminated TB, is seen in all age groups. Patients may be acutely ill with fever, dyspnea, and cyanosis, or be chronically ill with systemic symptoms. Miliary TB is recognized most often by the diffuse, finely nodular, uniform infiltrates visible on the chest radiograph. However, fever and systemic signs and symptoms may antedate the miliary pattern.

2.3.2.2 Pulmonary Signs and Symptoms
• Typically, there is the almost imperceptible onset of a cough, which slowly progresses over weeks or months to become more frequent and associated with the production of mucoid or mucopurulent sputum. Occasionally there is recurring dull, aching pain, or tightness in the chest. Hemoptysis is unusual but prompts the seeking of medical attention. Dyspnea is also common and usually indicates either extensive parenchymal involvement, a massive pleural effusion, pericardial involvement or other underlying cardiopulmonary disease.
• Some patients present with the acute onset of productive cough, fever, chills, myalgia, and sweating similar to signs and symptoms of influenza, acute bronchitis, or pneumonia. Physical findings may or may not be present; they are non-specific and not diagnostic of TB. There may be acute recurrent pain with pleural effusion.

2.3.2.3 Other Organs Signs and Symptoms
• TB may affect any organ in the body, including genitourinary tract, lymphatic system, bones and joints, meninges, peritoneum, pericardium, and larynx. TB in other organs can occur at all ages. Symptoms of TB disease of other organs are variable and often similar to the symptoms of other infections. The severity of the disease may range from mild to life threatening.

2.4 Diagnostic Methods

2.4.1 Tuberculin Skin Test
2.4.1.1 The tuberculin skin test (TST) is the most widely available method to indicate TB infection. The tuberculin test is based on the fact that mycobacterial infection produces delayed-type hypersensitivity to certain products of the organisms contained in culture extracts called "tuberculin." This cell-mediated or delayed-type hypersensitivity reaction is manifested by induration in sensitized persons. Such persons are termed "reactors." Not all reactors are infected with M. tb; infection with mycobacteria other than the tuberculosis species may cause weak cross-reactions. The larger the reaction with a given antigenic dose, the higher the probability that the reaction is specific for that antigen.

2.4.1.2 Technique
• Purified Protein Derivative (PPD) Tuberculin stabilized Tween 80 and standardized by biologic assay to five tuberculin units (TU) is the recommended antigen. The standard technique (Mantoux) is the intradermal injection of 0.1mL of PPD-tuberculin containing 5 TU intradermally, usually on the volar surface of the forearm. After cleansing the forearm with disinfectant, allow the area to dry before administration. The injection is made with a short, bluntly beveled, platinum or steel needle with a plastic tuberculin syringe. The injection should be made just beneath the surface of the skin, with the needle bevel upward. Inject slowly. A discrete pale elevation of the skin (a wheal) 6 to 10mm in diameter should be produced when the prescribed mount of fluid (0.1mL) is accurately injected intradermally. Even though the detergent Tween 80 minimizes the absorption of tubercle-protein, tuberculin should never be transferred from one container to another, and skin tests should always be given immediately after the syringe is filled. Used needles and syringes should be placed in a puncture resistant container and disposed of as medical waste.
• The site of injection should be examined 48-72 hours after the injection, the time when the induration is usually most evident. Large reactions however will be evident up to seven days later. The reaction should be recorded as the diameter of induration in millimeters, measured transversely to the long axis of the forearm.
• Erythema without induration is not considered evidence of tuberculosis infection. However, if the injection is subcutaneous instead of intradermal, as evidenced by the lack of a wheal at the time of injection, erythema could result with little or no induration and the test should be repeated.

2.4.1.3 Reading a PPD
• A PPD reading should be read across the arm, in good light, with the forearm slightly flexed at the elbow. The presence or absence of induration may be determined by inspection (from a side view against the light as well as by direct light) and by palpation of the injection area.

2.4.1.4 Record Results of PPD
• Record the single reading across the arm in millimeters of induration. Do not record readings as negative or positive. Do not record the extent of erythema.
• Classification of the tuberculin reaction is determined not only by size of the reaction, but also by clinical and other risk factors. Knowledge of the significance of specific sizes of induration is based on large epidemiologic surveys of patients with TB and other mycobacterial diseases.
  • Reaction 0-4mm: Considered negative in most persons, but does not rule out TB infection or disease. Individuals with overwhelming TB, anergy, or incubating infection may have a negative PPD.
  • Reaction ≥ 5mm: A reaction of ≥5mm induration is considered positive when the patient has a high likelihood of infection with tuberculosis or has limited ability to respond immunologically. A reaction of ≥5mm is considered positive in the following groups:
    • High risk contacts of a person with infectious TB
    • Persons who also have a chest radiograph suggestive of previous TB and who have received inadequate or no treatment
    • Persons known or suspected of having HIV
    • Persons who inject drugs and whose HIV status is unknown
  • Reaction ≥10mm: A reaction ≥10mm of induration is considered positive when a person does not meet any of the above criteria, but has other risk factors for TB including:
    • Persons who inject drugs and are HIV negative
    • Persons with certain medical conditions e.g. diabetes mellitus, silicosis, hematologic and reticuloendothelial diseases, end stage renal disease
    • Persons taking prolonged corticosteroid therapy or other immunosuppressive therapy
    • Transplant recipients
    • Foreign-born persons from areas with endemic TB
    • Residents of long-term care facilities
    • Children under four years old
    • Medically underserved, low-income populations, high-risk ethnic groups
    • Locally identified high-prevalence groups
  • Reaction ≥15mm: A reaction ≥15mm of induration is classified as positive in persons with no known risk factors for TB. In general, persons with no known risk factors should not be routinely screened for TB.

Recent converters are defined on the basis of size induration. An increase of ≥10mm within a two-year period is classified as a recent conversion, regardless of age.

2.4.1.5 TST Results in Healthcare Workers (HCWs)
• In general, recommendations in the previous sections should be followed when interpreting TST results in HCWs. However, the prevalence of TB in a
facility should be considered when choosing the appropriate cut-point for defining a positive PPD reaction. In facilities where there is essentially no risk of exposure to TB, i.e. facilities that do not care for patients with active TB disease, an induration of ≥15mm may be a suitable cut-point for HCWs with no other risk factors. In facilities where active TB patients are cared for, an induration of ≥10mm may be a suitable cut-point for HCWs with no other risk factors.

- A recent conversion in a HCW should be defined as a ≥10mm increase in size of induration within a two-year period. For HCWs who work in a facility where exposure to TB is highly unlikely, an increase of ≥15mm of induration over a two-year period may be sufficient.

2.4.1.6 Booster Effect

- This technique is used to establish a baseline reading for the initial skin test of a series of annual skin tests. Subsequent tests, if indicated, should follow the usual single test procedure; if a person has a documented skin test results within the past 12 months, the two-step procedure is unnecessary.

- A person’s reactivity to tuberculin may wane over time. For example, adults who were infected during childhood may have a small reaction, which would be interpreted as negative. However, the PPD could boost the hypersensitivity, and the size of the reaction could be larger on a subsequent test. This boosted reaction may be misinterpreted as a positive PPD test due to newly acquired infection. Misinterpretation of a boosted reaction as a newly acquired infection could result in unnecessary investigations of laboratory and patient records in an attempt to identify the source case. Additionally the unnecessary treatment of TB infection may occur. The boost effect may occur at any point in one’s life, but the likelihood increases with age.

- When PPD testing of adults is to be repeated periodically, such as with HCWs, two-step testing can be used to reduce the likelihood that a boosted reaction is misinterpreted as new infection. An individual with an initial tuberculin induration above the reaction cut off point for person’s risk group or previously documented reaction should be considered as positive. Two-step tuberculin skin testing should be utilized in the initial test of the series as follows:

  - An individual with an initial tuberculin skin test induration of less than the cut point for the risk group should have a repeat skin test five days to three weeks after the first test was given. This boosts the first test. If the second induration is above the cut point for person’s risk group, the results should be considered as a positive boosted response. Subsequent skin testing in the future is not indicated and the individual should receive medical evaluation to diagnose or rule out TB infection or disease. If the second induration is less than the cut point, it should be considered a negative response and subsequent skin tests should be repeated at appropriate intervals.

2.4.1.7 Tuberculin Availability

- PPD 5 TU is the only antigen used by the Louisiana Office of Public Health. Other strengths of PPD may be available but are not recommended for TB screening. Always check to ensure 5TU is used.

- PPD should be stored in a refrigerator at 2-8°C when not in use. When protected from heat and light it retains its potency throughout the date of expiration. Special note should be taken of the expiration date upon receipt of the antigen. All vials should be dated and initialed when opened. Unused antigen should be discarded 30 days from the date opened.

- The multiple puncture tests (Heaf, Tine, Applitest, or Monovacc) are not recommended, because it is very difficult to standardize the amount of tuberculin injected. Results of these type tests should be verified by an IGRA or TST. Current state regulations now require the use of PPD by the
Mantoux method or an IGRA if testing for TB is required for employment purposes.

2.4.2 Interferon Gamma Release Assay (IGRA) Blood Test

2.4.2.1 IGRAs detect the presence of TB infection by measuring the immune response to TB proteins in whole blood. IGRAs cannot differentiate between TB infection and active disease. As with TST, further medical evaluation is still necessary to diagnose or rule out TB disease.

2.4.2.2 Two IGRAs are commercially available and approved by the U.S. Food and Drug Administration (FDA) as aids in diagnosing *M. tb* infection: (1) QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and (2) T-SPOT®. TB Test.

2.4.2.3 IGRAs may be used in place of the TST in all situations in which a recommendation is made to use TST as an aid in diagnosing TB infection. The IGRA is preferred for testing persons from groups that traditionally have poor rates of return for TST reading or testing of persons who received BCG as a vaccine or for cancer therapy. IGRA is preferred for use in children older than two years of age.

2.4.2.4 IGRAs may be used in place of TST to test recent contacts of persons with infectious TB disease with special considerations for follow-up testing:

- IGRAs offer the possibility of detecting TB infection with greater specificity than TST
- Data on ability of IGRAs to predict subsequent TB are limited
- If IGRAs are used in contact investigations, initial negative results should be confirmed by repeating testing 8-10 weeks after contact with the infectious source is broken
- Use of the same test for repeat testing will minimize misclassification errors that occur due to testing discordance

2.4.2.5 IGRAs may be used in place of a TST for periodic screening that addresses occupational exposure to TB disease.

2.4.2.6 IGRAs do not boost subsequent test results and can be completed in a single visit

2.4.2.7 Routine testing with both a TST and IGRA is not recommended

2.4.2.8 When there is clinical suspicion for TB disease and confirmation of *M. tb* infection is desired, results from both tests may be useful in the following situations:

- When the initial IGRA result is indeterminate, borderline, or invalid, and a reason for testing persists
- When an initial TST is positive, additional evidence of infection may be required to confirm TB infection for persons who believe their positive TST is due to previous BCG vaccination or treatment
- In healthy persons who have a low risk of both infection and progression to TB disease

2.4.2.9 Interpretation of TB Testing Results in BCG-Vaccinated Persons

- The Bacille Calmette-Guerin (BCG) vaccine is a live, attenuated vaccine derived from a strain of *Mycobacterium bovis*. The TST or IGRA are not contraindicated for persons who have been vaccinated or treated with BCG.
- TST and IGRA results are used to support decisions about the diagnosis of infection with *M. tb*. TST in persons vaccinated with BCG should be interpreted using the same criteria for those not BCG vaccinated. The booster effect may occur among persons who have had a prior BCG vaccine.
- Live virus immunization and tuberculin testing
  - Tuberculin skin testing is not a prerequisite for any immunization. Live virus vaccines and acute diseases diminish tuberculin sensitivity. This has been shown for measles, rubella, and influenza. If there is a need for TB testing in persons involved in an outbreak of one of these diseases, do not use the TST on individuals with definite or probable viral disease.
  - When immunizing in non-outbreak situations, both TST or IGRA and live virus immunization should be done at
the same time. The TST should be read 48-72 hours after injection. If the TST is not read within 72 hours, retesting should be postponed until one month after immunization. Likewise, a TST or IGRA is not valid in a person immunized with a live virus vaccine within the past 30 days.

2.4.2.10 Screening for TB during Pregnancy
- The screening for TB among pregnant women should only be done as indicated for any person within a high-risk group for TB infection or disease.
- A TST or IGRA may be used for screening of pregnant women.

2.4.3 Chest Radiograph

2.4.3.1 Some radiologic patterns are common in TB. TB may produce almost any form of pulmonary abnormality on a chest radiograph (CXR).

2.4.3.2 Therefore, a diagnosis based solely on an abnormal CXR is a presumptive diagnosis. Other diagnostic tests such as microbiological testing of sputum or other samples should be attempted in order to establish a definitive diagnosis, determine susceptibility, and serve as a source for molecular epidemiology.

2.4.3.3 To avoid unnecessary exposure to ionizing radiation, X-rays should only be used for diagnostic purposes when TB infection or disease are suspected. X-rays should be performed based on the classification of the patient.
- CXR should be performed on active disease cases as part of the initial diagnostic and evaluation process, and at least every three months during treatment, or at the request of the physician throughout treatment.
- Repeat CXR in persons with TB infection is not necessary, particularly in persons whose initial radiograph showed no abnormalities. Repeat CXR should only be done when indicated by the physician.
- All high risk contacts to infectious TB disease cases should be tested for M.tb infection or disease, including CXR, then referred for further medical evaluation.

- Those suspected of having TB disease should always have a CXR, and be referred for further medical evaluation.
- Among pregnant women, a TST or IGRA may be used to test for M.tb infection. If the test is positive, a CXR using an abdominal lead shield should be done to rule out disease.

2.4.4 Bacteriology

2.4.4.1 Recovery of the Mycobacterium tuberculosis bacilli in culture is the “gold standard” for confirming diagnosis of TB. It is of utmost importance that specimen collection be done carefully, efficiently, and regularly.

2.4.4.2 Sputum specimens must be handled and shipped to the diagnostic laboratory in a very specific manner, using very rigid guidelines established by the federal Clinical Laboratory Improvement Act (CLIA). Specimens handled and shipped not according to the guidelines will not be processed by the laboratory. For specimens other than sputa, the Louisiana Office of Public Health Regional TB Manager should be contacted for instructions. Only approved containers should be used for mailing/shipping. Ensure that all requested information is provided, including patient name, date of birth, address, source of specimen, collection date and sender’s return address.

2.4.4.3 Private providers such as hospitals, laboratories, clinics, and physician’s offices may use the services of the Louisiana Department of Health Laboratory Services for specimen identification without charge. Questions pertaining to the submission of specimens to the Louisiana Department of Health Laboratory should be directed to the Regional TB Manager or parish health unit.

2.4.4.4 Sputum Collection
- Each time a sputum specimen is collected from a patient, the HCW should give thorough instructions for sputum collection and handling.
- Inform the patient that saliva and nasopharyngeal discharge are not sputum. Only material brought up from
the lung after a cough constitutes the sputum specimen desired. At least 3-5mL of sputum per sample must be supplied for adequate study.

- A minimum of three separate sputum specimens should be collected from suspects and new cases in the early morning, on three consecutive days. These samples must be submitted on the day of collection. The following outlines the minimum schedule of bacteriologic examination for \textit{M.\textit{tb}} in suspected or confirmed cases of TB disease.

- Collect weekly sputum specimens for the first four weeks. Smear conversion at four weeks determines the adequacy of the gastrointestinal absorption of orally administered anti-TB medications.

- Collect weekly sputum specimens until three consecutive sputum smears are negative. The degree of infectiousness is proportional to the positivity level of the smear results. I.e., a negative smear result would indicate a very low level of infectiousness; while a “4+” smear results would indicate a very high level of infectiousness.

- Collect weekly sputum specimens until sputum culture results are negative. Sputum culture conversion at eight weeks indicates length of therapy.

- Monthly sputum examination is strongly recommended as long as the patient is on treatment. Non-conversion of a case’s smear at four weeks or non-conversion of culture at eight weeks is an indication that blood drug levels need to be tested. A problem of malabsorption or non-absorption of oral anti-TB medications may be occurring and leading to delayed conversion. Development of resistant microorganisms must also be considered.

2.4.4.5 Other Collection Methods
- Aerosol induction, gastric aspiration, tracheal suction, or bronchoscopy are satisfactory alternatives for persons having difficulty or unable to produce sufficient sputum samples.

- Persons with extrapulmonary disease should also have initial sputum specimen collected if possible. Persons with genitourinary, central nervous system, or meningeal TB may require additional samples for microbiological testing.

- Persons with extrapulmonary disease are not infectious unless they have:
  - Pulmonary disease in addition to extrapulmonary disease
  - Extrapulmonary disease is located in the oral cavity or larynx
  - Extrapulmonary disease that includes an open abscess or legion in which the concentration of organisms is high and there is a risk of fluid being aerosolized.

- Routine laboratory testing may include a microscopic examination of a stained smear of the concentrated specimen, culture, nucleic amplification test (NAAT), and drug susceptibility testing.

2.4.4.6 Microscopic Examination
- The detection of acid fast bacilli (AFB) on standard smears is the first bacteriologic evidence of mycobacterial infection. AFB smear is quick, easy, and provides clinicians with a preliminary confirmation of the diagnosis. The sputum smear is also has important epidemiologic significance. All new and suspect cases should have sputum or other source smear results documented as soon as possible.

The finding of AFB is not definitive evidence of TB. Mycobacterium other than TB (MOTT) may be present in the specimen. These other mycobacterium could include \textit{M. avium}, \textit{M. kansasii}, \textit{M. fortuitum}, etc. Some, but not all MOTT are pathogenic. Conversely the lack of a positive smear results does not rule out TB.

- The nucleic acid amplification test (NAAT) is a molecular test that detects the presence of TB bacteria DNA. This test uses a sputum sample and can provide results in less than two hours. It can also detect genetic mutations associated with resistance to the drug Rifampicin, a first line anti-TB drug.
Detection of *M.tb* by NAAT is a preliminary diagnostic tool. The NAAT only detects the presence of TB bacteria DNA, it does not differentiate between the DNA of living or dead organisms.

### 2.4.4.7 Culture Confirmation

- **Culture confirmation** is the “gold standard” for diagnosing TB disease. All culture specimens are inoculated into a primary culture medium to be incubated for a maximum of 49 days, or until AFB are detected. At 49 days the specimen is considered negative if AFB are not detected. If AFB are detected, a species determination is made and susceptibilities are determined if warranted. For diagnostic purposes a minimum of three bacteriologic specimens should be collected.

- **Once a TB diagnosis is confirmed** it is important to monitor the bacteriologic status of sputum for the following reasons:
  - **Efficacy of treatment.** The single best method for evaluation of response to treatment is serial sputum smears and cultures. Serial X-rays can be misleading in assessing the progress and eventual results of treatment. Patients may show radiographic improvement and still discharge tubercle bacilli. On the other hand, persons who complete treatment and are cured, may be misclassified as treatment failure because of residual cavitation or lesions on X-rays.
  - **Possibility of drug resistance.** Early detection of drug resistance is not possible without serial sputum submission. Monthly or more frequent specimen submission is imperative for proper patient management and cure.
  - **Length of Treatment.** Current TB therapy requires regular collection of sputum to determine length of therapy. Non-conversion of sputum culture at eight weeks indicates extending the length of therapy.
  - **Management of Contacts.** Repeat TB testing of non-infected high-risk contacts should be done 8-10 weeks after the index case’s first negative smear result, or 8-10 weeks after contact with the index case is broken.

- **Susceptibility Studies.** The performance and interpretation of susceptibility studies is essential for the physician in assessing the patient’s response to therapy, and choice of the most effective anti-mycobacterial agents. The LDH Laboratory will automatically perform drug susceptibility testing on all initial specimens submitted that are positive for *M.tb*. If resistance to first line drugs is detected, susceptibilities to second-line drugs are performed. In patients suspected to be at risk of primary drug resistance, e.g. contacts to known drug resistant cases, HIV positive persons, or persons from countries with higher prevalence of drug resistant TB, expedited sensitivities should be requested from the laboratory.

- **Susceptibility testing should be requested** if any of the following conditions exist:
  - All newly diagnosed cases of TB
  - Patients who show consistently positive results in their sputum smear after four weeks or sputum culture after eight weeks.
  - Patients on therapy who, after an initial decrease in bacterial content in sputum samples, revert to high bacterial loads.
  - Patients who have had previous anti-TB drug therapy and need treatment again, i.e. recurrent or re-infected cases.

- **At the end of a successful course of treatment,** some patients may yield isolated positive smears with cultures negative for *M.tb*. If three repeat sputum examinations are negative by culture, such isolated positive smears may not mean that relapse has occurred. Medical re-evaluation of the patient for active disease should be performed only if symptoms are present.
2.5 Treatment of Tuberculosis Infection and Disease

2.5.1 General Principles of Treatment

2.5.1.1 The Louisiana Office of Public Health follows the general guidelines of the United States Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics\(^2\) (AAP), and the American Thoracic Society/Infectious Diseases Society of America\(^3,4\) (ATS/IDSA) for treatment of TB infection and disease.

2.5.2 Treatment of Active TB Disease

2.5.2.1 Several key principles apply to treatment of active TB:

- Provide the safest, most effective therapy over the shortest possible duration
- Use multiple drugs to which organisms are susceptible
- Never add a single new drug to a failing regimen
- Ensure adherence to therapy

2.5.2.2 TB treatment requires consistent adherence to a regimen of regular medications and involves a small risk of serious drug reactions. Patient factors such as age, sex, nutrition, and potential for drug toxicity are also important in the selection of an appropriate regimen of anti-TB drug therapy.

2.5.2.3 The objectives of treatment for active TB disease, requiring a combination of drugs, are:

- To prevent mortality from TB and interrupt the transmission of \(M.\text{tb}\). It is crucial to reduce the bacillary load rapidly to reduce the patient’s level of infectiousness.
- To minimize the possibility of the bacilli developing drug resistance by ensuring that drug-sensitive bacilli are killed as quickly as possible, and to prevent the transmission of drug-resistant organisms.

- To achieve cure and prevent relapse after completion of treatment.

2.5.2.4 It is the recommendation of the Louisiana TB Control Program that the initial phase of treatment for active TB disease include the four drugs Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB). For information about drugs used in the treatment of TB disease and infection see Section 2.6: Drugs Used for Treatment of TB.

2.5.2.5 Treatment of Pulmonary TB

- Pulmonary TB is the most common form of TB. The lungs are the most common site, the pleura and/or mediastinal lymph nodes may also be involved.
- A six-month regimen of INH, RIF, PZA, and EMB is the recommended treatment for those with TB disease. The use of four drugs is to ensure that potentially drug resistant organisms are being killed.
- This six-month regimen is comprise of two phases.

- The “Intensive Phase.” The four drugs should be used until a negative culture result is obtained at approximately two months post treatment initiation. The culture results can provide information on drug sensitivities of the recovered organism. If sensitivity studies show that the \(M.\text{tb}\) organism is sensitive to INH, RIF, PZA, and EMB, the EMB can be discontinued. The PZA, along with INH and RIF, should be continued through the full two-month intensive phase.

- The “Continuation Phase.” After negative culture results have been received and the intensive phase has been completed, four months of INH and RIF complete the six-month treatment regimen.

- The goal of the continuation phase is to sterilize the remaining

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bacilli. The combination of INH and RIF is the most effective regimen for sterilizing these bacilli.

- The extent and severity of the patient’s disease, and their response to treatment may create exceptions to the time frame cited above for length of treatment. Longer treatment duration may be necessary for those who do not culture convert at eight weeks, have drug-resistant organisms, problems with adherence, or non-or malabsorption of drugs.

- If one or more of the four intensive phase drugs are not tolerated, are contraindicated, or if culture conversion has not occurred at eight weeks, then an alternative drug regimen may be prescribed, and a longer duration of treatment may be required.

2.5.2.6 Treatment of Extrapulmonary TB Disease

- As a general rule, regimens that are adequate for the treatment of pulmonary TB, in adults and children, will also be effective for treatment of extrapulmonary TB. Miliary TB, TB meningitis, and TB of the bones and joints requires longer treatment durations from 12-24 months, especially in children. The addition of corticosteroids is recommended by some authorities for treatment of meningal TB.

- Surgery may be necessary to obtain diagnostic specimens for extrapulmonary TB and obtaining specimens for follow up bacteriologic testing may not be feasible. Responses to treatment must be just based on clinical and radiographic findings.

2.5.2.7 Treatment of Clinical TB

- Not all cases of TB disease are symptomatic or have bacteriologic evidence of disease. These cases are classified as “clinical cases” and are defined by the following characteristics:
  - Evidence of TB infection based on a positive TST or IGRA -AND- 
  - Signs and symptoms compatible with current TB disease, such as abnormal chest radiograph or other imaging study -OR- clinical evidence of current disease, e.g. fever, night sweats, cough, weight loss, hemoptysis -AND-
  - The absence of smear, NAAT, or culture confirmation

- A four-drug regimen of INH, RIF, PZA, and EMB for two months, followed by INH and RIF for an additional two months is a sufficient treatment regimen for the treatment of a clinical case of TB. Response to treatment must be judged on clinical or radiologic improvement.

2.5.2.8 Recommendations for Treatment of Drug Resistant TB (DRTB)

- The basic principle of managing patients with drug resistant organisms is the administration of at least two, preferably three, drugs to which there is demonstrated susceptibility. The selection is based on in vitro susceptibility patterns of the organisms, and the potential for toxicity for the patient. If drug resistance is suspected prior to receiving susceptibility testing results, at least two new drugs, which the organisms has not previously been treated with, should be added until results are available.

- A single drug should never be added to a failing regimen. Adding a single drug could add to the microorganisms gaining resistance to other drugs.

- If there is confirmed resistance to INH, a regimen of RIF, PZA, and EMB for 6 months or RIF and EMB for 12 months can be used.

- If there is confirmed resistance to RIF, three or four drugs to which the organism is susceptible should be given for a total of 18 months, or at least 12 months after sputum culture conversion.

- In all cases involving drug resistance, decisions on drug combinations and duration of therapy should be determined on a case-by-case basis. Consultation with a physician experienced in the treatment of DRTB is recommended.
2.5.2.9 Treatment of TB in Persons Co-infected with HIV/AIDS

- Persons with Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) are at a higher risk of TB infection and disease. All HIV/AIDS patients should be tested for TB as part of their routine HIV/AIDS medical care. All persons 13 years of age and older, newly diagnosed with TB infection or disease should be tested for HIV, if their status is unknown.

- Anti-TB therapy should be started whenever AFB are detected in respiratory tract samples in persons with, or at high-risk of HIV/AIDS. Persons with HIV/AIDS currently taking antiretroviral drugs and needing treatment for TB require an alternative TB treatment regimen. Rifabutin (RBT) is generally substituted for Rifampin (RIF), but consultation with a physician specializing in treatment of HIV-TB co-infected individuals should occur before any alteration to the standard treatment regimen are made.

- TB patients co-infected with HIV/AIDS are at a higher risk of developing drug resistance to TB medications. Therefore, therapy in HIV-TB co-infected individuals should include INH, RIF or RBT, and PZA for two months, with EMB and streptomycin (SM) until drug susceptibilty results are available. Treatment with INH and RIF or RBT should continue for at least six months after culture conversion.

- In treating TB patients with HIV, it is critically important to assess clinical and bacteriologic response. Treatment should be prolonged if the response is slow or otherwise suboptimal. It is recommended that the treatment of persons with HIV/AIDS who are receiving antiretroviral therapy and need anti-TB drug therapy be treated by a physician specializing in the treatment of HIV-TB co-infection.

- DOT is highly recommended for TB cases co-infected with HIV/AIDS.

2.5.2.10 Treatment of TB During Pregnancy and Lactation

- Untreated TB disease presents a far greater risk to a pregnant woman and her fetus than treatment for TB. Prompt initiation of treatment is crucial. Congenital TB, while rare, can occur in an infant born to a woman with untreated TB during pregnancy. This risk is higher among pregnant women with extensive disease or TB of the uterus.

- Treatment with INH and RIF is recommended for pregnant women, with the addition of EMB if INH or RIF resistance is suspected. The addition of Pyrazinamide (PZA) is contraindicated with pregnancy. It should not be used in treatment of pregnant women with TB. The exact teratogenic effects of PZA are not yet known.

- It is preferable to avoid Streptomycin because of its ototoxicity for the developing fetus. However, should any of the first line drugs be unsatisfactory or contraindicated, Streptomycin can be used. In such cases, the infant should be evaluated for possible side effects, e.g. damages to the eighth cranial nerve. Ethionamide and cycloserine should be avoided pending further information about the use of these drugs during pregnancy.

- Standard TB treatment regimens using most first and second line drugs have not been proven to have teratogenic effects on the human fetus. Their use generally does not call for medically indicated abortion.

- Breast-feeding should not be discouraged for women being treated for TB. TB cases should receive treatment during lactation. Several TB drugs pass into breast milk, but have not been proven to be deleterious to the infant. Conversely, drugs in breast milk should not be considered adequate therapy for disease in the nursing infant. Close follow-up of the mother and infant is necessary. Pyridoxine, vitamin B6, supplementation is recommended for all pregnant or lactating women taking INH.

- To avoid unnecessary exposure to ionizing radiation, pregnant women with TB infection or disease should be given
2.5.2.11 Treatment of TB in Children and Adolescents

- Children and adolescents should be treated for TB if a diagnosis of disease is suspected anywhere in the body. Children can develop serious and potentially lethal forms of TB very quickly. Gastric washings can be used to obtain bacilli for bacteriological testing since children usually do not produce sputum. Gastric washings are best performed in a hospital setting. When properly done, gastric washings can provide a positive culture in 40-60% of cases.

- Children may develop active TB at more than one site in the body concurrently. Infants and children should be carefully examined for signs of secondary sites of infection, including lymph nodes, joints, and cranial nerves. Symptoms of meningitis should be investigated.

- The current treatment recommendation for children and adolescents with TB disease is patterned after carefully studied regimens in adults with pulmonary TB. Whenever possible, information should be obtained from the drug susceptibility studies from the infectious source case. Active cases of TB with or without radiologic evidence, should be treated with INH and RIF for at least six months, with the addition of PZA for the first two months, if drug resistance has been ruled out. Twice weekly dosages are effective and can be utilized in patients after two or three weeks of daily drugs. Certain types of disseminated disease, specifically bone and joint, miliary, and meningeal TB should be treated for 12-24 months.

- TB disease in children indicates recent transmission from an infectious index case. If the index case is suspected or confirmed of having drug-resistant organisms, then it is recommended to add a fourth drug, streptomycin or EMB, to the child’s treatment regimen. Once the susceptibility pattern of the index case is confirmed, the regimen can be adjusted appropriately. EMB should be used cautiously in children too young to identify colors, as changes in visual acuity includes red/green color vision changes, are an early sign of ocular side effects due to EMB. If EMB must be continued throughout treatment, the minimal dose should be used.

- All children with suspected or confirmed TB disease should be treated with DOT as follows:
  - The daily dosage of anti-TB drugs can be given all at one time. Tablets should be well crushed with a large spoon, the contents of the capsules added and mixed with a diluent
  - Give the medication directly from the spoon
  - Never put drugs in a drinking glass or formula bottle
  - Ensure all medication is ingested.
  - Note that it is possible for some medication adhere to the container. If necessary rinse the container with a small amount of water and have the child ingest this also.

- The syrups of INH and RIF are not stable and are not recommended.

- Parenteral drugs are usually used only in seriously ill, hospitalized patients who are vomiting or comatose. Parenteral forms of INH and RIF are available and streptomycin is likewise useful in these circumstances.

- Second-line drugs are sometimes needed. For example, if a child has been infected with INH and RIF resistant organisms, Ethionamide can be added to a regimen of PZA and EMD-or-streptomycin. Ethionamide, related to INH, is used in the same dosage, and usually well tolerated by children despite its unpleasant taste. Consultation with a specialist experienced in treating drug resistant pediatric TB is recommended.

- Toxic side effects of anti-TB drugs are rare in children, so liver function tests are infrequently needed in children. Repeated blood tests in children adversely affect adherence. Follow-up should be monthly.
• Weight gain is by far the most useful measure of the child’s progress. Steady weight loss may indicate:
  • Progress of the disease due to drug resistance
  • Non-adherence on the part of the child or parent/guardian
  • Failure to ensure that the child ingests the total prescribed dosage of medication.
  • Drug absorption problems
• While the officially recommended duration of treatment is six months, it is sometimes necessary to prolong treatment if adherence is questionable. Repeated chest X-rays are indicated if the initial radiographic test was abnormal, however treatment should not be prolonged solely on the presence of an abnormal CXR. Some CXR abnormalities can take 2-3 years to resolve fully after successful treatment. Some scarring may remain permanently in those with extensive disease.

2.5.2.12 Treatment of TB with Other Associated Disorders
• TB commonly occurs in association with other diseases. Medical conditions that predispose individuals to TB may include malignancies, immunosuppressive therapy, chronic renal failure, malnutrition, and alcoholism.
• In patients with impaired renal function, Streptomycin, Kanamycin, or Capreomycin should be avoided. If given, reduced doses should be calculated.
• The potentially hepatotoxic drugs used in the treatment of TB e.g. INH, PZA, and RIF, are not contraindicated in patients with liver disease, but such patients should have close monitoring of liver function.
• Patients with co-morbid neuropsychiatric disorders must receive DOT.

2.5.2.13 Recurrent or Relapsing TB
• Patients with recurrent or relapsing disease should be evaluated to identify the probable cause. Some patients who are being treated for TB may experience a relapse of disease during treatment and some patients who have successfully been treated for drug-susceptible disease may suffer a recurrence of disease. Patients who suffer a recurrence or relapse of disease are at greater risk for having acquired drug resistance to previously used drugs. Likewise, patients who have successfully completed treatment may be re-infected upon exposure to a person with infectious TB.
• Organisms in patients treated initially with INH and RIF usually remain susceptible if relapse occurs. Thus, management of these patients generally consists of reinstitution of a regimen including ING and RIF. Drug susceptibility testing should be performed and the regimen modified if resistance is detected.
• Consultation is recommended with a specialist in the treatment of TB for patients who have relapse, recurrence, or re-infection. DOT should always be used in patients with recurrent disease.

2.5.3 Treatment of Tuberculosis Infection (TBI)
2.5.3.1 Several key principles apply to treatment of TBI:
• Provide the safest, most effective therapy over the shortest possible duration
• Ensure adherence to therapy
2.5.3.2 Every person with significant exposure to TB and every person with a positive TST or IGRA is at risk of developing TB disease. Such persons will benefit from treatment of TB infection, since the risk of progressing to disease is lifelong.
2.5.3.3 Treatment of TBI is used to reduce the risk that TB infection will progress to active disease. Treatment of TBI can prevent development of TB disease. Persons with certain risk factors must be given priority for treatment of TBI, regardless of age. There is a consistent reduction in TB morbidity when treatment of TBI is provided to high-risk groups. Every effort should be made to ensure that patients adhere to treatment of TBI.
2.5.3.4 The current recommendation of a six-month regimen of INH for treatment of TBI is the most cost-effective regimen.
For children through adolescents, pregnant women, and HIV positive persons at least nine-months of INH is recommended. If a patient is a known contact to a drug-resistant case, treatment should be altered accordingly. The Regional TB Program Manager should be consulted about providing DOT for TBI treatment. Patients should be assessed monthly or more frequently if indicated, for adverse reactions. Monthly assessments also provide more information of the patient’s adherence to the prescribed regimen. The initial beneficial effect of INH in persons with TBI is thought to be very long lasting, possibly lifelong.

2.5.3.5 Persons in the following high-risk groups should be prioritized for treatment of TBI:
- Persons who have a positive IGRA or TST reaction that is interpreted as positive based on the guidelines in Section 2.4.1.4 Record Results of PPD.
- High risk contacts of persons with infectious TB disease
- HIV infected individuals
- Persons with fibrotic changes on chest radiograph consistent with prior TB disease (once active disease has been excluded)
- Immunosuppressed individuals e.g. those on steroid therapy
- Patients with organ transplants and other immunosuppressed patients receiving the equivalent of 15 mg/day of prednisone for greater than or equal to one month, and patients anticipating taking tumor necrosis factor-alpha (TNF-α) inhibitor drugs
- Recent arrivals to the United States from areas with high TB prevalence
- Injection drug users
- Residents and employees of high-risk congregate settings, e.g. correctional facilities, long-term care facilities, residencies for migrant workers, etc.
- Mycobacteriology laboratory personnel
- Persons with medical conditions that increase the risk for progression to TB disease, including silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphomas, cancer, etc.
- Children younger than five years of age, immunosuppressed children, or children and adolescents exposed to adults in high-risk categories
- Persons who have been known to convert their TST or IGRA from negative to positive within the past two years

2.5.3.6 Standard Regimens for Treatment of TBI
- INH six to nine months
  - Self-administered INH for six months for adults is the recommended therapy.
  - Nine months, self-administered INH should be utilized for the following groups:
    - Children and adolescents
    - Persons co-infected with HIV/AIDS
    - Persons with abnormal CXR not suggestive of TB, e.g. a non-tuberculous stable parenchymal lesion or calcification
    - Persons receiving prolonged adrenocorticosteroids or other immunosuppressive therapy
    - Persons on immunotherapy, including TNF-α therapy, if TNF-α therapy will begin while the patient is on TBI treatment or prophylactic treatment
    - Persons with silicosis, diabetes mellitus, or end stage renal disease
    - Persons with hematologic and reticuloendothelial diseases such as leukemia or Hodgkin’s lymphoma
    - For children and HIV co-infected individuals who are at especially high risk for TB, twice-weekly DOT should be considered.
- INH/RPT 12 weeks
  - INH and RPT (Rifapentine) once weekly for 12 weeks for treatment of TBI is an alternative to INH daily for six to nine months.
  - For otherwise healthy persons two years of age or older, who have a positive TST or IGRA, this regimen is recommended. The two drugs are taken orally under DOT once weekly for 12
weeks. This regimen should not be used in children under two years of age, any HIV co-infected persons taking anti-retroviral medicines, any persons with presumed INH or RPT resistant organisms, pregnant women or women expecting to become pregnant within the 12-week period.

- If a woman on either the INH or INH/RPT TBI treatment should become pregnant, reassure the patient of the safety of INH during pregnancy. Consultation should be done with a physician experienced in treatment of TB in pregnant women. A physician may delay INH treatment for TBI until after delivery, unless the patient is at high risk for progressing to active disease, e.g. HIV co-infected or recent conversion. After delivery, the woman should be evaluated and started on treatment for TBI.

- Once the decision has been made to place a person on TBI treatment, the following must be ensured:
  - Evaluation of patient adherence to determine need for initiation of DOT
  - Motivation and help in developing a system of reminders for taking the medications
  - Issuance of monthly drug supply
  - Counselling regarding continuity of TBI treatment and risk of developing TB disease in the future
  - Monthly nursing assessments to monitor for adverse drug reactions and adherence to therapy

- Monitoring for side effects consists of careful questioning for the following symptoms:
  - Hepatotoxicity
  - Nausea, vomiting or unexplained anorexia of greater than three days duration
  - Fatigue or weakness of greater than three days duration
  - Persistent dark urine (coffee or tea colored) or jaundice (icterus eyes and/or skin)
  - Rash or pruritus
  - Elevated temperature of greater than 101°F for more than three days duration without explanation

  - Symptoms of neurotoxicity such as persistent paresthesia of the hands and feet
  - Nausea and vomiting unrelated to hepatotoxicity

  - The patient should be advised that immediately upon developing any such side effects during treatment of TBI, medications should be discontinued and side effects should be reported to a healthcare provider as soon as possible.

- After completion of treatment for TBI the patient should be educated about the risk of developing TB in the future. No further medical follow-up is necessary unless the patient develops symptoms of TB disease. The patient should be advised that further testing for TB infection is unnecessary and that yearly CXR are not necessary. If symptoms occur, an evaluation including CXR should be conducted.

### 2.5.7 Treatment of TBI in Contacts to Known INH-Resistant Cases

- Contacts who are known to be exposed to INH-resistant cases of TB disease may be treated with daily RIF for six to nine months. If the initial skin test is ≤5mm. or the IGRA is negative, begin RIF therapy and repeat the TB test eight weeks after the source case converts to negative sputum smears or contact with the source case is broken. If the skin test or IGRA remain negative, discontinue RIF treatment for TBI. If the skin test converts to ≥5mm or the IGRA converts to positive, continue RIF for six to nine months. DOT should be used for this regimen.

### 2.5.8 Treatment of TBI in Infants and Children

- All infants and children recently exposed to any sputum smear positive suspect or case should be preventatively treated, regardless of the initial TST or IGRA result. Exposure of an infant or child to an adult with active TB disease living in the household may be inevitable. If so, the infant or child should be started on treatment. This primary prevention should be continued for at least eight weeks beyond
documented smear conversion in the source case or after contact is broken, i.e. the adult source case has left the household. If this occurs before the infant is three months of age, the infant should be re-tested at three to six months of age.

- INH only is used to treat children under two years of age with a negative TST or IGRA, and no clinical or radiographic evidence of infection, who has recently been or is currently being exposed to a sputum smear positive case.
- If an infant is exposed to someone with active disease in the communicable state and has a negative test for TB infection, INH treatment must be started and the TST should be repeated in eight weeks. If the test is still negative after eight weeks and contact to the infectious case have been eliminated, INH therapy may be discontinued. If the repeat test is positive, nine months of INH should be completed.
- INH or INH/RPT may be used in children at least two years of age or older who have a positive TST or IGRA, but have no clinical or radiological manifestation of disease.
- Note: the BCG vaccine is of limited usefulness in the United States. However, it may be considered for children from a family with a history of INH and RIF resistant organisms. The use of BCG may prevent serious forms of TB disease, e.g. miliary or meningeal, but the vaccine should only be given in consultation with a physician experienced in managing pediatric TB. For more information about BCG see Section 4.7 Bacillus of Calmette and Guerin.

2.5.3.9 Treatment of TBI in Pregnant, Post-Partum, and Lactating Women

- Although no harmful effects of INH on the fetus have been observed, it is prudent to prescribe only therapeutically necessary drugs during pregnancy. The exception is for pregnant women likely to have been recently infected with TB or women who are HIV-TB co-infected. In this situation, INH treatment for TBI should begin when infection is documented. Pregnant women receiving INH should also receive Vitamin B6. Pregnant women intolerant of INH should be treated in consultation with a physician experienced in the treatment of TB in pregnant women. INH treatment for TBI in pregnant women, in the absence of other risk factors should be delayed until two to three months post-partum.
- There is a potential for increased hepatotoxicity in the first two to three months of the post-partum period. It is recommended that TBI treatment be delayed until this period is over, unless there is a high risk of progression to TB disease.
- INH daily self-administered or INH/RPT twice weekly with DOT are equally preferred regimens. Vitamin B6 should be given to women being treated for TBI and to the infant if the infant is being breastfed.
- It should be noted that the amount of INH in breast milk is inadequate to treat an infant in need of TBI treatment.

2.5.3.10 Treatment of TB Exposure without Infection (Prophylactic Treatment)

- Persons who are high risk contacts to an infectious case, may have been infected but have not yet developed a positive TST or IGRA test result, since not enough time has elapsed to develop the necessary immune response. High risk contacts with an initial negative TST or IGRA should receive a chest radiograph and should be considered for treatment of TBI in any of the following situations:
  - Circumstances suggest high probability of infection
  - Evaluation of other contacts with a similar degree of exposure demonstrates a high prevalence of infection
  - The contact is a child or adolescent, or an immunosuppressed individual. These individuals should receive INH daily self-administered or twice weekly with DOT.
  - These contacts should have a repeat TST or IGRA eight weeks after contact with the infectious case is broken, or the infectious case converts smears. If
the TST or IGRA remain negative, prophylactic treatment should be stopped. If the TST or IGRA become positive, TBI treatment should continue.

2.5.3.11 Prior to Starting Treatment for TBI

- Rule out progressive TB disease
- Rule out history of adequately treated TBI
- Rule out contraindications, such as chronic or acute liver disease or severe adverse reaction to previous TB treatment of TBI
- Identify patients who may require special attention, such as persons with chronic co-morbidities, epilepsy, alcoholism, drug-addiction, liver disease, or women who are pregnant or breastfeeding

2.5.4 Monitoring Treatment Adherence

2.5.4.1 Non-adherence is a major problem in TB control. Inadequate treatment for TB disease can lead to continued transmission, emergence of drug resistance, and recurrent disease. Inadequate treatment for TB infection can lead to progression to TB disease. Checkpoints for non-adherence can include:

- Two weeks on therapy having urine specimen without orange-red color indicates RIF not being taken
- One month on therapy and sputum smear remaining positive indicates non-adherence with the prescribed regimen, that drug-resistance may be developing, and/or that the drugs are not being absorbed after oral ingestion
- Two months on therapy not having conversion from positive to negative sputum culture result indicates non-adherence with the prescribed regimen, that drug-resistance may be developing, and/or that the drugs are not being absorbed after oral ingestion
- Monthly pill counts revealing more than 10% of pills remaining in the bottle for individuals on daily self-administered regimens indicates patient may not be taking medicines at the prescribed frequency

2.5.4.2 Directly Observed Therapy (DOT)

- DOT is a method used to ensure that patients diagnosed with TB take their medications as prescribed by the physician.
- Patients must be initiated on daily DOT. This regimen may be changed from daily to twice-weekly DOT after at least 14 daily doses have been observed, unless contraindicated. The drugs that can be used for twice-weekly DOT include INH, RIF, EMB, PZA, and SM (streptomycin).
- Refer to the CDC’s “Core Curriculum on Tuberculosis: What the Clinician Should Know” for all recommended drug dosages.
- DOT should be used for the treatment of active TB disease whenever possible, especially when:
  - Patient has suspected or confirmed pulmonary TB in the communicable state
  - Patient has a history of non-adherence
  - Adherence with self-administered medication is unlikely
  - Hospitalization or inpatient care is not practical or recommended.
- The Louisiana Standard of Care for the treatment of TB is DOT.
- If sufficient staff is not available to provide DOT to all persons with active pulmonary TB disease, priority for DOT should be given to the following:
  - Smear positive pulmonary patients with drug resistance to one or more first line anti-TB drugs.
  - Smear positive pulmonary TB patients
  - HIV co-infected patients
  - Children and adolescents
- DOT is important in ensuring adherence throughout the course of treatment for TB. DOT may be observed in many settings. Under the direction of the Regional TB Program Manager, DOT may be provided in a Parish Health Unit, or other locations using public health personnel. Utilization of personnel other than
nurses and DIS may be considered for DOT, with the consultation and approval of the Regional TB Program Manager. Prepackaged or unit dosages of medications allow responsible persons of ancillary public health personnel to directly observe and assist with a patient’s therapy whenever possible.

- Successful treatment results have been demonstrated when using DOT twice weekly or daily, Monday through Friday.

2.5.4.3 Directly Observed Preventative Therapy (DOPT)

- Patients with TBI on certain medications should be placed on DOPT. As with DOT, DOPT is primarily conducted in patient’s homes, workplaces, or Parish Health Unit or LDH/OPH clinic. Other locations may be utilized but must be approved by the Regional TB Program Manager prior to initiation of therapy.
- Consult with the Regional TB Program Manager is any medication other than INH is used for treatment of TBI.
- DOPT should be used for the treatment of TBI when the following medications are used: RIF and RPT.

2.5.5 Monitoring Response to Treatment

2.5.5.1 For patients who are sputum smear positive before treatment, three weekly sputum specimens should be obtained until the criteria for non-infectiousness are satisfied; including three consecutive negative sputum smears. Refer to Section 3.1 Definitions of Infectious and Non-Infectious for the criteria of non-infectiousness.

2.5.5.2 Patients whose sputum culture has not converted at two months should be evaluated for possible treatment failure. Susceptibility tests should be obtained on a current sputum specimen. While results are pending, the original drug regimen may be augmented by at least two drugs not previously prescribed in the treatment regimen, one of which should be an injectable. The regimen should be adjusted in accordance with results of the susceptibility tests and drug blood level tests should be done.

2.6 Drugs Used for Treatment of TB

2.6.1 The following descriptions are a brief, yet useful summary of information about the drugs used to treat TB infection and disease in the United States. A medically reliable compendium of drugs and the package insert or a medically reliable reference should be consulted regarding indications, contraindications, and possible side effects, if a complete review of a particular drug is needed.

2.6.2 First Line Drugs

2.6.2.1 The four “first line” drugs used for the treatment of TB are isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA).

2.6.2.2 Isoniazid, INH, Isonicotinic acid hydrazide

- INH is the most valuable and most widely used drug for the treatment of TB. INH is a bacteriocidal drug that kills the TB bacilli, and is indicated in all types and stages of TB. INH is available in 100mg and 300mg tablets.
- Metabolism
  - INH is easily absorbed from the gastrointestinal tract with good diffusion to all tissues and cavities (CSF, pleural fluid, peritoneal fluid, and breast milk), and crosses the placenta. It is partially conjugated in the liver by acetylation into an inactive form. Some people are rapid activators, which occasionally can cause for treatment failure.
- Toxicity and Side Effects
  - Nervous System: Administered at high doses, INH may cause peripheral neuritis (paresthesia in hands and feet and weakness). Convulsions, toxic encephalopathy, toxic psychosis, or optic neuritis is rarely seen. At the low doses currently used, there is minimal risk except in persons with:
    - Renal insufficiency that may result in having higher blood levels of INH
    - Alcoholic neuropathy
    - Malnutrition
    - Simultaneous administration of
Pyridoxine (vitamin B6) prevents the neurotoxic effects of INH. It is given orally at a daily dose of 25-50mg. It should be used whenever a reasonable risk of neurotoxicity exists. Pyridoxine supplements are not usually necessary in children.

- Liver: INH may cause toxic hepatitis, which usually is mild. This effect is not dose related and is observed at therapeutic dosage. Mild hepatic dysfunction, as evidenced by low and transient elevation of Aspartate Aminotransferase (AST) up to 2.5 times the upper limits of normal (2.5xULN), occurs in 10-20% of persons taking INH. In some cases, toxic hepatitis will develop with signs or symptoms consistent with those of liver damage or other toxic effects, e.g. jaundice (icterus of eyes or skin), persistent dark urine (coffee or tea colored), nausea, vomiting, fatigue or weakness lasting more than three days, unexplained anorexia.

  - The frequency of toxic hepatitis increases with age: 1 per 1,000 at age 25, 5 per 1,000 at age 35, and up to 23 per 1,000 above age 50; it is extremely rare in young children. In cases of toxic hepatitis, physician consultation should be sought immediately and the drug should be discontinued immediately to prevent progressive liver damage. Alcoholics and patients with chronic liver diseases are more susceptible to liver toxicity of INH. These persons should be monitored for side effects even more closely then patients with no history of alcoholism or chronic liver disease.

- Other rare adverse reactions include:
  - Hypersensitive reactions
  - Fever
  - Skin eruption
  - Hematologic reactions

- Metabolic reactions
- Paraneesthesia of the hands and/or feet

- Drug Interactions
  - INH may interact with other medications administered on a long-term basis. INH may reduce excretion of some drugs, e.g. phenytoin, and enhance their effects. For a more complete description of interactions with INH, a reputable medical pharmacology reference book should be consulted.

- Precautions
  - Ask the patients for the following possible risk factors: alcoholism, chronic or acute liver disease, renal insufficiency, peripheral neuritis, or long-term drug administration, especially drugs known to be hepatotoxic.
  - Inquire about early symptoms of liver toxicity during periodic assessment. Multiple drug therapy patients need not have periodic liver function studies after an initial baseline test is done, unless symptoms suggestive of liver toxicity. If symptoms of liver toxicity occur:
    - Advise stopping medication
    - Obtain liver function studies
    - Physician consultation is indicated immediately

2.6.2.3 Rifampin, RIF
  - RIF is one of the most potent and useful anti-TB drugs available. RIF is bactericidal and accelerates the sterilization of bacilli in infectious cases.

- Metabolism
  - Presence of food in the stomach delays absorption, hence it is recommended that RIF be taken either one hour before or two hours after a meal. RIF diffuse throughout the body, somewhat less in body fluids. RIF crosses the placenta. It crosses the blood-brain barrier poorly, except when there is inflammation of the meninges.

- Toxicity and Side Effects
  - Liver: RIF is hepatotoxic. During the
first month of treatment, elevation of bilirubin is common; the AST level is less likely to be elevated. The risk of hepatitis with clinical jaundice is low. In alcoholics or in combination with INH the risk of hepatitis is higher. RIF can be restarted after resolution of symptoms.

- Red/orange coloration of secretions: Patients should be warned that RIF may give urine, feces, saliva, sputum, sweat, and tears a red/orange color. RIF may cause permanent discoloration of soft contact lenses.
- Cutaneous syndrome: Flushing, rash, and pruritus involving particularly the face and scalp, often with redness and watering of the eyes may occur. Cutaneous episodes usually start during the first month. They are self-limiting and do not usually require more than symptomatic treatment.
- Abdominal syndrome: Abdominal pain and nausea, sometimes accompanied by vomiting or diarrhea, may occur. It requires only symptomatic treatment as long as it occurs alone. If the patient has been taking the drug on an empty stomach, as is generally recommended, the reaction may be stopped by giving the drug with a meal.
- Respiratory syndrome: Shortness of breath, rarely with collapse and shock can occur. Respiratory syndrome is very uncommon. Caution is required as hospitalization may be necessary. In severe cases, RIF should be permanently discontinued.
- Flu syndrome: Attacks of fever, chills, malaise, headache, and bone and joint aches are observed only during intermittent regimens. It is rare at current dosage levels. It is usually mild and requires no treatment. If it persists, a reduction of dosage and a change to daily chemotherapy is recommended. RIF therapy rarely has to be interrupted.
- Hematologic crises: Hemolytic anemia or purpura and renal dysfunction are extremely rare. If they develop, RIF therapy should be permanently discontinued.

- Drug Interactions
  - RIF increases the metabolism of other drugs.
  - Oral contraceptive effectiveness is decreased. Women should be counselled to use an additional method of contraception while taking RIF.
  - Anticoagulants, dosages of coumarin type drugs may need to be adjusted prothrombin time should be checked more frequently.
  - Hypoglycemic drugs, digitalis, steroids, methadone, antiarrhythmic agents e.g. quinidine, verapamil, mexiletine, theophylline; anticonvulsants, ketoconazole, and cyclosporine. For a more complete description of interactions with RIF, a reputable medical pharmacology reference book should be consulted.

- Precautions
  - Inquire about possible risk factors such as alcoholism, chronic liver disease, renal insufficiency, and long-term drug administration.
  - Warn patient about coloration of secretions, about possible drug interaction (chiefly oral contraceptive and anticoagulants) if relevant. Women taking oral contraceptives should be counselled to use other contraceptive methods during RIF therapy.
  - At least monthly, inquire about early symptoms of liver dysfunction, thrombocytopenia, hematuria or renal dysfunction, and flu-like symptoms.
  - Obtain pretreatment liver function tests, including AST, ALT, and bilirubin, if RIF and INH are to be combined. Routine laboratory monitoring for subclinical drug toxicity is not necessary. If symptoms suggesting drug toxicity
occur, appropriate laboratory testing should be performed to confirm or exclude such toxicity. 

- In case of hematologic crises, anuria, and/or respiratory crisis stop RIF and do no administer again. In case of other adverse reactions, try symptomatic treatment first. If adverse reactions persist and are troublesome, RIF should be discontinued and more than one other drug to which there is sensitivity should be added. Further consultation with a physician experienced in the treatment of TB may be indicated.

2.6.2.4 Pyrazinamide, PZA

- PZA has a special sterilizing effect on tubercle bacilli that grow very slowly inside the macrophage cells in an acidic environment. Thus, PZA is able to kill tubercle bacilli that could not otherwise be attacked by other current drugs. PZA is bacteriostatic.
- Metabolism:
  - PZA penetrates well into most tissues including CSF.
- Toxicity and Side Effects
  - PZA is always given in combination with several other drugs. It is difficult to ascertain to what extent PZA contributes to adverse effects observed. It carries a certain risk of hepatotoxicity, but this risk is very low at the recommended dosage. PZA inhibits excretion of uric acid. Elevated uric acid occurs frequently, occasionally accompanied by arthralgias. Gout is uncommon. PZA should not be stopped for asymptomatic elevations of uric acid. The frequency of arthralgias is about 7% in those on daily regimens and 3% in those on twice-weekly regimens of PZA. These disturbances are easily managed with acetylsalicylic acid (aspirin) or other analgesics or allopurinol. Occasionally hypersensitivity reactions such as fever, rash, and other cutaneous manifestations may be seen.

- PZA can lead to phototoxicity in some patients. Patients should be cautioned against excessive sun exposure as exposing their skin to sunshine could cause a phototoxic reaction of reddish-brown coloration of the exposed areas of skin resembling sunburn.
- Precautions
  - Obtain pretreatment liver function studies and uric acid levels.
  - Close monitoring is necessary in patients with liver disease and/or severe alcoholism.
  - Repeat uric acid levels if joint symptoms appear.

2.6.2.5 Ethambutol, EMB

- EMB activity on the tubercle bacilli is modest. It is widely used in the initial treatment of TB when resistant strains of tubercle bacilli are suspected. EMB is bacteriostatic.
- Metabolism
  - EMB is easily absorbed even with food.
- Toxicity and Side Effects
  - Neuro-optic toxicity. About 1% of patients receiving EMB experience a decrease in visual acuity. It is reversible if the drug is discontinued. Visual symptoms such as red-green color blindness, blurring of vision, and spots in front of the eyes commonly precede a measurable decreased visual acuity. Patients should be informed to report any changes in vision immediately. The change may be unilateral or bilateral, so vision in each eye should be tested separately. High blood levels of EMB due to renal deficiency may be responsible for toxic reactions.
- Precautions
  - Inquire about co-morbid conditions that would contraindicate EMB. Active optic neuritis is the only definite contraindication.
  - Cataracts, diabetic retinopathy, inflammatory eye conditions, and renal insufficiency make the evaluation of visual acuity more difficult. Care should be taken to ensure that variations in vision are
not due to underlying co-morbid conditions.

- During treatment, always inquire about blurred vision, decreased color perception, spots in the visual field, and unusual ocular pain.
- Check visual acuity of both eyes separately before beginning EMB. Snellen eye charts are recommended for testing. Visual symptoms commonly precede a measurable decreased visual acuity. Patients should be informed to report any changes in vision. If changes are reported, then visual acuity testing should be repeated immediately. In testing visual acuity of patients receiving EMB, if there is a change of two lines or more in the Snellen chart test, then results should be reported to the attending physician and/or ophthalmologist immediately.
- Check gross red-green color perception before treatment and monthly thereafter. Other forms of color blindness, e.g. blue-yellow color blindness occur occasionally as well. Ishihara tables can be used to test for forms of color blindness. If Ishihara tables are not available, common objects can be used to test for color blindness. If even mild color blindness is suspected the attending physician and ophthalmologist should be alerted.
- In children who are too young for assessment of visual acuity and red-green color discrimination, EMB should be used with caution and after consideration of possible alternative drugs. Given at the typically recommended dose there is no evidence that EMB is especially toxic to children.

2.6.2.6 Rifabutin, RBT

- This drug is very similar in its action to rifampin, but has far fewer drug-drug interactions with anti-retroviral drugs. Therefore, it is primarily used in regimens for susceptible organisms in HIV-TB co-infected individuals who are also taking anti-retroviral therapy during the course of their TB treatment.

2.6.2.7 Rifapentine, RPT

- This drug is rarely used in combination with INH for treatment of TB disease in selected patients. If used, it should be in consultation with a recognized expert in the treatment of TB. This drug is primarily used with INH in a once weekly regimen for 12 weeks to treat TBI in selected patients.

2.6.3 Second Line Drugs

2.6.3.1 Streptomycin, SM

- Streptomycin was the first practical drug discovered for the treatment of TB. SM is bacteriocidal in an alkaline environment.
- Metabolism
  - SM is not absorbed by the gastrointestinal tract. Therefore, it must be administered parenterally. It does not diffuse well into the tissues and body cavities, e.g. it does not appear at useful concentrations in the CSF except when the meninges are inflamed. Excretion is primarily through the kidneys.
- Toxicity and Side Effects
  - The toxicity of SM is a limiting factor for its prolonged use, as the toxicity is dose-related and cumulative. Intermittent therapy is preferable to avoid sustained blood levels. Toxicity is enhanced in patients with renal insufficiency with increased blood urea nitrogen levels.
  - Ototoxicity. The eighth cranial nerve, both auditory and vestibular branches, is especially susceptible. The onset of symptoms may be insidious. Vestibular symptoms usually precede auditory symptoms. Many persons have unrecognized impairment of auditory and vestibular function prior to treatment. Therefore, it is important to evaluate these two functions prior to starting SM. The symptoms of ototoxicity are:
    - Auditory branch: hearing loss, roaring noises, sense of fullness in the ears, tinnitus. These side effects are often irreversible.
• Vestibular branch: vertigo, unsteady gait, dizziness accompanied by nausea and vomiting.
• Hypersensitivity to SM is an unusual but potentially serious complication of treatment. Generalized morbilliform type of rash, rarely exfoliative dermatitis, fever and malaise may occur. After cessation of treatment, there is a prompt return to normal. The person giving the injection should avoid skin contact with the drug.
• Nephrotoxicity is uncommon and usually reversible.
• Both ototoxicity and nephrotoxicity are relative to cumulative dose. A total dose of more than 120 grams should not be given unless other therapeutic options are not available.
• Other adverse reactions have been reported and are uncommon such as rash, fever, numbness and tingling around the mouth.
• Precautions
  • Conduct audiometric testing prior to starting treatment with SM. Then at the time of each injection, inquire about vestibular or auditory symptoms. If symptoms are reported, withhold medication and obtain audiometric tests immediately.
  • Check regularly for vestibular symptoms. Some simple tests are making the patient walk on tiptoe, make the patient walk and turn around suddenly or the eye-wiggle test for bedridden patients. Pour cold water in ear, close the ear for 30 seconds, let it drain, and watch for nystagmus.

2.6.3.2 Other Anti-TB Agents
• These are for use only in selected patients, primarily those infected with certain drug-resistant organisms. Use of any second line drug should be undertaken only upon consultation with a physician experienced in the treatment of TB.
• Such second line drugs include:
  • Amikacin
  • Bedaquiline
  • Capreomycin
  • Ciprofloxacin
  • Cycloserine
  • Ethionamide
  • Gatifloxacin
  • Kanamycin
  • Levofloxacin
  • Moxifloxacin
  • Ofloxacin
  • P-Aminosalicylic Acid (PAS)

2.6.4 Anti-TB Drug Distribution
2.6.4.1 Medicines for treatment of TB disease and infection are available at no out-of-pocket cost to all patients. Such medications may be requested by the patient at a local parish health unit upon presentation of a properly written prescription signed by a physician. Prescriptions written by any Louisiana licensed physician, whether in public or private practice, are acceptable. Prescriptions for medications under this program are filled and kept on file at the Louisiana Department of Health, Office of Public Health, Pharmacy Services in New Orleans.

3 Infection Control
3.1 Definitions of Infectious and Non-infectious

3.1.1 The main goal of an infection control program is to detect TB disease as early as possible and to isolate and promptly treat those patients who have suspected or confirmed TB. The level of infectiousness is directly related to the number of tubercle bacilli expelled into the air. In general a person would be considered infectious if they met one of the following criteria:
  • Coughing
  • Undergoing cough-inducing procedures
  • Positive acid-fast bacilli (AFB) on sputum
    -AND-
  • Not on anti-TB therapy
  • Just started anti-TB therapy
  • Has poor clinical or bacteriological responses on therapy
3.1.2 Patient who have or are suspected of having TB are not considered infectious if they meet all of the following criteria:

- They have received adequate therapy for two to three weeks
- They have a favorable clinical response to therapy
- They have three consecutive negative sputum smear results from sputum samples collected on different days

3.1.3 Please note that the above criteria are reserved for pulmonary and laryngeal TB. Persons with extrapulmonary TB are not infectious for a patient to remain in the hospital for TB treatment or isolation unless clinical status warrants.

3.1.4 Patients should be instructed to remain at home to avoid any unnecessary public contact until it is determined they are not infectious. Patients may continue to have contact with household members and travel directly to and from medical appointments. Consideration must be given to home circumstances when deciding whether or not a patient should be separated from family members; e.g. if there are children under the age of five in the household, there must be serious consideration to have them live separately from the infectious source, until that person meets the criteria for non-infectious. Ideally, all family members who have been in close contact with a patient with active TB disease should be tested as soon as infectious TB is suspected or confirmed in that person.

3.1.5 Patients with MDR-TB may be infectious for months due to failure of the treatment regimen. For all patients with TB disease, response to therapy must be closely monitored.

3.2 Hierarchy of Infection Controls

3.2.1 An effective TB infection control program requires early detection, isolation, and treatment of persons with infectious TB disease. An effective infection control plan should achieve these goals through a hierarchy of direct and indirect control measures:

- Administrative Control Measures
- Environmental Control Measures
- Personal Infection Control Measures

3.2.2 Administrative Control Measures

3.2.2.1 Infectious Patients

- All health care facilities must have guidelines for the prompt and effective detection of suspected TB cases. All clinicians should suspect TB in patients who demonstrate any signs or symptoms suggestive of respiratory disease. It is critical to isolate suspected TB patients away from other patients in an appropriately engineered TB isolation room. These patients should be evaluated for TB with the usual diagnostic methods. In order to determine infectiousness of a suspect, a microscopic examination of sputum for the presence of acid-fast bacilli (AFB) must be performed. Review the results of other tests, e.g. X-ray, IGRA, etc., as they are performed for diagnostic purposes and analyze this information to determine the potential for transmission of TB. Patient history should be reviewed to determine previous exposure, diagnosis, and treatment of TB infection or disease. If TB disease is suspected in light of patient history and radiological findings, the patient should be considered as a potential transmitter and appropriate infection control measures should be instituted. The early initiation of an effective regimen of TB therapy is the best means of preventing contamination in the air. Therefore, TB therapy should be initiated at the time a presumptive diagnosis is made, rather than waiting for a final culture identification.
3.2.2.2 Non-infectious Patients
- Non-infectious pulmonary or laryngeal TB patients are persons on anti-TB medications whose symptoms and laboratory reports indicate sputum has converted from smear positive to smear negative. If a patient is in the hospital because of other conditions, it is important to maintain the following:
  - Patient’s anti-TB drug therapy should be continued
  - Patient’s sputum should continue to be monitored by weekly sample collection and microscopic examination, with follow-up cultures as necessary
  - Patient should not be restricted to the room or required to wear a mask
  - Patients who have a history of completing TB treatment may be considered non-infectious and no immediate precautionary measures are required, unless symptoms suggestive of recurrent or relapsing TB are present. If symptoms are present sputum should be collected, a new chest X-ray should be taken and compared to any available previous radiographic films. Previous completion of treatment should be documented if possible.

3.2.2.3 Patient and Staff Education
- Patients who are infectious to others should be educated about the transmission of TB, the reasons for isolation, and the importance of remaining isolated from the population. The patient should be instructed that TB is spread through the air, not by fomites, i.e. any nonliving object or substance capable of carrying infectious organisms. The patient should be instructed to cover their mouth and nose with disposable tissue when coughing or sneezing. If there is any unwillingness or inability to cover the cough, the patient should be instructed to wear a surgical mask. All tissues and masks should be placed in bags for sanitary disposal. Follow universal precautions and procedures for waste disposal. Sterilization of personal items or utensils is not necessary as TB is spread through the air, not by fomites. Usual and customary cleaning and washing of personal items with soap and water is sufficient for infection control.
- It is critical that the patient is aware of the risk of transmitting TB to others. Emphasize that as few persons as possible should enter the TB isolation room.

3.2.2.4 Non-emergency surgery
- For non-emergency surgery, it is advisable to wait until the TB patient is responding to therapy and is non-infectious. Precautions should include use of a disposable unit in a closed circuit anesthesia system with sterilization of inner parts of equipment when in contact with the patient’s breath. Exterior parts of equipment and exterior areas of the room do not require additional decontamination or sterilization.

3.2.2.5 Discharge Planning
- Persons who are suspected of having TB may be discharged to their home after therapy has been initiated. In some cases, the patient may still be infectious at time of discharge. However, if therapy is adequate, the patient is less likely to transmit the disease to household contacts. The health care facility should work closely with the Region TB Program Manager to coordinate the best possible discharge plan for the patient.

3.2.2.6 Health Care Worker Education
- All health care workers should be educated about the basic concepts of TB. This includes transmission, pathogenesis, signs and symptoms, treatment, TB infection vs. disease, and infection control procedures. HCWs should understand the importance of participating in yearly TB testing programs that may be required by law and offered at their health care facility.

3.2.2.7 Health Care Facility Employee Screening
- New employees, prior to or at time of employment are required to have a TST or IGRA test for *M. tuberculosis*. Many authorities recommend that the
booster, or a two-step technique should be used if new employees cannot provide documentation of previous PPD within the past year. A previous positive TST or IGRA must be documented, including size of induration for TST, in order to excuse an employee from further testing. Annual CXRs are not recommended for employees with previously positive TST or IGRA.

- Employees with a negative TST of IGRA upon hire are required to have annual testing using TST or IGRA, or must answer a brief TB symptoms related questionnaire.
- Employees with positive TST or IGRA upon hire will have CXR and medical evaluation to determine the need for treatment of TB infection or disease.

3.2.2.8 Infection Control Program

- It is the responsibility of the Infection Control Program of the health care facility to:
  - Establish an employee TB testing program
  - Establish an isolation protocol for HCWs caring for patients who are suspected or confirmed of having infectious TB
  - Provide an in-service education program for health care professionals and allied health personnel outlining the current medical management of TB.

3.2.3 Environmental Control Measures

3.2.3.1 Prevention of Transmission

- Airborne infections such as TB can be prevented by killing the infectious microorganisms in the air. The concentrations of *M. tb* in a room can be controlled with mechanical ventilation and/or ultraviolet irradiation. Both methods are effective reducing the risk of transmission of *M. tb*. They may be used separately or in combination, but environmental controls will not replace conventional interventions such as prompt detection and treatment of cases and contact investigations.

3.2.3.2 Air Control Demands

- Air control is necessary in:
  - Rooms of known or suspected infectious TB patients
  - Intensive care units
  - Emergency rooms
  - X-ray units
  - Respiratory therapy units

3.2.3.3 Air Control Considerations:

- Patients should have fresh air introduced through a central or window unit
- Patients’ rooms should have air exhausted to the outside through an individual room exhaust or central exhaust system. Air should not move into a hallway or return to a central air condition or heating system, i.e. air from a TB patient’s room should not be recirculated within the room or building.
- An exhaust system should move air out of the room at an appropriate rate of air changes per hour (ACH). Calculations must be made for individual rooms. Air consultation should be sought from a heating, ventilation, and air conditioning system specialist.
- Any room with proper air control can be used for TB patients. Air control rooms do not need to be set aside exclusively for use by TB patients.

3.2.3.4 Mechanical and Engineering Controls

- Mechanical and engineering controls may be utilized in order to reduce the concentration of infectious droplet nuclei in the air. This would help prevent the suspension of droplet nuclei or actually kill tubercle bacilli in the droplet nuclei. Engineering controls are based primarily on the use of adequate ventilation systems. High-efficiency particulate air (HEPA) filters and ultraviolet germicidal irradiation (UVGI) are excellent instruments that can supplement existing ventilation systems in high-risk areas.

- Exhaust Ventilation

- Exhaust ventilation should be used to remove contaminated air from a room. Negative pressure relative to other rooms is mandatory. For booths, cabinets, or small rooms, exhaust ventilation may be preferred to ultraviolet irradiation for
decontamination.

- For complete explicit guidelines for exhaust ventilation refer to the “Guidelines for Environmental Infection Control in Health-Care Facilities Recommendations of the CDC and the Healthcare Infection Control Advisory Committee,” U.S. Department of Health and Human Services Centers for Disease Control and Prevention (CDC), Atlanta, GA 30329.

- High Efficiency Particulate Air (HEPA) Filtration

  - HEPA filters may be used in a number of ways to reduce or eliminate infectious particulates in the air or exhaust. These methods include placement of HEPA filters in:
    - Exhaust ducts
    - Fixed recirculation air systems
    - Portable air cleaners
    - Manufacture and CDC installation and cleaning instructions for HEPA filters should always be followed.

- Ultraviolet Irradiation (UV)

  - UV is an acceptable means of decontaminated air. Overhead UV lamps are useful in crowded, poorly ventilated areas where conventional control measures are not adequate. UV light is appropriate in areas where air volume is too large for exhaust ventilation, such as homeless shelters, correctional facilities, long-term care facilities, or health care facility waiting rooms.

  - UV lamps must be maintained to function properly and must be turned off before cleaning. The tubes and the trough of the fixture must be cleaned monthly with a cloth dampened with water or alcohol. If fixtures are in areas with excessive dust, more frequent cleaning may be necessary. Bulbs should be changed every year or earlier if malfunctioning.

  - To reduce UV exposure in occupied portions of a room, install baffles to prevent people from looking directly at the tubes.

3.2.4 Personal Infection Control Measures

3.2.4.1 Personal Respirators

- In some circumstances, administrative and environmental/engineering methods may not be wholly effective in the protection of HCWs from infectious TB. HCWs should be advised to use personal respirators when they are in the following areas:
  - TB isolation rooms
  - Rooms where cough-inducing procedures are done
  - Homes of infectious TB patients

- Every precaution should be taken to prevent the airborne transmission of tubercle bacilli during and immediately following procedures that involve sputum collection and induction, bronchoscopy, and aerosolized treatments by persons at risk for TB. Personnel performing these procedures should wear personal respirators, N-95 or above.

3.2.4.2 General Specifications

- Masks: approved masks should be worn during cough producing procedures

- Gowns: not necessary for personnel treating TB patients.

- Hands: hands should be washed upon entering and exiting a patient’s room, as otherwise indicated during patient care

- Gloves: not necessary for personnel treating TB patients

- Needles and Syringes: universal precautions for blood borne pathogens should be followed as otherwise indicated during patient care

- Dressing and Tissues: should be discarded in bags which should be closed securely in a wastebasket lined with an impervious plastic bag; this bag should be sealed upon removal and

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treated as potentially infectious waste
- Urine and feces: universal precautions should be followed as otherwise indicated during patient care
- Universal precautions should be followed on all patients regardless of diagnosis.

4 Surveillance

4.1 Mandated Reporting

4.1.1 The Louisiana Administrative Code 51:II.105 (Public Health – Sanitary Code) mandates reporting of all suspected and confirmed cases of TB within one business day of suspicion or diagnosis. TB cases must be reported to the health department by any physician, other health care provider, or any person knowing of the case. All positive bacteriology culture results, including drug susceptibility results when available, should be forwarded to the health department. The health department uses this information for the overall management, reporting, and statistical analysis of TB cases.

4.2 Definition of a TB Case

4.2.1 A case is any individual with a culture positive for *Mycobacterium tuberculosis*, or both a positive TST or IGRA and radiographic evidence for current disease.

4.3 Case Finding

4.3.1 The fundamental activity in TB control is case finding. It is extremely important to detect the undiagnosed person with current disease and initiate treatment to reduce infectiousness as quickly as possible. The priority is to identify those who have TB in a communicable state, as they are the ones who can spread the infection to others.

4.4 Case Screening

4.4.1 It is not effective from a public health or funding standpoint to screen the general population for TB infection as was done previously.

4.4.2 Groups in which focused screening for TB is recommended are:
- Close contacts of sputum smear positive TB cases. These contacts should have first priority when screening for TB infection as they are at highest risk of being infected.
- Contacts of sputum smear negative and extrapulmonary cases bear only a slightly higher risk of infection than the general population. For this reason, such contacts are not usually considered high risk, but should be prioritized over the general population for TB screening.
- Groups identified using epidemiologic methods as having a higher prevalence of TB, e.g. persons with HIV, homeless individuals, and injection-drug users.
- Immigrants or refugees from countries with endemic TB, regardless of prior vaccination with BCG.
- Occupants and employees of long-term care facilities, e.g. residential nursing homes, should be screened according to the Louisiana Sanitary Code.
- Employees of the Louisiana Department of Health, Office of Public Health, Public Health Units in accordance with the Louisiana Sanitary Code.

4.4.3 Systematic screening is not necessary in the following groups:
- Employees of medical offices, dental offices, out-patient clinics, or home health agencies
- Non-medical professionals contact with the public, e.g. food handlers, beauticians, barbers, school employees, daycare workers, etc., and other groups of workers with no epidemiologic evidence of high rates of TB.
4.4.4 Screening Procedures
- The TST or IGRA for *M. tb* are the methods of choice for screening for TB. It is followed by medical evaluation, CXR, and other diagnostics procedures outline in Section 2.4 Diagnostic Methods, as necessary for those individuals with a positive TB test.

4.4.5 Screening Responsibilities
- The formerly mentioned institutions are responsible for their own screening programs. The LDH/OPH Public Health Unit staff are able to assist in the preparation and establishment of the screening program and provide follow-up for positive reactors or suspects.
- The Regional TB Program Managers have the responsibility to ensure that the appropriate identification, screening, and follow-up are provided to contacts of suspects and cases. These contacts are then referred to the LDH/OPH Regional TB Medical Clinic for evaluation and diagnosis.
- Recommendation: Facilities licensed by the Louisiana Department of Health should refer to the state Sanitary Code for employee screening and follow-up.

4.5 Case Management

4.5.1 The care of patients with TB involves the same process involved in treating patients with other diseases: assessment, diagnosis, planning and implementation of treatment, and evaluation of progress. The patient’s care must be individualized according to the extent of the disease with consideration of personal needs and lifestyles. Essential to successful treatment is participation in care by the physician, the public health personnel, the patient, and the patient’s family.

4.5.2 Fundamental to all case management is adherence.

4.5.2.1 Adherence is defined as the extent to which a person’s health related behaviors, e.g. taking medication, coincides with medical advice. Non-adherence is a serious problem. It can lead to treatment failure, drug resistance, continued transmission, increasing disability or morbidity, and death.

4.5.2.2 Factors affecting adherence can include:
- Clinical setting, referral process, and/or the patient or medical provider
- Duration complexity, frequency, and side effects of therapy
- Lifestyle, social support, demographics, and health beliefs of patient

4.5.2.3 Methods for ensuring adherence can include:
- Education for the patient and the patient’s family/social support
- DOT
- Appointment reminders

4.5.3 Hospitalization

4.5.3.1 There is no need to routinely hospitalize all new TB cases. Hospitalization for diagnostic or isolation purposes is unnecessary in most cases. The risk of infection to contacts exists prior to diagnosis. Once the case is diagnosed and placed on treatment, the infectiousness dwindles rapidly.

4.5.3.2 Inpatient care may be recommended for
- Cases requiring 24 hour nursing care
- Cases with co-morbidities making the initial plan of care too complicated to be carried out on an outpatient basis
- Cases where a period of supervised drug administration is deemed necessary.
- Relapse cases with drug resistant strains of *M. tb*, where non-adherence to prescribed treatment was previously a problem.

4.5.4 Decision to Discharge

4.5.4.1 Patients can be discharged when hospitalization is no longer deemed necessary by the physician. Several factors must be evaluated when deciding to discharge a TB patient, to ensure completion of the prescribed therapy.
- Patient’s likelihood of adherence to TB treatment regimen
- Patient’s understanding of TB disease, including transmission and the importance of completing the full course of treatment
• Patient’s living situation

4.5.5 Prior to Discharge

4.5.5.1 Once the decision to discharge a TB patient has been made, the following actions should be completed prior to discharge

• Determine the outpatient facility to which the patient will be referred for follow-up of TB care as soon as possible.
• Advise that facility in writing or by phone of the anticipated discharge and referral of the patient, and provide that facility with the patient’s names, diagnosis, current clinical status, and anticipated date of discharge.
• If anti-TB drugs are to be provided by the LDH/OPH Pharmacy, appropriate prescriptions for a 30-day supply should be forwarded to the Parish Health Unit in the parish where the patient resides or to the Regional TB Program Manager as soon as possible.

4.5.6 Discharging the Patient

4.5.6.1 Instruct the patient to report to the Parish Health Unit as soon as possible to arrange outpatient care and treatment.

4.5.6.2 The discharging institution’s infection control practitioner should prepare a case summary that includes patient history, discharge summary, and all appropriate laboratory and radiographic reports. This should be forwarded to the Region TB Program Manager or Parish Health Unit of the parish where the patient resides.

4.5.7 Anti-TB Medications

Anti-TB medications are available at no out-of-pocket cost to suspects and confirmed cases of TB in Louisiana. This applies to patients under regional clinic care, private medical care, or hospital outpatient clinic care. Such medications may be requested by the patient at their Parish Health Unit upon presentation of a properly written prescription, signed by a physician licensed to practice medicine in Louisiana. Prescriptions for medications under this program are filled and kept on file at the LDH/OPH Pharmacy.

4.6 Suspect Management

4.6.1 A suspect is any individual for whom a diagnosis of TB disease should be considered.

4.6.2 Symptomatic individuals should have a TST or IGRA, a chest radiograph, sputum collected for bacteriologic testing, and an HIV test if their HIV status is unknown.

4.6.3 Patients who have AFB positive sputum smear results should have a contact investigation done immediately to identify any persons who may have been exposed to or infected by the suspected case. Contact investigations are the responsibility of the Regional TB Program Manager.

4.6.4 All patients regardless of site of disease should have at least three consecutive daily sputum specimens collected to rule out pulmonary disease.

4.7 Bacillus of Calmette and Guerin (BCG)

4.7.1 The Bacillus of Calmette and Guerin (BCG) was derived from a strain of Mycobacterium bovis attenuated through years of serial passages in culture by Calmette and Guerin at the Pasteur Institute in Lille, France. It was first administered to humans in 1921. Since that time, many different strains have been derived and used throughout the world.

4.7.2 BCG vaccination is not generally recommended in the United States because:

• There is a low risk of infection with Mycobacterium tuberculosis in the U.S.
• The vaccine has variable efficacy against pulmonary TB
• There is a low risk of severe disseminated TB disease in young children in the U.S.
• The BCG vaccine can produce a false positive result of the TST. History of BCG vaccine does not interfere with IGRA testing. It is recommended that an IGRA test be performed for any
person with a history of BCG vaccination and a positive reaction to PPD.

4.7.3 Many TB-endemic countries distribute the BCG vaccine among infants as part of their TB control efforts to prevent children from contracting severe disseminated TB or meningeal TB.

4.7.4 The BCG vaccine is not recommended for use in HIV positive persons. An IGRA should be used when screening HIV positive persons for *M. tb* infection.

4.7.5 In the Louisiana TB Control Program case detection, drug therapy, preventative treatment, and contact investigation are the proper and sufficient methods to decrease the burden of TB morbidity and mortality in the state.
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