TUBERCULOSIS CONTROL MANUAL

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This Manual is dedicated to:

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MERETTA WILSON

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

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1. OUTLINE

1.1 Goal

The goal of the Tuberculosis (TB) Control Program is to lower the morbidity and mortality from tuberculosis and ultimately obtain eradication of the disease. To reach this goal the program's objectives are:

- To reduce the risk of becoming infected for persons not yet infected.
- To reduce the risk of developing the disease once a person has been infected.
- To reduce the risk of severe complications and death once the disease has developed.

1.2 Methods

The methods used to reduce these risks are:

- Case finding among symptomatic persons, in groups with high prevalence of tuberculosis infection or disease (close contacts of tuberculosis cases for example) or in groups where the presence of an infectious case could provoke a major tuberculosis outbreak, such as:
  - Nursing Homes
  - Prisons
  - Homeless
  - Drug Treatment Programs
  - Immunosuppressed.
- Early diagnosis, treatment, and follow-up of patients with tuberculosis disease to stop transmission and reduce the risk of complication 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.
- Early detection of latent tuberculosis infection combined with treatment to reduce the risk of developing disease.
- Preventive treatment of "not infected" high-risk contacts to reduce the risk of infection/disease.
- Education of persons with infection/disease and the general population, a major component of a sound prevention program, to help to reduce the risk of non-compliance.

1.3 Services Available

To implement tuberculosis control activities in Louisiana, the Office of Public Health (OPH) offers the following:

- Tuberculosis Control Section Central Office staff to plan and coordinate tuberculosis control activities, provide consultation to regional and local public health staff, evaluate program progress, and control the program budget.
- Regional TB Program Managers, formerly Regional Tuberculosis Disease Intervention Specialist (DIS) Supervisors, responsible for managing and directing the regional tuberculosis

programs to assure compliance with programmatic policies and procedures. The Regional TB Program Manager is responsible for managing and monitoring surveillance and containment activities including sanitary code and quarantine regulations within the region. This includes parish health units, public and private hospitals, nursing homes, home health agencies, correctional facilities, private medical offices or facilities, and other public and private agencies where tuberculosis may occur or be a concern. The Regional TB Program Manager directly supervises the Regional TB DIS staff and provides programmatic direction to clerical, professional and other staff involved in TB control activities. The Tuberculosis Medical Clinics provide medical care and supervision to tuberculosis suspects, cases and contacts attending those clinics. Tuberculosis Medical Clinics accept referrals from all public and private sites.

- Surveillance and containment activities are essential to control tuberculosis in a community. Activities related to case finding, screening, case reporting and counting are surveillance activities. Activities related to treatment and follow-up of cases and contacts are containment activities. These activities are accomplished by the combined efforts of TB DIS staff and parish health unit staff of each region.

- Long-term hospitalization may be available for TB patients who have failed special TB control measures established by the Office of Public Health. The decision for long-term hospitalization of a TB patient who has failed special control measures, must be made by the Regional TB Program Manager and the State TB Control Program Office.

- Diagnostic Services available under the direction of the Office of Public Health at no expense to outpatients include:

    - Tuberculin skin testing available for TB suspects/cases and persons exposed to these suspects/cases.

    - X-Ray services for those patients receiving TB care through TB medical clinics or contractual sites.

    - Medical evaluation and treatment provided by regional clinicians.

    - Laboratory services including:

        - Microscopic examination, culture and sensitivities of specimens submitted for acid-fast bacilli (AFB).

        - Testing of blood for antibodies to Human Immunodeficiency Virus (HIV) in all adult and adolescent patients receiving TB services.

        - Testing of blood for liver function studies according to guidelines.

- Anti-tuberculosis drugs available with a written prescription from a Louisiana licensed physician at no expense to persons residing in Louisiana.

2. TUBERCULOSIS

2.1 Classifications - Definitions

(From Core Curriculum on Tuberculosis Centers for Disease Control and Prevention, 4th Edition, 2000)

The classification of tuberculosis is based on the broad host-parasite relationships as described by exposure history, infection, and disease. It includes all persons. It applies to both children and adults.

- Class 0: **No Tuberculosis Exposure, Not Infected.** No history of exposure, negative reaction to tuberculin skin test.

- Class 1: **Tuberculosis Exposure, No Evidence of Infection.** History of exposure, reaction to tuberculin skin test negative.

- Class 2: **Tuberculosis Infection, No Disease.** Positive reaction to tuberculin skin test, negative bacteriological studies (if done) no clinical or radiographic evidence of active tuberculosis.

- Class 3: **Tuberculosis, Clinically Active.** *Mycobacterium tuberculosis* cultured; otherwise, both a positive reaction to tuberculin skin test and clinical and/or radiographic evidence of current disease.

- Class 4: **Tuberculosis, Not Clinically Active.** History of previous episode(s) of tuberculosis, or abnormal but stable radiographic findings in a person with a positive reaction to tuberculin skin test, negative bacteriologic studies, no clinical and/or radiographic evidence of current disease.

- Class 5: **Tuberculosis Suspect.** Diagnosis pending.

2.2 Transmission and Pathogenesis

Tuberculosis is an airborne communicable disease caused by *Mycobacterium tuberculosis*. Tuberculosis can affect any organ of the body. The most common source of transmission is the patient with pulmonary or laryngeal tuberculosis who produces sputum that is smear positive with acid fast bacilli.

Infectious droplet nuclei: Infectious particles are created when the person with pulmonary or laryngeal TB coughs, sneezes, talks or sings. Small droplets (1-5 microns) may remain suspended in the air for hours and, when inhaled, may reach the alveoli starting a new infection. The probability that TB will be transmitted depends on three factors:

- The infectiousness of the person with TB (determined by direct smear result of a sputum specimen)

- The duration of exposure in an environment appropriate for transmission (the shared air principle)

- The presence of a susceptible host (exposure of uninfected or immuno-compromised contacts).

There is a low risk of infection in casual contacts unless the source case proves very infectious. Infection/disease occurs more often among household contacts or other high-risk contacts.

About 5% of the persons recently infected

with tuberculosis bacilli will develop the disease within 2 years if not treated. The risk is higher in infants and toddlers than in adolescents and adults. Among those who do not develop the disease in the first 2 years after infection, another 3% to 5% may develop the disease at a later time in life. **Individuals infected with HIV and tuberculosis develop active disease at a rate of 8-10% each year.** A majority of active tuberculosis cases occur in elderly persons previously infected, and in high-risk individuals such as contacts, immigrants, alcoholics, drug addicts, or persons with debilitating diseases.

Tuberculosis infection: If droplet nuclei pass down the bronchial tree they may settle in the alveoli beyond the mucociliary blanket. Then the bacilli are phagocytized and multiply locally. From there the tubercle bacilli may spread through the lymphatic channels and bloodstream.

The initial lesions in the lung and draining lymph nodes are of limited duration and heal without treatment.

Hypersensitivity: The host develops delayed-type hypersensitivity which is a cell-mediated reaction to the tubercle bacilli. This is associated with a tuberculin skin test that becomes positive within 2 to 10 weeks after infection. Along with hypersensitivity the normal host develops immunity against subsequent infection.

Relation between hypersensitivity and immunity: Although no definite proof is yet available, it seems that the reaction of hypersensitivity plays little, if any, role in acquired immunity to tuberculosis. The role of hypersensitivity is insignificant when compared with the high degree of specific immunity that can develop in animals. Both phenomena involve a cellular type of immune response, but separate "T" lymphocyte populations mediate the response.

New infection: Factors that prevent individuals from controlling the dividing bacilli are poorly understood.

Immune response may be altered:

- By certain diseases (HIV infection, silicosis, diabetes, cancer, diseases associated with immunosuppression or post-gastrectomy, malnutrition, or other infections)
- By treatment with corticosteroids or other immunosuppressants
- During the first 2 years of life, puberty and adolescence, and postpartum.

Primary disease: In a small percentage (2 to 3%) of recently infected persons, the initial control of tubercle bacilli by the body is inadequate. There is direct progression of infection to primary pulmonary tuberculosis, with or without dissemination outside the lungs to the pleura, to the meninges or to other organs.

Dormant bacilli: Tubercle bacilli may remain viable but dormant within the tissues for years or even a lifetime.

The immunocompetent response inhibits the 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 individuals previously infected, there is a breakdown in resistance to the tubercle bacilli and bacilli multiply (sometimes referred to as recrudescence). The reasons for this breakdown are not known. As mentioned above, tubercle bacilli from a remote infection, shift from a dormant state to

multiply and cause disease.

Recurrence: Tuberculosis should be designated as recurrent if a patient has previously had verified tuberculosis, responded to therapy and was discharged (or lost to supervision) for more than 12 months and again has active tuberculosis.

2.3 Clinical Information

Active tuberculosis is an infectious disease that usually presents with symptoms. However, many patients, even some with extensive disease, have insidious symptoms that they ignore. Other patients may be truly asymptomatic. The asymptomatic patient and the person who does not recognize insidious or even frank symptoms can be identified only through a history of exposure, an abnormal chest X-ray, the confirmation of infection with a tuberculin skin test, or cultures positive for *Mycobacterium tuberculosis*. Symptomatic patients can be characterized as having generalized systemic signs and symptoms, pulmonary signs and symptoms, signs and symptoms related to other organs, or a combination of these characteristics.

Generalized signs and symptoms: Frequently patients are first aware of fatigue, anorexia, weight loss, night sweats, or low-grade fever that persists over weeks to months. These signs and symptoms are often attributed to stressful lifestyles. 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. Acute symptoms may be superimposed on the more chronic pattern. Erythema nodosum may occur rarely with the acute onset of tuberculosis. At times, non-specific systemic symptoms associated with fever of unknown origin may be the only manifestation of tuberculosis. This syndrome can defy intensive diagnostic evaluation in the hospital, and may be resolved only through a systematic evaluation of diagnostic studies such as repeated chest X-rays, 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 is usually asymptomatic and may be far advanced before fever and weight loss begin. A productive cough in children is extremely rare; obtaining a gastric aspirate to support diagnosis may be considered.

Miliary tuberculosis is seen in all age groups. Patients may be acutely ill with fever, dyspnea, and cyanosis, or be chronically ill with systemic symptoms. Miliary tuberculosis is recognized most often by the diffuse, finely nodular, uniform infiltrates visible on the chest X-ray. However, fever and systemic symptoms and signs may antedate the miliary pattern.

Pulmonary signs and symptoms: Characteristically, 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 uncommon 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 the 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 tuberculosis. There may be acute or recurrent pleuritic pain with pleural effusion.

Other organs: Tuberculosis may affect several other organs of the body, including the genitourinary tract, lymphatic system, bones and joints, meninges, peritoneum, pericardium, and larynx. Symptoms of tuberculosis disease of other organs are variable and are often similar to the symptoms of other infections. The severity of the disease may be from mild to life threatening and can occur in all ages. (See Core Curriculum 2004)

2.4 Diagnostic Methods

2.4.1 Tuberculin Skin Test and Blood Assay for *Mycobacterium tuberculosis (M.tb)*

The tuberculin skin test is most widely available method to diagnose *M.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 at the site of the antigen injection in sensitized persons. Such persons are termed **"reactors."** Not all reactors are infected with *M.tb;* infection with mycobacteria other than tuberculosis, common in many parts of the world, may cause weak cross-reactions. The larger the reaction with a given antigenic dose, the greater is the probability that the reaction is specific for that antigen.

Technique: Purified Protein Derivative (PPD) Tuberculin, stabilized with Tween 80 and standardized by biologic assay to 5 tuberculin units (TU) is the recommended antigen. The standard technique (Mantoux) is the intracutaneous injection of 0.1 ml of PPD-tuberculin containing 5 TU into the skin, usually the volar surface of the forearm. If the injection site is cleansed with alcohol, it should be allowed 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 amount of fluid (0.1ml) is accurately injected intradermally. Even though the detergent Tween 80 minimizes the adsorption of tuberculo-protein, tuberculin should never be transferred from one container to another, and skin tests should be given immediately after the syringe is filled. Used needles and syringes should be placed in a puncture-resistant container.

The site of injection should be examined 48 to 72 hours after the injection, the time when the induration is usually most evident. Large reactions, however, will still be evident up to seven days later. The reaction should be recorded as diameter of induration in millimeters, measured transversely to the long axis of the forearm. Erythema without induration is not considered evidence of tuberculous infection. If, however, the injection is subcutaneous, instead of intradermal, as evidenced by the lack of a wheal at the time of the injection, erythema could result with little or no induration, and the test should be repeated.

Readings: A PPD reading should be read across the arm, in a 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 with a gentle stroking with the finger.

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 (redness).

The Mantoux PPD must be recorded in millimeters (mm) of induration.

Classification of the tuberculin reaction is determined not only by its size, but by the clinical circumstances and the intended use of the result. For example, we record the actual measured value of blood glucose, or blood urea, etc., and interpret the significance in various ways utilizing the information available. Knowledge of the significance of specific sizes of induration is based on large epidemiologic surveys of patients with tuberculosis and other mycobacterial diseases.

- When evaluating an individual, a reaction of 5mm or more is considered positive when the patient has a high likelihood of infection with tuberculosis or has limited ability to respond immunologically. A tuberculin reaction of ≥5mm of induration is classified as positive in the following groups:
    - Close contacts of a person with infectious TB
    - Persons who have a chest radiograph suggestive of previous TB and who have received inadequate or no treatment
    - Persons known to have or suspected of having HIV infection
    - Persons who inject drugs and whose HIV status is unknown.
- A tuberculin reaction of ≥10mm of induration is classified as positive in persons who do not meet the preceding criteria but who have other risks factors for TB. These include:
    - Persons who inject drugs (if HIV negative)
    - Persons with certain medical conditions (diabetes, silicosis, prolonged corticosteroid therapy, other immunosuppressive therapy, hematologic and reticuloendothelial diseases, end stage renal disease, transplant recipients, intestinal bypass, low-body weight, malnutrition)
    - Foreign-born persons from areas where TB is common
    - Residents of long-term care facilities (nursing homes, correctional facilities, etc.)
    - Children younger than 4 years of age
    - Medically underserved, low-income populations, including high-risk minority and ethnic groups
    - Locally identified high-prevalence groups (*e.g.*, migrant farm workers or homeless persons).
- A tuberculin reaction of ≥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 tuberculosis.**

- Recent converters are defined on the basis of size of induration:
  - ≥10mm increase within a two year period is classified as a recent conversion regardless of age.
- PPD skin-test results in health-care workers (HCWs):

  In general, the recommendations in the preceding sections should be followed when interpreting skin-test results in HCWs. However, the prevalence of TB in the facility should be considered when choosing the appropriate cut-point for defining a positive PPD reaction. In facilities where there is essentially no risk for exposure to *M.tb* (i.e., facilities that do not care for patients with active tuberculosis), an induration ≥15mm may be a suitable cut-point for HCWs who have no other risk factors. In facilities where patients with active TB receive care, the cut-point for HCWs with no other risk factors may be ≥10mm.

- A recent conversion in an HCW should be defined generally as a ≥10mm increase in size of induration within a two-year period. For HCWs who work in facilities where exposure to TB is very unlikely (i.e., facilities that do not care for patients with active tuberculosis) an increase of ≥15mm within a two-year period may be more predictive for defining a recent converter because of the lower positive predictive value of the test in such groups.

- **Booster effect:** This technique is used to establish a baseline reading for the initial skin test of a series of annual tests. Subsequent tests, if indicated, should follow the usual single test procedure. **If a person has recent documented skin test results (within a 12 month period), the two-step procedure is unnecessary.**

  A person's reactivity to tuberculin may wane over a period of time. For example, if tested with PPD, adults who were infected during their 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 PPD test conversion from a newly acquired infection. Misinterpretation of a boosted reaction as a new infection could result in unnecessary investigations of laboratory and patient records in an attempt to identify the source case. Additionally, the unnecessary treatment of latent tuberculosis infection may occur. The booster 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 HCW's, two-step testing can be used to reduce the likelihood that a boosted reaction is misinterpreted as a new infection. **An individual with an initial tuberculin induration above the cut-point for his risk group or previous documented reaction should be considered as positive.** There is no need for a repeat skin test. Boosting is not required or indicated.

Two-step testing should be utilized in the

initial test of the series as follows:

- **An individual with an initial tuberculin induration of less than the cut-point for his risk group** should have a repeat skin test five days to three weeks after the first test was given. This then is boosting the first skin test.

- If the second induration is above the cut-point for his risk group, consider it a positive boosted response. Subsequent skin testing in the future is not indicated.

- 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.

A reaction of 0 to 4 mm does **not rule** out the diagnosis of *M.tb* infection or disease. Individuals with overwhelming tuberculosis, anergy, or incubating infection may have a negative PPD.

- **Bacille Calmette-Guerin (BCG) Vaccine:** Recommendations are to assume that any reaction greater than 10 mm in a person vaccinated with BCG more than a year before is due to TB infection.

- **Live virus immunization and tuberculin testing:** Tuberculin skin testing is **not** a prerequisite for measles 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 tuberculin skin testing during an epidemic of one of these diseases, do not skin test an individual with definite or probable viral disease.

When immunizing in other than epidemic situations, both the PPD and live virus immunization should be done at the same time. The tuberculin test should read 48-72 hours later. If the test is not read within 72 hours, retesting should be postponed until one month after immunization.

Tuberculin availability: PPD 5TU is the only antigen used by the Office of Public Health. Other strengths of PPD are available but are not recommended for TB screening. Always check to be sure 5TU is used.

PPD should be stored in a refrigerator at 2-4°C when not in use. When protected from heat and light it retains its potency through the date of expiration. Special note should be taken of the expiration date upon receipt of antigen. All vials should be dated and initialed when opened. **Unused antigen should be discarded thirty days from this date**.

The multiple puncture tests (Heaf, Tine, Applitest, or Monovacc) are not recommended because it is impossible to standardize the amount of tuberculin injected. Results of these type tests should be verified by a Mantoux PPD. Current State regulations now require the use of Mantoux method PPD for employment purposes. (Refer to Sanitary Code State of Louisiana)

Blood assay for *Mycobacterium tuberculosis* (BAMT): The United States Food and Drug Administration approved blood assay for *Mycobacterium tuberculosis* is QuantiFERON-TB Gold (QFT-G). QFT-G results are reported as positive, negative, or indeterminate. (Refer to Centers for Disease Control, Morbidity and Mortality Weekly Report, "Guidelines

for Using the QuantiFERON-TB Gold Test for Detecting Mycobacterium tuberculosis Infection, United States" December 2005; 54 (No. RR-15, 49-55)

2.4.2 Chest X-ray

Some radiographic patterns are common in tuberculosis. Tuberculosis may produce almost any form of pulmonary abnormality on the chest X-ray. Therefore, a diagnosis based on X-ray alone is a presumptive diagnosis. Other diagnostic tests such as sputum cultures, bronchial washes, gastric washes or collection of other body fluids, or biopsies should be attempted in order to establish a definitive diagnosis, to determine susceptibility, and to serve as a source for molecular epidemiology.

Before 1975, routine screening for tuberculosis was done by systematic X-ray surveys identifying cases in the general population. This became a very non-productive way of finding new cases and was abandoned. In order to avoid unnecessary exposure of patients to ionizing radiation, to reduce expenditures, and to save personnel time, X-rays should be limited to specific situations.

Tuberculosis Cases

- Chest X-rays should be performed as an initial diagnostic method and during chemotherapy when requested by a physician (minimum within three months after initiation of therapy).

- If initial chest X-ray had abnormalities suggestive of tuberculosis, a repeat chest X-ray should be done at the end of therapy to provide a new baseline X-ray.

- If the patient presents with symptoms of tuberculosis after being discharged, sputa (x 3) should be collected. The decision to repeat a chest X-ray will be made by the physician on a case-by-case basis according to clinical presentations.

Tuberculosis infections (routine reactors identified through tuberculin skin testing) If initial X-ray shows no abnormality, repeat only on medical request or suspicion of activation of disease.

All close contacts to infectious pulmonary cases should be tuberculin skin tested, X-rayed, and referred for medical evaluation.

Tuberculosis suspects should always have sputa collected, be skin tested, X-rayed, and referred for medical evaluation.

No X-rays are to be performed for anyone coming to the health unit requesting a chest X-ray for other reasons (*e.g.,* employment, personal convenience, etc.).

2.4.3 Bacteriology

Recovery of the Mycobacterium tuberculosis bacilli is essential for establishing a definitive diagnosis of tuberculosis. It is of utmost importance that specimen collection be done carefully, efficiently, and regularly.

The efficiency of laboratory methods used to isolate mycobacteria depends in part on the manner in which a specimen is handled after collection.

For optimum results, the specimen must be mailed to the laboratory on the day of collection. Ideally, if the specimen is not brought into the health unit someone from the health unit or a Disease Intervention Specialist should pick it up from the patient. All specimens should be placed in

an inside drop box at the post office in order to preserve the specimen. Immediate mailing is of utmost importance. Do not send specimens via the OPH truck or any courier service. Specimens should not be held from the mail because of weekends or holidays.

Only approved containers should be used for mailing/shipping. Be sure that all requested information is provided: including patient name, date of birth, address, source of specimen, collection date and sender's return address.

Public health units are to obtain sputum collection containers and lab slips from the Regional TB Program Manager.

Private providers such as hospitals, laboratories, clinics, and physician's offices may use the services of the Texas Laboratory Services Section for specimen identification without charge. An introductory kit may be obtained by requesting in writing, by telephone, or fax request directly from the laboratory:

Texas Laboratory Services Section
1100 West 49th Street, MC-1947
Austin Texas 78756-3194
Phone: 512-458-7318

The introductory kit will contain information regarding refill supplies.

Sputum collection: Each time a sputum specimen is collected from a patient, the health care worker should give thorough instructions for sputum collection and handling.

- Inform the patient that saliva and nasopharyngeal discharge are not sputum. Only the material brought up from the lung after a cough constitutes the material desired. 5-10 ml is a sufficient quantity.

- At least three single early morning specimens should be collected from suspects and new cases on succeeding days. These should be submitted on the day of collection and mailed without delay. According to standards as set forth by the "Governor's Task Force on Tuberculosis" the following is a minimum schedule of bacteriologic examination for *Mycobacterium tuberculosis* culture positive pulmonary patients:

  - Weekly sputum exams on culture positive patients for the first eight weeks. **(Culture conversion at eight weeks determines length of therapy)**

  - After eight weeks, continue weekly sputum exams on all patients who remain smear positive until three consecutive negative sputum smears have been obtained.

  - Monthly sputum examination as long as the patient is on treatment.

  - Single monthly sputum specimens are sufficient, unless non-compliance or drug resistance is suspected.

  - When noncompliance or drug resistance is suspected, weekly specimens should be collected until completion of therapy.

The Office of Public Health prefers weekly sputum collection until sensitivities on MTB positive patients are returned. Changes in the sputum collection schedule should be discussed with the Regional TB Program

Manager.

Other collection methods: Aerosol induction, gastric aspiration, tracheal suction, or bronchoscopy are satisfactory alternatives for patients having difficulty producing sputum spontaneously.

Aerosol induction is the only mechanical method currently used in public health clinics. Water (bottled, non-bacteriostatic) is nebulized. Such specimens may appear watery and thin. These should be labeled "Induced" and submitted to the laboratory. The cough induced by this method is often violent and uncontrolled. Local exhaust ventilation devices (*e.g.,* booths or special enclosures) or, if local exhaust devices are unavailable, a room that meets the ventilation requirements for TB isolation should be used. Before the booth, enclosure, or room is used for another patient enough time should be allowed to pass for at least 99% of airborne contaminants to be removed. This time will vary according to the efficiency of the ventilation or filtration used (MMWR, 1994 / Vol. 43 / No RR-13; Suppl.3, Table S3-1). **If local ventilation devices are not available or feasible, collection should be attempted outdoors.**

Patients can often produce a good regular specimen the morning after an induction, and should be given an approved container for collection and submission of this specimen.

During initial sputum collection, the health care worker should review the sputum collection instruction sheet (TB-11) with the patient and coach the patient to ensure that:

- An adequate specimen is obtained
- The patient understands how to collect and submit future specimens.

Patients with any extra-pulmonary disease should also have initial sputum specimen collection as previously stated. These patients have a 20% chance of pulmonary involvement. Patients with GU TB, CNS TB, or TB meningitis require follow-up urine or CNS specimens for culture.

Routine Laboratory testing includes a microscopic examination of a stained smear of the concentrated specimen, culture, identification, and drug susceptibility testing.

Microscopic Examination: The detection of acid fast bacilli (AFB) on stained smears is the first bacteriologic evidence of the presence of mycobacteria in a specimen. It is easy, quick, and provides the clinician with a preliminary confirmation of the diagnosis. The sputum smear is also of important epidemiologic significance. All new and suspect cases should have sputum smear results documented as soon as possible. This may require direct communication with the hospital laboratory, state laboratory, or private physician.

The finding of acid fast bacilli is not definitive evidence of tuberculosis. Mycobacteria other than tuberculosis (MOTT) (*Mycobacterium avium intracelluare, M. kansasii, M. fortuitum, etc.*) may be present in the specimen. Some MOTT are pathogenic, some are not. Conversely, the lack of a positive smear does not rule out the possibility of tuberculosis. Only 60% of culture positive specimens are also smear positive microscopically.

Culture Isolation: 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 susceptibility determination is made if warranted.

The Central Lab currently uses solid media for primary cultures and liquid and solid media for all smear positive specimens.

Identification: Techniques for species detection include: FL-HPLC, UV-HPLC, DNA probe, and amplified DNA testing.

For diagnostic purposes at least 3 bacteriologic specimens should be collected. Once the diagnosis is established 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, patients completely treated and cured may be misclassified as failures because their X-rays still show residual lesions including cavitation. Sputum follow-up is preferred over X-ray for treatment evaluation.

- Possibility of drug resistance: Early detection of drug resistance is not possible without routine serial sputum submission. Monthly or more frequent specimen submission is imperative for proper patient management and cure.

- Conversion of sputum culture and length of therapy: Modern tuberculosis therapy requires the regular collection of sputum to determine the length of therapy and combination of drugs.

- Management of contacts: Repeat PPD testing of non-infected close contacts should be done two months after first negative smear is obtained, or contact is broken.

The performance and interpretation of drug susceptibility testing is essential for the physician in appraisal of the patient's response to chemotherapy and choice of the most effective anti-mycobacterial agents. The Central Laboratory will perform rapid determination by radiometric drug susceptibility testing on all initial specimens submitted that are positive for *Mycobacterium tuberculosis* complex.

Susceptibility studies should be requested whenever any of the following conditions exist:

- All newly diagnosed cases of tuberculosis

- Patients who show consistently positive results in their sputum

- Patients on therapy who, after an initial decrease in bacterial content of their sputum again become heavily positive

- Patients who have had previous anti-tuberculosis chemotherapy and need treatment again (recurrences)

- In patients suspected to be at risk of primary resistance, expedited sensitivities can be requested from the lab. This includes the following situations:

    - Known contact with a drug resistant case

- Residents from countries with high prevalence of resistant *Mycobacterium tuberculosis*

- HIV positive persons

Susceptibility request: Indirect/direct radiometric drug susceptibilities will automatically be performed on all *Mycobacterium tuberculosis* isolates from new patients. Follow-up drug susceptibilities should be performed approximately every three months for patients with normal immune systems and every two months in those who are immunodeficient. When drug resistance develops to the primary drugs Isoniazid (INH), Rifampin (RIF), Ethambutol (EMB), Pyrazinamide (PZA), and Streptomycin (SM), then drug susceptibilities to second-line drugs are performed automatically.

Occasionally, a positive culture of bacilli resistant to one or more drugs of a regimen may be observed in the course of successful chemotherapy. The resistant culture is composed of a few colonies (less than five) usually obtained shortly before complete sputum conversion occurs. This finding could be due to resistant organisms that for unknown reasons outlived the sensitive part of the bacterial population. If the clinical response to treatment suggests transient drug resistance it is justified to repeat culture and drug susceptibilities before altering the course of therapy.

If transient drug resistance is confirmed, (subsequent bacteriologic exams confirm decrease in mycobacterial content of sputum, and/or resistant bacteria are no longer present) it may not be necessary to change treatment since it carries a good prognosis.

At the end of a successful course of chemotherapy, or even after termination of chemotherapy, some patients may yield **isolated positive smears** with cultures negative for *Mycobacterium tuberculosis*. If repeat sputum examinations time three are negative by culture and smear, such isolated positive smears do not necessarily mean that a relapse has occurred. The infectiousness of isolated, positive sputum smear patients is low.

2.5 Treatment of Tuberculosis Disease and Latent Tuberculosis Infection

2.5.1 General Principles

The Louisiana Office of Public Health follows the general guidelines of the Centers for Disease Control and Prevention, the American Thoracic Society (ATS), and the Infectious Diseases Society of America (IDSA). The latest statements "Treatment of Tuberculosis" and "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" are available in the Morbidity and Mortality Weekly Report, or from the Office of Public Health, TB Control Program.

Information concerning diagnosis, treatment, and compliance is available on request from the Office of Public Health, TB Control at (504) 568-5015 or the Regional Tuberculosis Control Programs. An outline of current treatment recommendations can be found in the appendix. Specific treatment schemes are discussed in Section 2.5.3.

Several key principles apply to successful treatment of active tuberculosis:

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

2.5.2 Monitoring for Adherence

Non-compliance is a major problem in TB Control. Inadequate treatment can lead to continued transmission, emergence of drug resistance, and recurrent disease.

Evidence of non-compliance includes:

- **Two weeks:** urine specimen without orange red color.
- **One month:** pill count reveals more than 10% remaining in bottle (for individual on self-supervised daily therapy); sputum smear remains positive.
- **Two months:** sputum culture remains positive.

Directly Observed Therapy

Patients with suspected or confirmed active pulmonary tuberculosis should be placed on Directly Observed Therapy (DOT). Highest priority should be given to the following categories:

- Smear positive pulmonary patients.
- HIV positive patients.
- Children under the age of 15.

DOT is especially important in defeating non-compliance as in Section 4.3. 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 setting or other locations through the use of field personnel.

Directly observed therapy has demonstrated acceptable results when given two or three times a week. DOT provides a tool to address the problem of "on again, off again treatment" and non-compliance. Non-compliance contributes to the emergence of resistant organisms and is a major factor in the development

and transmission of resistant strains of bacilli.

DOT should be used for the treatment of active disease whenever possible, especially when:

- Patient history indicates prior non-compliance
- Compliance with self-administered medications is unlikely
- Hospitalization is not practical or recommended.

Patients must be initiated on daily DOT. This regimen may be changed from daily to twice weekly DOT anytime after 14 daily doses have been observed. The following drugs/dosages may be used twice weekly:

INH	15 mg/kg up to 900mg
RIF	10 mg/kg up to 600mg
PZA	50-70 mg/kg up to 4gm
SM	25-30 mg/kg up to 1.5gm
EMB	50 mg/kg
PAS	120 mg/kg up to 12gm.

(See Appendix for details)

Utilization of personnel other than nurses and DIS may be considered for directly observed therapy. Prepackaged or unit dosages of medications allow responsible persons or ancillary public health personnel to directly observe and assist with a patient's therapy wherever possible.

2.5.3 Pulmonary Tuberculosis

Treatment Schemes: The decision to recommend treatment for tuberculosis is a crucial decision to be made by a physician. Tuberculosis treatment requires faithful compliance to a program of regular medications and involves a small risk of serious drug reaction. Diagnosis by "therapeutic trial" with specific anti-tuberculosis drugs is a procedure generally to be avoided. Host factors such as age, sex, nutrition, and potential for drug toxicity are also important in the selection of an appropriate regimen of chemotherapy.

Treatment of Active Tuberculosis: A successful chemotherapy regimen for tuberculosis requires a combination of drugs for the following reasons:

- It is of crucial importance to the outcome of therapy to put a rapid stop to bacterial multiplication and ensure that drug sensitive bacilli are killed as soon as possible ("early kill"). This initial phase of treatment is especially critical in patients harboring a large bacterial population (smear positive sputum and/or cavitary disease). The recommended drugs for the initial phase are INH, RIF, and PZA.

- At the start of treatment, an appreciable number of drug resistant bacilli may be present. The drug regimen must include at least two drugs, preferably three or four to which all bacilli are likely to be sensitive (INH, RIF, PZA, and EMB). If there is any suspicion that a fair proportion of bacilli are resistant to a given drug, at least two additional drugs should be given. **The Centers for Disease Control and Prevention recommends a four drug regimen in areas with an initial INH resistance rate of 4% or greater. Louisiana has a primary INH resistance rate above this threshold.**

- In any population of tubercle bacilli, there are some bacilli whose growth has almost come to a standstill. These bacilli are called "dormant bacilli".

They may persist for weeks, months or years. When dormant bacilli become active and start multiplying, during therapy they are killed by bactericidal drugs (INH, RIF). If dormant bacilli revive and multiply after chemotherapy has been stopped, they may cause a relapse.

The inclusion of Pyrazinamide (PZA) during the initial 2 months of therapy is necessary if short course chemotherapy (six months) is planned. In addition, a fourth drug (either Ethambutol or Streptomycin) is recommended while sensitivities are pending. Patients who are compliant, and whose organisms are sensitive to **INH** and **RIF** should receive a total of 6 months of therapy. Longer periods of treatment are required for patients who have resistant organisms, who exhibit non-compliance, who are unable to tolerate one or more of the initial drugs, or who have not converted sputum culture at eight weeks.

- During the continuation phase of therapy the goal of successful chemotherapy is the sterilization of the remaining bacilli. INH and RIF is the most effective sterilizing regimen. The bacteriostatic drugs (*e.g.*, EMB) have a very low sterilizing potency.

Treatment Schedules: A six-month regimen of INH, RIF, and PZA is used for the treatment of active tuberculosis. If PZA is not tolerated, contraindicated, or sputum conversion has not occurred at eight weeks, then a chemotherapy regimen using INH and RIF for a **minimum of 9 months duration** is recommended. Non-compliance and drug resistance require longer periods of treatment.

- **Six Month Regimen:**

  Treatment should begin with INH-RIF-PZA-EMB daily. Drug susceptibility testing should be carried out because of the increased chance of initial drug resistance, especially to INH. ALL initial drugs should be continued until drug susceptibility studies confirm sensitivity to INH and RIF. If susceptibility tests show the organisms to be sensitive to INH and RIF, PZA should be continued for a total of two months. Discontinue EMB at this time.

  The Louisiana Standard of Care for the treatment of Tuberculosis is Directly Observed Therapy (DOT).

  If resistance is found, a revision of regimen is required. (See Recommendations for Drug Resistant Tuberculosis, Section 2.5.8). The Regional TB Program Manager must be notified if resistance is found.

- **Four Month Treatment of Smear and Culture-negative Pulmonary TB in Adults**

  A 4-month regimen, including INH, RIF, PZA, and EMB for the initial 2 months and INH and RIF for the continuation phase of 2 months, is an acceptable regimen for smear negative and culture-negative tuberculosis in the TB infected person when there is clinical or radiographic evidence of TB disease, no other etiology is identified, and improvement clinically and radiographically is noted.

2.5.4 Drugs Used for the Treatment of Tuberculosis

Isoniazid (INH), (Isonicotinic acid hydrazine)

INH is the most valuable and most widely used drug for the treatment of tuberculosis. INH kills the tuberculosis bacilli (bacteriocidal) and is indicated in all types and stages of tuberculosis. 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 (especially Asians) are rapid activators, which occasionally is a cause for treatment failure.

Toxicity: 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 are rarely seen.
  At the low doses currently used, the risk is practically zero except in persons with:
  - Renal insufficiency that may result in having higher blood levels of INH
  - Alcoholic neuritis
  - Malnutrition
  - Diabetes.

Simultaneous administration of pyridoxine (vitamin B_6) prevents the neurotoxic effects of INH. It is given orally at daily dose of 25mg to 50mg. It should be used whenever a reasonable risk of neurotoxicity exists. Pyridoxine supplements are not necessary in children under 11 years of age.

- **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 Amino-transferase (AST) up to 2.5 X Upper Limits of Normal (ULN), occurs in 10 to 20% of persons taking INH. OPH staff should refer to Appendix Section, pages A-6 and A-7. Private providers should refer to the two treatment statements in the bibliography. In some cases, toxic hepatitis will develop with signs or symptoms consistent with those of liver damage or other toxic effects *i.e.*:
  - Jaundice (icterus of eyes or skin)
  - Persistent dark urine (coffee or tea colored)
  - Nausea, vomiting, fatigue or weakness of greater than 3 days duration
  - 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 these cases 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. They should be monitored more closely than other patients.

INH may interact with other medications administered on a long term basis. INH may reduce excretion of some drugs (for instance Dilantin[7] and enhance their

effects, see Physician's Desk Reference).

Other rare adverse reactions ascribed to INH include:

- Hypersensitivity reactions
- Fever
- Skin eruption
- Hematologic reactions
- Metabolic reactions
- Paraesthesia of the hands and/or feet.

Precautions:

- Ask the patient 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 monthly assessment). Multiple drug therapy patients need not have periodic liver functions studies after an initial baseline test is done unless symptoms suggestive of liver toxicity occur. If symptoms of liver toxicity occur:
- Obtain liver function studies
- Advise to stop medication
- Notify Regional TB Program Manager immediately
- Refer to the attending physician immediately (refer to AST follow-up guidelines in appendix).

(See Core Curriculum 2004 for details)

Rifampin (RIF)

RIF is one of the most potent and useful anti-tuberculosis drugs available. RIF is bacteriocidal 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 diffuses well 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: 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.

- **Drug Interactions:**

  RIF increases the metabolism (breakdown) of other drugs:

- Oral contraceptive effectiveness is decreased. Women should be counseled 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 *i.e.,* quinidine, verapamil, mexiletine, theophylline; anticonvulsants, ketoconazole, and cyclosporin.

- **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. This is completely harmless except for its psychological impact.

- **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 recommended) the reaction can be stopped by giving the drug during a meal.

- **Respiratory syndrome:** Shortness of breath, rarely with collapse and shock, can occur. Respiratory syndrome is very uncommon. Caution is required when it occurs because shock may develop. Careful evaluation 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 or joint pains 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.

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 anticoagulant) if relevant. **Women taking oral contraceptives should be counseled to use barrier-type birth control methods during RIF therapy.**

- At least monthly, inquire about early symptoms of liver dysfunction, thrombocytopenia, hematuria or renal dysfunction, and flu-like syndrome.

- Obtain pretreatment liver function studies to include AST 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.

(See Core Curriculum 2004 for details)

- **In case of adverse reaction:**

- Hematologic crises, anuria, and/or respiratory crises: Stop Rifampin, do not

administer again.

- Other reactions: Try symptomatic treatment first. If symptoms persist and are troublesome, RIF should be discontinued and three other drugs to which there is sensitivity should be added. A regimen change will lengthen the recommended treatment time. Further consultation may be indicated.

PYRAZINAMIDE (PZA)

This drug 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 penetrates well into most tissues including CSF.

Toxicity: Side Effects

PZA is always given in combination with several other drugs. It is difficult to ascertain to what extent PZA contributes to the 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 arthralgia is about 7% in daily regimen and 3% in twice weekly regimens. 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. Patients should be cautioned against exposing their skin to sunshine since phototoxicity may occasionally cause a reddish-brown coloration of the exposed areas 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.

(See Core Curriculum 2004 for details)

ETHAMBUTOL (EMB)

Ethambutol activity on the tubercle bacilli is modest. It is widely used in the initial treatment of tuberculosis when resistant strains of tubercle bacilli are suspected. EMB is bacteriostatic.

Metabolism: Easily absorbed even with food.

Toxicity: Side Effects

Neuro-optic toxicity: About 1% of patients receiving Ethambutol (15mg/kg) experience a decrease in visual acuity. It is reversible if the drug is discontinued. Visual symptoms (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 change in vision immediately. The change may be unilateral or bilateral, so vision in each eye should be tested separately. High blood levels of Ethambutol due to renal deficiency may be responsible for toxic reactions.

Precautions:

Before starting treatment inquire about conditions that would contraindicate Ethambutol.

- 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 assure that variations in vision are not due to underlying disease 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 Ethambutol. Snellen eye charts are recommended for testing. If corrective glasses are used by the patient, they should be worn during visual acuity testing. Visual symptoms commonly precede a measurable decreased visual acuity. Patients should be informed to report any change in vision. If changes are reported, then visual acuity testing should be repeated. In testing visual acuity of persons not receiving Ethambutol there are definite fluctuations of one or two lines of the Snellen chart. In patients receiving EMB, if there is a change of two lines or more, retest and refer to the attending physician.

- Check gross red-green color perception before treatment and monthly thereafter. Ishihara Tables are inappropriate for this purpose. Red and green pieces of paper, yarn, or Mardi Gras beads are appropriate.

- 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 15 mg/kg there is no evidence that EMB is especially toxic for children.

(See Core Curriculum 2004 for details)

STREPTOMYCIN (SM)

Streptomycin was the first practical drug discovered for treatment of tuberculosis. Streptomycin is bacteriocidal in an alkaline environment.

Metabolism: Streptomycin 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 concentration in the cerebrospinal fluid except when the meninges are inflamed). Excretion is primarily through the kidneys.

Toxicity: Side Effects
Toxicity of streptomycin is a limiting factor for its prolonged use. Toxicity is dose-related and cumulative. Intermittent therapy is preferable to avoid sustained blood level. Toxicity is enhanced in patients with renal insufficiency with increased blood urea nitrogen (BUN) levels.

- Ototoxicity: The eighth cranial nerve (both auditory and vestibular branches) is especially susceptible. Onset of symptoms may be insidious. The symptoms of toxicity are:

- Vestibular branch: vertigo, unsteady gait, dizziness accompanied by nausea and vomiting.

- Auditory branch: hearing loss, roaring noises, sense of fullness in the ears,

tinnitus. These side effects are often irreversible.

- 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 undertaking Streptomycin treatment.

- Hypersensitivity to Streptomycin 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.

- Other adverse reactions have been reported and are uncommon such as fever, rash, numbness and tingling around the mouth.

- Both ototoxicity and nephrotoxicity are related to cumulative dose. A total dose of more than 120 grams should not be given unless other therapeutic options are not available.

Precautions:

Check regularly for vestibular symptoms. Some simple tests are:

- Make the patient walk and turn around suddenly.

- Make the patient walk tiptoe.

- Eye wiggle test for bedridden patients: pour cold water in one ear, close ear for 30 seconds, let it drain, watch for nystagmus (eyes wiggling).

- Prior to starting treatment an audiometric test is required. Then at the time of each injection, inquire about vestibular or auditory symptoms. If symptomatic withhold medication and obtain audiometric test immediately.

(See Core Curriculum 2004 for details)

Other Anti-tuberculosis Agents

Additional drugs are used only in selected patients, such as those whose organisms have multiple-drug resistance. Their recommended dosages and common side effects can be found in the appendix.

2.5.5 Extrapulmonary Tuberculosis

As a general rule, regimens that are adequate for the treatment of pulmonary tuberculosis in adults and children will also be effective in extrapulmonary disease. Surgery may be necessary to obtain diagnostic specimens. Miliary TB, TB meningitis, and bone and joint tuberculosis, may require longer therapy (12 months), especially in infants and children.

The addition of corticosteroids is recommended by some authorities for treatment of meningeal tuberculosis. In patients with extrapulmonary TB, obtaining specimens for bacteriologic follow-up may not be feasible. Response to treatment often must be judged based on the clinical and radiographic findings.

2.5.6 Tuberculosis During Pregnancy and Lactation

Untreated TB represents a far greater hazard to a pregnant woman and her fetus than does the treatment of the disease. In a pregnant woman with TB, it is essential that effective treatment be given as soon as possible. Congenital TB, although extremely unusual, can occur in an infant born to a woman with untreated TB during pregnancy, particularly when the woman has very extensive disease or TB of the uterus.

In pregnant women it is essential that effective therapy be given. Begin with INH and RIF with the addition of Ethambutol (EMB) if resistance is suspected. **The addition of PZA is contraindicated in pregnancy.** Information on the teratogenic effects of PZA is not available. Pyridoxine (vitamin B_6) is recommended for pregnant women taking INH.

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 may be used. In that case, the infant should be evaluated for possible side effects (damages to the 8th cranial nerve). Ethionamide and cycloserine should be avoided pending further information.

Standard regimens using first and second-line drugs have not been proven to have teratogenic effects on the human fetus; therefore, their use does not justify therapeutic abortion.

TB cases should receive treatment during lactation. Several TB drugs pass into the breast milk, but have not been proven to be toxic to the infant. Conversely, drugs in breast milk should not be considered as adequate therapy for disease in the nursing infant. Close follow-up for the mother and infant is necessary.

In order to minimize unnecessary X-ray exposure, the following policy should be followed for pregnant women:

- Routine chest X-ray for the screening of tuberculosis among pregnant women should not be done. Instead, a **Mantoux PPD tuberculin skin test should be performed** if a history of tuberculosis exposure is suspected.

- Pregnant women with tuberculosis infection or suspicion of active tuberculosis disease should be X-rayed immediately at any time during

pregnancy using a lead shield.

2.5.7 Tuberculosis in Children and Adolescents

Indications for anti-tuberculosis treatment in children and adolescents include the following:

- A diagnosis of disease anywhere in the body, even if only provisional (since children can develop lethal forms of tuberculosis very quickly)

- Immunosuppression or immuno-depression (steroid therapy, antileukemic therapy, HIV infection, *etc.*) in a child with tuberculosis infection.

Children may develop active tuberculosis at more than one site 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, including progressive lethargy.

The current recommended treatment for infants, children, and adolescents with tuberculosis disease is patterned after carefully studied regimens in adults with pulmonary tuberculosis. Whenever possible, information should be obtained from the drug susceptibility studies from the infectious source case. Disease, clinical and/or radiologic, should be treated with INH and Rifampin for 6 months, with Pyrazinamide for the first two months, if drug resistance has been ruled out. Certain types of disseminated disease, specifically bone and joint disease, miliary disease, and meningitis, should be treated for a minimum of 12 months. If the infectious source case appears likely to have resistant organisms, then it is wise to add a fourth drug (streptomycin or ethambutol) to the child's regimen. Once the susceptibility pattern of the organisms of the source case is established, then the child's regimen can be appropriately adjusted. Ethambutol should be used cautiously in children too young to identify colors, since red/green color vision changes are the earliest sign of visual damage from Ethambutol. If Ethambutol must be used, the minimum dose should be selected. **All children suspected of having active tuberculosis should be treated with Directly Observed Therapy as follows:**

- The daily dosage of anti-tuberculosis drugs can be given all at one time. Tablets should be well crushed in a large spoon, the contents of capsules added, mixed with "something good" (mashed banana, applesauce, ice cream, sugar syrup, grits, *etc.*).

- Give directly from the spoon.

- **Never** put drugs in a drinking glass or formula bottle.

- Assure that all medication is ingested.

NOTE: It is possible for some medication to adhere to the container. If necessary rinse container with a small amount of water and have the child ingest this also. The syrups of INH and Rifampin are not stable and are not recommended. Twice weekly dosages are effective and can be utilized in patients after two or three weeks of daily drugs.

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

The second-line drugs are sometimes needed. For example, if the child has been

infected with tubercle bacilli resistant to both INH and Rifampin, Ethionamide can be added to a regimen of PZA and EMB or SM. Ethionamide, related to INH, is used in the same dosage, and usually well tolerated by children despite its unpleasant taste.

If no identified adult source is found and drug resistance is a clear possibility, gastric aspirate may be used to aid in the recovery of the TB organism for culture. Gastric aspirate can be performed in a hospital. Properly done gastric aspirates can provide a positive culture in 40-60% of cases.

Toxic effects of the anti-tuberculosis drugs are rare in children. Liver function tests are not recommended in children because toxic complications are so rare. Repeated blood tests adversely effect compliance. Follow-up should be monthly. The weight is by far the most useful measure of the child's progress. Steady weight loss means:

- Progress of the disease due to drug resistance
- Non-compliance on the part of the parent/guardian or child
- Failure to assure that the child ingests the total prescribed dosage
- Drug toxicity.

While the officially recommended duration of treatment is 6 months, it is sometimes necessary to prolong treatment if compliance is questionable. Repeated chest X-rays are indicated if the initial film was abnormal. Treatment should not be prolonged solely on the basis of an abnormal X-ray, since some abnormalities may take 2-3 years to finally resolve after successful treatment. Some scarring may remain permanently in those with extensive disease.

Further information concerning the treatment of a newborn whose mother has active tuberculosis can be found in the current ATS treatment statement located in the Appendix Section.

2.5.8 Recommendations for Drug-Resistant Tuberculosis

The basic principle of managing patients whose organisms are resistant is the administration of at least two, or preferably three, drugs to which there is demonstrated susceptibility. If the organism is susceptible to both INH and RIF, a first line regimen is usually successful. In the case of resistance to either INH or RIF, a combination of other effective drugs must be used. The selection is based on in-vitro susceptibility pattern of the bacteria and the potential for toxicity for any given patient. If drug resistance is suspected, but not confirmed, at least two new drugs with which the organism has not previously been treated should be added until susceptibility results are available. **Never add a single drug to a failing regimen.** In the presence of documented resistance to INH, a regimen of RIF, EMB, and PZA for 6 months can be used, or RIF and EMB can be used for 12 months. In the presence of documented resistance to RIF, three or four drugs to which the organisms are susceptible should be given for 18 months or 12 months after conversion of sputum to negative culture at a minimum. In the presence of drug resistance, decisions on drug combinations and duration of chemotherapy should be made on a case-by- case basis. The Regional TB Program Manager must be notified if resistance is found.

2.5.9 Treatment of Tuberculosis in HIV/AIDS and Other Associated

Disorders

- **Treatment of Tuberculosis in Patients with AIDS or HIV Infection**

Patients with Acquired Immunodeficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV) infection are at high-risk for tuberculosis. All HIV infected patients should be tested for tuberculosis as part of their medical care for HIV. All new TB patients 13 years of age and older should be tested for HIV. Anti-TB therapy should be started whenever acid-fast bacilli are seen in specimens from the respiratory tract of a person with AIDS, HIV-infection, or those at high risk for HIV-infection.

Tuberculosis patients with HIV infection are at high risk of developing drug resistance. Therefore, therapy should include INH and RIF, with an initial two months of PZA. Include EMB or Streptomycin until drug susceptibility tests are available. Continue treatment with INH and RIF for at least 6 months after conversion to negative sputum. In treating patients with HIV infection, it is critically important to assess clinical and bacteriologic response. Treatment should be prolonged if the response is slow or otherwise suboptimal. **Directly Observed Therapy for this group is essential.** Close coordination with the HIV medical provider is imperative to address treatment issues. (Protease Inhibitors etc.)

- **Treatment of Tuberculosis with Other Associated Disorders**

  Tuberculosis commonly occurs in association with other diseases. Medical conditions which predispose individuals to tuberculosis include malignancies, immunosuppressive therapy, chronic renal failure, malnutrition, and alcoholism. Therapeutic decisions for the impaired host must be individualized. In patients with impaired renal function, Streptomycin, Kanamycin, or Capreomycin should be avoided. If given, reduced doses should be calculated. The potentially hepatotoxic anti-TB drugs (INH, PZA, RIF) are not contraindicated in patients with liver disease but such patients should have close monitoring of liver function. Patients with neuropsychiatric disorders must receive DOT.

2.5.10 Recurrent Tuberculosis

Patients with recurrent disease should be evaluated to identify the probable cause. Such patients are at risk of having organisms resistant to previously used drugs. Treatment should follow these principles:

- Best results are obtained with a 3-4 drug regimen, usually two oral drugs plus one parenteral drug.

- Continue use of parenteral drug for 4 to 6 months after sputum becomes negative.

- The oral drugs in order of effectiveness are:
  - INH, RIF
  - PZA
  - EMB, Cycloserine, PAS.

- If less effective drugs are used (EMB, Cycloserine, PAS) combine at least two of them to attempt to obtain effectiveness of one first line drug.

- Organisms in patients treated initially with INH and RIF usually remain susceptible if relapse occurs. Thus, management of these patients generally consists of re-institution of a regimen

including INH and RIF. Drug susceptibility testing should be performed and the regimen modified if resistance is detected. **Directly observed therapy must be used in patients with recurrent disease!** Patients who relapse after taking regimens that did not contain both isoniazid and rifampin should be assumed, until proven otherwise, to have organisms that are resistant to the agents previously used.

2.5.11 Monitoring Response to Treatment

For patients who are sputum smear positive before treatment, three weekly sputum specimens should be obtained until the criteria of non-infectiousness is satisfied, including three consecutive negative smears. Thereafter specimens should be obtained monthly until the completion of therapy.

Patients whose sputum has not converted after 2 to 3 months of treatment 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 continued or may be augmented by at least 2 drugs not given previously (one of which should be an injectable). The regimen should be adjusted in accordance with results of the susceptibility tests. **Patients should be treated using Directly Observed Therapy whenever possible.** Drug absorption levels should be performed.

2.5.12 Treatment of Latent Tuberculosis Infection

Every person with significant exposure and every positive tuberculin reactor is at risk of developing tuberculous disease. Each will benefit from treatment of latent tuberculosis infection, since the risk of developing disease is lifelong. Treatment of latent tuberculosis infection is utilized to reduce the risk that TB infection will progress to disease. Certain groups should be considered candidates for treatment of latent tuberculosis infection. Certain risk factors must be given priority for treatment of latent tuberculosis infection, regardless of age. The current recommendation of a six-month regimen of INH treatment for LTBI is the most cost effective regimen. For children through adolescence, pregnant women, and HIV positive persons, 9 months of INH is recommended. If a patient is a known contact to drug-resistant organisms, therapy should be altered accordingly (Consult the Regional DIS Supervisor). Patients should be assessed monthly (or more frequently, if necessary) for adverse reactions. Monthly assessments also provide more information of the patient's adherence to the prescribed regimen. The beneficial effect of INH in persons with a positive tuberculin skin test persists for up to twenty years, and presumably for life.

2.5.13 Candidates for Treatment of Latent Tuberculosis Infection

- **Treatment of Tuberculosis Exposure Without Infection:**

  Persons who are close contacts may have been infected but have not yet developed a positive PPD skin test since not enough time has elapsed for the tuberculin test to convert to more than 5mm. Close contacts with an initial tuberculin reaction of <5mm should receive a chest radiograph and should be considered for treatment of latent tuberculosis infection in any of the following situations:

- Circumstances suggest a 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 an adolescent, or the contact is immunosuppressed (*e.g.,* HIV infected).These individuals should receive INH (daily self-administered or twice weekly Directly Observed Therapy [DOT]) for at least 8 weeks after documented smear conversion of the source case or contact with the source case has been broken. At the end of this period, the PPD test should then be repeated. If <5mm, prophylaxis should be stopped. If ≥5mm, the patient should continue the appropriate preventive regimen.

- **Treatment of Latent Tuberculosis Infection Without Disease:**

  Persons in the following high-risk groups should be given high priority for treatment of latent tuberculosis infection if they have positive skin test results, **regardless of their age** (the criterion for a positive reaction, in millimeters of induration, is given in parentheses):

  - Persons known to have or suspected of having HIV infection, including persons who inject drugs and whose HIV status in unknown (≥5mm).

  - Close contacts of a person with infectious TB (≥5mm). The risk of developing TB is approximately 5% the first 2 years after infection, and an additional 5% over lifetime.

  - Persons who have chest radiograph findings suggestive of previous TB and who have received inadequate or no treatment (≥5mm). The rate of reactivation ranges from 1-4.5% per year in this group.

  - Persons who inject drugs and who are known to be HIV negative (≥10mm).

  - Persons with certain medical conditions which increase the risk of developing TB infection (≥10mm).

  - Persons whose tuberculin skin test reactions have converted from negative to positive within the past 2 years (≥10mm increase).

  In addition, in the absence of any of the preceding risk factors, persons in the following high-prevalence groups should be evaluated for treatment of latent tuberculosis infection if their reaction to the tuberculin skin test is ≥10mm:

  - Foreign-born persons from areas of the world where TB is common (*e.g.*, Asia, Africa and Latin America)

- Medically underserved, low-income populations, including high-risk racial and ethnic groups
- Residents of long-term care facilities (*e.g.,* correctional facilities and nursing homes)
- Children younger than 4 years of age
- Other groups identified locally as having an increased prevalence of TB (*e.g.,* migrant farm-workers or homeless persons).

Persons with no known risk factors for TB should be evaluated for treatment of latent tuberculosis infection if their reaction to the tuberculin test is ≥15mm. This group should be given a lower priority for prevention efforts than the groups already listed.

Isoniazid treatment of latent tuberculosis infection is recommended for infected persons at high-risk of developing TB disease.

Before Starting Treatment of Latent Tuberculosis Infection:

- Rule out progressive tuberculosis disease
- Rule out a previous history of adequate treatment of latent tuberculosis infection
- Rule out contraindications:
  - Previous treatment of latent tuberculosis infection related hepatotoxicity
  - Severe adverse reaction to treatment of latent tuberculosis infection
  - Acute liver disease
- Identify patients who may require special attention:
  - Patient on any long-term treatment
  - Patient on Dilantin
  - Alcoholics
  - Chronic liver disease
  - Pregnancy

The risk of complications occurring in these groups is not increased. However, if toxicity occurs, the severity of complications may be greater.

Standard Regimens: Treatment of infection can prevent TB from progressing from infection to disease. Extensive trials have shown a consistent reduction in TB morbidity when treatment of latent tuberculosis infection is provided to high-risk groups. Every effort should be made to ensure that patients adhere to treatment of latent tuberculosis infection for at least 6 consecutive months. For treatment of latent tuberculosis infection Isoniazid is normally used alone in a single daily dose of 300mg for adults and 10-20mg/kg body-weight in children, not to exceed 300mg per dose. The length of therapy is at least 6 months for adults, and 9 months for children. Nine months of therapy should be utilized for the following groups:

- Patients with abnormal radiographs (*i.e.,* stable parenchymal lesions, calcifications)
- Patients with AIDS, antibodies to HIV, or at high risk for HIV infection
- Patients receiving prolonged adrenocorticosteroid or

immunosuppressive therapy

- Patients with silicosis, diabetes mellitus, or end stage renal disease
- Injection drug users known to be HIV-seronegative
- Patients with hematologic and reticuloendothelial diseases, such as leukemia or Hodgkin's disease.

It should be noted that for children <15 years of age and HIV infected individuals who are at especially high risk for TB, DOT should be considered. INH can be given twice weekly (DOT) at a dosage of 15mg/kg for adults and 20-40mg/kg for children. Intermittent INH treatment of latent tuberculosis infection is an effective form of therapy.

Treatment of Latent Tuberculosis Infection Follow-up: Once the decision has been made by the physician to place a person on LTBI treatment, the following must be assured:

- Evaluation of patient compliance to determine the need for initiation of DOT
- Motivation and help in developing a system of reminders for taking the drugs daily
- Issuance of monthly drug supply
- Counseling regarding continuity of LTBI treatment and the risk of developing tuberculosis in the future
- Monthly nurse assessment to monitor for drug side effects, compliance, etc.

Side Effect Monitoring: Monitoring for drug side effects consists of careful questioning for the following:

- Hepatotoxicity:
  - Nausea, vomiting, or unexplained anorexia of greater than 3 days duration
  - Fatigue or weakness of greater than 3 days duration
  - Persistent dark urine (coffee or tea color) or jaundice (icterus eyes and/or skin).
- Other signs and symptoms:
  - Rash or pruritus
  - Elevated temperature of greater than 101° for 3 days duration without explanation
  - Symptoms of neurotoxicity such as persistent paresthesia of the hands and feet
  - Nausea or vomiting unrelated to hepatotoxicity.

The patient should be advised that immediately on development of any such signs or symptoms during treatment of latent tuberculosis infection, he should discontinue the drug and report to the public health nurse.

A standardized form (TB-27) is used by the nurse for accessing patients at each visit. It helps insure alertness to all signs and symptoms, expedite the interview process, and provide standard data collection.

At completion of treatment of latent tuberculosis infection the patient should be educated about the risk of developing tuberculosis in the future. No further medical follow-up is necessary unless the patient develops symptoms of tuberculosis. Please advise the patient that further skin

testing is unnecessary and that yearly chest X-rays are not indicated. If symptoms occur, an evaluation including chest X-ray should be obtained.

- **Treatment of Contacts to Known INH-Resistant Cases**

Contacts who are known to be exposed to cases with INH-resistant disease may be treated with daily RIF. The dosage for RIF is 600mg for adults and 10-20mg/kg for children. If the initial skin test is less than 5mm, begin RIF and repeat the skin test 8 weeks after the index case converts to negative sputum smear or contact is broken. If the repeat skin test remains under 5mm, discontinue RIF treatment of latent tuberculosis infection (LTBI). If the repeat skin test is ≥5mm, continue RIF for a total of 6 to 9 months. DOT should be used for this regimen.

- **Pediatric Treatment of Latent Tuberculosis Infection**

Treatment with one drug alone, namely INH, is reserved for treatment of latent tuberculosis infection:

- In the child with a positive Mantoux but no manifestation of disease, either clinical or radiologic
- In the tuberculin negative child with no clinical or radiographic evidence of disease who has been recently or currently exposed to a sputum smear positive source case.

All children recently exposed to any sputum smear positive suspect or case should be preventively treated regardless of skin test interpretation. Exposure of a newborn to an adult with active tuberculosis living in the household may be inevitable. If so, the infant should be started on daily INH, which has been found to be remarkably effective under these circumstances. This primary prevention should be continued for 8 weeks beyond documented sputum conversion of the adult, or after the adult has left the household (see Candidates for Treatment of Latent Tuberculosis Infection, as found earlier in this section).

BCG is of limited usefulness in the United States. However, it should be considered for children from a family with a history of INH and Rifampin resistant organisms. Its use may prevent the serious forms of disease, *i.e.,* miliary and meningeal tuberculosis.

- **Pregnancy and Treatment of Latent Tuberculosis Infection**

INH LTBI Treatment: 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 or infected with HIV and tuberculosis; in this situation, INH treatment of latent tuberculosis should begin when the infection is documented, but after the first trimester. Pregnant women receiving INH should receive B_6.

The increased risk of tuberculosis for the woman is during the postpartum period, not during pregnancy. INH LTBI treatment for routine reactors should be started after delivery. Persons infected with no disease may be placed on INH LTBI treatment during lactation without detriment to the infant's health, however, B_6 supplement should be given to the infant. It is important to continue the LTBI treatment postpartally because the mother is at high risk of developing tuberculosis disease. The amount of INH in the breast milk is inadequate to treat the infant.

If a woman on INH LTBI treatment should become pregnant, reassure the patient about the safety of INH and refer to a physician for final decision. Physicians may delay INH treatment for LTBI until after delivery unless the patient is at high risk for developing active disease *e.g.,* HIV positive or recent conversion. After delivery, the patient should be evaluated and started on treatment of latent tuberculosis infection.

Routine chest X-ray for the screening of tuberculosis among pregnant women should not be done. Instead, **a Mantoux PPD tuberculin skin test should be performed if a history of tuberculosis exposure is suspected.**

2.5.14 Anti-tuberculosis Drug Distribution

- **Policy**

Drugs for LTBI treatment and treatment of tuberculosis disease are available at no cost to patients who are residents of Louisiana. 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 DHH/OPH Pharmacy Services in New Orleans.

- **New Prescriptions**

Upon receipt of prescriptions for anti-tuberculosis medication(s) at the local health unit, personnel will retrieve, check and update the patient's record, or initiate a new record if necessary. Personnel should always check for an existing record prior to opening a new chart. Use an existing medical record number when one has already been established.

Health Unit personnel are requested to check prescriptions for legibility, completeness, and accuracy, especially with regard to patient's name and physician's name (please print or type any name that is written illegibly, this will speed processing and reduce the chance for errors). Where no authorized refills are noted on the new prescription, no medication can be dispensed subsequent to the initial filling. Health Unit personnel should confirm refills if none are indicated. Problems or discrepancies should be resolved through DHH/OPH personnel, pharmacist, and physician contact.

Note: When submitting new prescriptions for anti-tuberculosis medication(s) please indicate the patient's weight at the top right corner of the all prescriptions.

- **Refills:** Physicians may order up to eleven (11) monthly refills of the original 30 day supply.

- **Prescription Quantities**: The large number of patients served and prescriptions filled under this program makes it necessary to standardize dispensing procedures. Therefore, the quantity of medication dispensed on each prescription for each patient is limited to a 30-day supply, with refills issued on a monthly basis. Orders should be written for the quantity sufficient for thirty days. In those cases where the quantity indicated on the original prescription exceeds a month's supply, the pharmacist will adjust the prescription to indicate a 30-day supply plus a number of refills equating to the total original quantity prescribed by the doctor, up to a

maximum of a one-year supply.

The 30-day medication limitation serves the additional purpose of having the patient return to the health unit once a month for assessment and refills. **This affords a mutual opportunity for the patient to report any adverse effects experienced with medications, and for the public health nurse to check on the course of treatment. For this reason it is imperative for patients to pick up their own medications.**

- **Form PH-104**

The PH-104 is a form that provides the required pharmacy data on the patient. Identification, allergies, and other medical information are documented on the front side , and the reverse side of the card serves as the prescription receipt.

The patient's PASPORT label may be affixed to the front side of the PH-104 or all identification data must be printed by DHH/OPH personnel. The patient signs on the appropriate line at the bottom of the back side of the form upon receiving medications. The person delivering the medication(s) should initial the card and enter the patient's next appointment date on the appropriate lines. The public health nurse should review the medication/allergy information at every monthly nursing assessment visit.

Any change in prescription status should be indicated. If a prescription is not to be refilled because of discontinuation or change in order, please indicate this on the receipt card before returning it to the pharmacy. **All prescriptions and PH-104 cards should be mailed to the pharmacy on a daily basis**. Prescriptions and receipt cards should not be accumulated from day to day as this will cause delays and backlogs in the pharmacy. Use a 28 day cycle for appointments.

- **Form PH-127**

The PH-127 is the prescription form used by public health physicians (usually in Tuberculosis Medical Clinics). Private physicians may use their own prescription forms or hospital or clinic prescription form. All identification information or patient's PASPORT label must be on every prescription. Each prescription must include the physician's name and the health unit pharmacy code. If the physician's signature is not legible, the physician's name should be printed underneath signature line.

- **Prescriptions Originating in Tuberculosis Medical Clinics**

Prescriptions written for a patient who is being treated in a Tuberculosis Medical Clinic should be sent to the pharmacy following the same procedure outlined under new prescriptions (see above).

Since these medications may be picked-up by the patient at the parish health unit, be sure to indicate where the filled prescription is to be sent by entering the pharmacy code of the health unit, at the top of the PH-127 (prescription form). A list of all health units and their unique pharmacy code is available on request from the pharmacy.

- **Medication "Starter Supplies" in Tuberculosis Medical Clinics**

Tuberculosis Medical Clinics are stocked with a "starter supply" of anti- tuberculosis medications which the physician may dispense to a patient during clinic. Refills will be sent to the patient's health unit by the DHH/OPH Pharmacy in New Orleans.

These "starter supplies" may be obtained from the pharmacy by submitting a signed prescription to the pharmacy without a patient's name. Several bottles of a given drug and dosage may be ordered on a single prescription blank.

"Starter supplies" are labeled with incomplete prescription labels that must be completed by the physician before being dispensed to the patient. To complete the label the physician must add his or her own name, the patient's name, and the date.

The prescription number(Barcode) from the label(s) must also be recorded in the patient's medical record at the time it is dispensed.

DHH/OPH personnel should initiate appropriate action where exceptional patient needs exist. Prescriptions and PH-104s for initial anti-tuberculosis medications for new cases/suspects or immediate changes in prescriptions for cases may be faxed to the pharmacy. Faxing is for priority cases/suspects who will be without medications. The prescription and PH-104 must be completed as previously noted under 2.5.14 New Prescriptions.

On receipt of faxed prescription and PH-104, the pharmacy will fill and expedite the prescription based on this information. The original prescription must be mailed immediately to the pharmacy with the original PH-104 and must be marked that it is confirmation of faxed information. Please indicate on all documents that it is a confirmation to avoid duplication or confusion. The prescription and PH-104 should be placed in a stamped envelope addressed to: DHH/OPH, 325 Loyola Ave. (Room 404), New Orleans, LA 70112 and mailed the same day. Original prescriptions and PH-104s are kept on file in the pharmacy.

- **Failure of Patient to Pick up Medication**

If medications are not called for or picked up by the patient within 45 days after the patient's appointment date, a notation to that effect should be made on the receipt card, and the medication, with the card attached, returned to the pharmacy. The reason for the return should always be noted on the receipt card. Medications should not be returned to the pharmacy without an explanation.

If a patient comes to the clinic within 45 days after prescriptions have been returned to the pharmacy (within 90 days after the missed appointment), the nurse may restart therapy by calling or writing the pharmacy and requesting that the prescriptions be refilled. Be sure to have the prescription numbers for reference. If a patient is delinquent more than 90 days after the appointment date a new prescription will be necessary.

3. INFECTION CONTROL

3.1 Definition of Infectiousness and Non-infectiousness

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 infectiousness is directly related to the number of tubercle bacilli expelled into the air. In general, a person would be considered infectious if he meets one of the following criteria:

- Coughing
- Undergoing cough-inducing procedures

- Positive AFB on sputum smears

And is

- Not on therapy
- Just started therapy
- Or has poor clinical or bacteriological responses to therapy.

Patients who have or who are suspected of having TB are not considered infectious if they meet **all** the following criteria:

- They have received adequate therapy for 2-3 weeks.
- They have a favorable clinical response to therapy.
- They have three consecutive negative sputum smear results from sputum collected on different days.

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

Sputum smear examinations should be done weekly during therapy to monitor for recurrence of tuberculosis or the development of drug resistance until three consecutive negative sputum smears are documented. Sputum should be collected monthly thereafter unless clinical condition worsens. Until sputum conversion is documented, the patient should remain at home to avoid any unnecessary public contact. Patients are allowed contact with household members and direct travel to and from TB medical appointments In patients with MDR-TB, infectiousness may last for months. These patients are more likely to experience treatment failure or relapse. If this occurs, hospitalization may be required since infectiousness may be prolonged. Response to therapy should be closely monitored.

3.2 Hierarchy of Controls

An effective TB infection control program requires the early detection, isolation, and treatment of persons with infectious TB. 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.

3.3 Administrative Control Measures

3.3.1 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 the infectiousness of a suspect, a microscopic examination of sputum for the presence of acid-fast bacilli must be performed. Review the results of other tests (X-ray, skin test, and bronchoscopy) as they are performed for diagnostic purposes and correlate this information to determine the potential for transmission of tuberculosis. Patient history should be reviewed to determine previous

disease, exposure to tuberculosis, skin test reaction and drug treatment. If tuberculosis is suspected in light of history and radiologic findings, consider the patient a potential transmitter and provide appropriate infection control measures. **The early initiation of an effective regimen of TB therapy is the best means of preventing contamination of the air. Therefore, TB therapy should be initiated at the time a presumptive diagnosis is made, rather than waiting for final culture identification.**

3.3.2 Non-infectious Tuberculosis Patients

Non-infectious pulmonary or laryngeal TB patients are persons on chemotherapy whose symptoms and laboratory reports indicate sputum has converted from positive to negative. If a patient is in the hospital because of other conditions, it is important to maintain the following:

- The patient's chemotherapy should be continued.
- The patient's sputum should be continued to be monitored by weekly microscopic examinations and follow-up cultures.
- The patient should not be restricted to the room or required to wear a mask.
- The patient who has had a history of completed treatment for tuberculosis may be considered a non-transmitter and no immediate precautionary measures are required, unless symptoms suggestive of tuberculosis are present. Then sputa should be collected. A new chest X-ray should be obtained and compared with previous films if available. Previous completion of treatment should be documented if possible.

3.3.3 Patient Education

Patients should be educated about the transmission of TB, the reasons for isolation, and the importance of remaining isolated from the population. 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. The patient should be instructed that TB is spread through the air rather than by fomites. The patient should be instructed to cover his mouth and nose with disposable tissues when coughing, raising sputum, or sneezing. If there is an unwillingness or inability to cover the cough, the patient should wear a surgical mask. All tissues and masks should be placed in bags for sanitary disposal. Follow universal precautions and procedures for waste disposal. **Tuberculosis is transmitted by airborne droplet nuclei not by fomites.** Sterilization of personal items or eating utensils is not necessary.

3.3.4 Non-emergency Surgery

For non-emergency surgery it is advisable to wait until the patient is responding to chemotherapy. 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 require no unusual routine.

3.3.5 Discharge Planning

Persons who are suspected of having TB may be eventually discharged to their home after therapy has been initiated. In some cases, the patient may still be deemed infectious. However, if therapy is adequate, the patient is less likely to transmit the

disease to members of his household. The health care facility should work closely with the Regional TB Program Manager to coordinate the best possible discharge plan for the patient.

3.3.6 Health Care Worker (HCW) Education

All health care workers should be educated about the basic concepts of TB. This includes transmission, pathogenesis, signs and symptoms, treatment of infection and disease, and infection control procedures. HCW's should understand the importance of participating in yearly skin testing programs that may be offered at their health care facility.

3.3.7 Hospital Employee Screening

- New employees prior to or at the time of employment are required to have a Mantoux PPD tuberculin skin test. The booster technique (2-step) should be used if the new employee can not provide documentation of PPD testing within the past year. A previous positive PPD must be documented (date and millimeters) in order to excuse the employee from further testing. Annual chest X-rays are not recommended for employees with previous documented positive PPD's.

- Employees with negative skin tests are required to have annual Mantoux PPD skin tests.

- Employees with positive skin tests will have chest X-rays and medical evaluations to determine the need for tuberculosis prophylaxis or case therapy.

3.3.8 Infection Control Program

It will be the responsibility of the Infection Control Program of Health Care Facilities:

- To establish an employee tuberculin skin testing program

- To establish a presumptive/positive tuberculosis isolation routine

- To provide an in-service education program for professionals and allied health personnel outlining the modern management of tuberculosis.

3.4 Environmental Control Measures

3.4.1 Prevention of Transmission

Airborne infections such as tuberculosis can be prevented by killing the infectious microorganisms in the air. The concentrations of *Mycobacterium tuberculosis* in a room can be controlled with mechanical ventilation and/or ultraviolet irradiation. Both methods are effective for reducing the risk of transmission of tuberculosis. They may be used separately or in combination. Environmental controls will not replace conventional interventions such as prompt detection and treatment of cases, and tracing of contacts.

3.4.2 Air Control Demands

- Air Control is necessary in:
    - Rooms of known or suspected transmitters
    - Intensive care units
    - Emergency rooms
    - X-ray units
    - Respiratory therapy units and/or any unit performing aerosolized pentamidine treatment for immuno-compromised patients.

Mechanical ventilation is the preferred method of air control.

- Air Control Considerations:
    - Patients should have fresh air introduced through a central or window unit.
    - Patient's room should have air exhausted to the outside through an individual room exhaust or central exhaust system. Air should not move out of the patient's room into a hallway or return to a central air conditioning or heating system (recirculating).
    - An exhaust system should move air out of the room at an appropriate rate of air changes per hour (ACH). This must be calculated for each room. Air control consultation is available through the Tuberculosis Control Section.
    - Any room with proper air control can be used for tuberculosis patients. Air control rooms do not have to be set aside for exclusive use by tuberculosis patients.

3.4.3 Engineering Controls

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 the 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 rooms smaller than 200 cubic feet, exhaust

ventilation is preferred to ultraviolet irradiation for decontamination.

- Air flow should be from the room to the outdoors with the outlet at least 25 feet away from any air intakes. Air should move from adjacent rooms and/or hallways through the contaminated room to the outdoors. Respiratory isolation rooms in existing buildings built before 2001 should have an ACH of and $\geq$6. The Centers for Disease Control and Prevention recommends $\geq$12 ACH in all buildings constructed or renovated since 2001. Adjusting or modifying the ventilation system in buildings older than 2001 with ACH less than 12 is recommended. Twenty ACH are recommended for high-risk areas where sputum induction or aerosolized pentamidine treatments are performed.

- The formula for calculating the cubic feet per minute (CFM) fan capacity necessary for proper ventilation is as follows:

  $$\frac{\text{(room volume) x (\# of ACH)}}{\text{60 min/hour}} = \text{CFM}$$

  For example, a room 20 ft by 10 ft with 9 ft ceilings would need 180 CFM exhausted to the outside in order to provide 6 ACH.

  $$\frac{\text{(20' x 10' x 9') x (6 ACH)}}{\text{60 min/hour}} = 180 \text{ CFM}$$

  To check whether airflow is adequate to produce negative pressure, stand in the doorway with a smoke producing device. Smoke should move into the room and not into the hallway. This should be checked twice a year, in summer and winter.

- HEPA filtration:

  HEPA filters can be used in a number of ways to reduce or eliminate infectious room air or exhaust. These methods include placement of HEPA filters in:

  - Exhaust ducts
  - Fixed recirculation air systems
  - Portable air cleaners

  Follow manufactures installation and cleaning instructions. (See Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health Care Facilities, 1994)

- Ultraviolet Irradiation:

  Ultraviolet irradiation (UV) is an acceptable means of decontaminating 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:

  - shelters for the homeless
  - correctional institutions
  - nursing homes
  - waiting rooms in
    - hospitals
    - TB clinics
    - AIDS clinics.

Ultraviolet lamps must be maintained to function properly. The tubes and the trough of the fixtures 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.

- The formula for calculating fixture size is as follows:

  200 ft^2 of floor area = 30 watts ceiling or wall fixture.

- To reduce UV exposure in occupied portions of a room, install baffles to prevent people from looking directly at the tubes. If necessary, use paints containing titanium dioxide (TiO_2) to reduce reflection from ceilings and walls.

3.5 Personal Infection Control Measures

3.5.1 Personal Respirators

In some circumstances, administrative and engineering methods may not be totally effective in the protection of HCW's from infectious TB. HCW's 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 after procedures that involve sputum collection and induction, bronchoscopy , and aerosolized pentamidine treatments by persons at risk for TB. Personnel performing these procedures should wear personal respirators (N-95 or above).

3.5.2 General Specifications

- **Gowns: Not necessary for personnel treating patient. Approved masks should be used during cough producing procedures.**
- **Hands:** Should be washed on entering and leaving room, and as otherwise indicated during patient care.
- **Gloves:** Not necessary.
- **Needles and syringes:** Universal precautions for blood borne pathogens, as for non-tuberculosis patients.
- **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 treated as potentially infectious waste.
- **Urine and feces:** Usual precautions as for non-tuberculosis patients.
- **Universal Precautions Should Be Followed on All Patients Regardless of Diagnosis.** (Refer to the SANITARY CODE STATE OF LOUISIANA and to Centers for Disease Control, Morbidity and Mortality Weekly Report, "Guidelines for Preventing the Transmission of Tuberculosis in Health-Care Settings", December 2005, Vol. 54, No. RR-17).

4. SURVEILLANCE

4.1 Definition of Surveillance

Chapter 2, "THE CONTROL OF DISEASES," of the SANITARY CODE STATE OF LOUISIANA section 2:003 requires reporting of all new tuberculosis cases and suspected cases of tuberculosis. Cases should be reported promptly to the health department by any physician or any other health care professional as listed in section 2:006 of the Sanitary Code. All positive laboratory results including drug susceptibility results should be forwarded to the health department. The health department uses this information for the overall management, reporting, and statistical analysis of TB cases.

- **Definition**: A case is any individual with culture positive *Mycobacterium tuberculosis* or, alternately, both a positive reaction to tuberculin skin test and radiographic evidence of current disease.

- **Case Finding:** The fundamental activity in tuberculosis control is case finding. It is extremely important to detect the undiagnosed person with current disease and initiate treatment so that the person is made non-infectious as soon as possible. **The priority is to identify those who expel tubercle bacilli,** as they are the ones who expose others.

- **Case Screening:** Tuberculosis control programs no longer utilize the mass campaigns of the past aimed at screening large portions of the population. A more productive approach is to identify subgroups of the population which are at risk of developing tuberculosis and screen the individuals in these groups for the presence of tuberculosis infection and disease.

- **High-Risk Groups** in which systematic screening is recommended are:

  - Close contacts of sputum smear positive tuberculosis cases should have first priority when screening for tuberculosis infection (see contact investigation section to follow). These contacts are at highest risk of being infected (about 30% to 50% of such contacts are infected).

  - Contacts of sputum smear negative and extrapulmonary cases bear only a slightly higher risk of infection than the general population. For this reason these contacts are not considered high risk.

  - Areas or groups identified by epidemiologic methods as having a high prevalence of tuberculosis:

    - HIV-infected individuals
    - Homeless individuals
    - Injecting drug users (IDUs)

- Immigrants and refugees from areas of high tuberculosis endemnicity regardless of prior BCG vaccination

- Occupants of long-term residential facilities (such as prisons, nursing homes, and mental hospitals). All new occupants should be screened on admission with a Mantoux PPD tuberculin skin test utilizing the booster technique and, in addition, if symptomatic receive a chest X-ray and sputum.

- Tuberculin skin testing is considered essential in symptomatic patients or in patients with medical conditions predisposing to tuberculosis (diabetes, silicosis, Hodgkin's Disease, etc.).

- Employees of long term residential facilities such as nursing homes, mental institutions, and prisons must be screened at the time of employment and yearly thereafter with a Mantoux test. Employees with positive skin tests should be X-rayed and evaluated. **No further annual skin testing or X-rays are needed for the skin test positive employees.** If symptoms of TB should occur, a new chest X-ray is required. Skin test positive employees should be evaluated annually for signs and symptoms of TB by employer questionnaire.

- Employees of health related nonresidential facilities or services such as public health units, outpatient clinics, and visiting nurse and home health agencies should be screened systematically. Only those with the likelihood of close contact with sputum positive cases need to be evaluated at regular intervals (at least yearly).

- **Screening not Necessary**

  Requirements of screening among non-medical professionals in contact with the public (such as barbers, beauticians, cosmetologists, food handlers, school employees, daycare workers *etc.*) and other categories of workers not known to have a high incidence of tuberculosis infection are not necessary.

- **Screening Procedures and Responsibilities**

- Procedures: Mantoux PPD tuberculin testing is the method of choice as recommended by the Centers for Disease Control and Prevention and the American Lung Association. It is followed by an X-ray of the tuberculin positive individuals and other diagnostic procedures if necessary.

- Responsibilities:

- The above mentioned institutions are responsible for their own screening programs. The health unit should assist in the preparation and establishment of the program and provide follow-up for positive reactors and suspects.

- The Regional TB Program Manager has the responsibility to assure that the appropriate identification, screening, and follow-up are provided to contacts of suspects and cases. These contacts are then referred to TB Medical Clinics for evaluation and diagnosis by a physician.

- **Recommendations:** Facilities licensed by the Department of Health and Hospitals should refer to the requirements of the SANITARY CODE STATE OF LOUISIANA for employee screening.

- **Follow-up:** Reactors identified by screening will be followed as indicated in Section 2.5.12.

4.2 Case Reporting and Counting

- Tuberculosis Register

- **Parish register:** A tuberculosis register provides an accurate up to date record on all persons in the parish who require treatment for tuberculosis infection or disease. By keeping current data on the register, one is able to maintain complete information on the status of the persons involved. Such information is necessary

for an effective tuberculosis control program. One would be unable to determine the magnitude of the tuberculosis problem or to assess the community's success in controlling the disease without a well-maintained register.

- The Parish Health Units must submit the regional copy of all TB-9's as soon as completed to the Regional TB Program Manager.

- **Regional register:** A computerized regional register will be maintained by the Regional TB Program Manager.

- This system is dependent upon timely submission of accurate and complete TB-9's from the parish health units. Functions of this system are as follows: case reporting, case management, contact follow-up, and contact management.

- The Regional TB Program Manager will furnish the Tuberculosis Control Section with electronic case reports, regional management reports, and regularly scheduled electronic updates.

- The Regional TB Program Manager should furnish the parish health unit with delinquent medication, sputum, and medical evaluation reports.

- **State register:** The State Tuberculosis Control Section has a computerized case registry system, which is dependent upon the parish and regional case registers.

- The electronic Case Register will furnish case reports to the Centers for Disease Control and Prevention, will furnish statistical data for analysis of tuberculosis in Louisiana, and will compile management reports for more efficient case and contact follow-up.

- **Parish Health Unit Register Structure** All suspects and cases, whether followed privately or publicly, will have a health unit record with an appropriate health unit ID number. The TB Register is a vital component of TB case management. The register will be maintained on TB-8 Forms in the Veri-Visible file in each parish health unit.

    - The **Case File** contains TB-8's for cases presently requiring public health management.

    - The **Suspect File** contains TB-8's for suspects requiring public health management.

    - The **Prophylaxis File** contains TB-8's for latent tuberculosis infected patients requiring public health management. This file will also contain high risk contacts to suspected or known TB cases who have either negative PPD's or positive PPD's while still under investigation.

    - The **Closed File** contains TB-8's on all tuberculosis patients no longer requiring public health management. **These cards are not to be destroyed.**

      NOTE: These TB-8's are to be kept in the closed file. They are never to be stored in patient's records.

4.3 Case Management

The care of the patient with tuberculosis involves the same process used 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 his 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. **Fundamental to all case management is compliance.**

Compliance: Compliance is defined as the extent to which a person=s health related behaviors (taking medications and keeping appointments) coincide with medical advice. Noncompliance is a serious problem. It can lead to treatment failure, drug resistance, continuing transmission, increasing disability, and death.

Factors Affecting Compliance:

- Clinical setting, referral process, and features of the provider
- Duration, complexity, frequency, and side effects of therapy
- Lifestyle, social support, demographics, and health beliefs of the patient.

Methods For Improving Compliance:

- Patient education
- Directly Observed Therapy (DOT)
- Appointment reminders
- Incentives (Refer to Appendix, IDM 755)

For additional information refer to the document: IMPROVING PATIENT COMPLIANCE IN TUBERCULOSIS TREATMENT PROGRAMS found in the appendix.

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

Inpatient care may be recommended for:

- Cases requiring 24 hour nursing care
- Cases with other diseases making the initial plan of care too complicated to be carried out on an outpatient basis.
- Cases where a period of supervised drug administration and indoctrination about the disease is deemed necessary.
- Relapse cases with drug resistant strains of *Mycobacterium tuberculosis* when noncompliance with the prescribed regimen of treatment was the problem.

Discharge: Patients are discharged when hospitalization is no longer deemed necessary by the physician. Several factors must be evaluated prior to discharge to insure completion of prescribed therapy:

- Patient's compliance
- Patient's understanding of the disease
- Patient's living situation.

Adequate provision for completion of therapy must be made prior to discharge. This can be arranged by contacting the Regional TB Program Manager or the health unit in the patient's parish of residence in conjunction with the patient's physician.

Prior to Discharge:

- Determine the outpatient facility to which the patient will be referred as soon as possible.

- Advise that facility in writing or by phone of the anticipated discharge and referral and furnish that facility with patient's name, diagnosis, current clinical status and approximate date of discharge.

- If anti-tuberculosis drugs are to be furnished by the Tuberculosis Control Section, appropriate prescriptions for a thirty-day supply should be forwarded to the health unit in the patient's parish of residence as soon as possible.

When The Patient Is Discharged:

- Instruct the patient to report to the health unit as soon as possible to pick up his medications and to be advised of his first outpatient appointment. All patients regardless of site of disease should have at least three consecutive daily sputum specimens collected to rule out pulmonary disease.

- Prepare a case summary (that includes patient history, discharge summary, and all appropriate laboratory and radiographic reports) and forward to the Regional TB Program Manager or health unit in the patient=s parish of residence.

Drugs: Anti-tuberculosis drugs are available at no cost to new suspects and confirmed cases of tuberculosis who are residents of Louisiana whether under regional clinic supervision, private medical care, or hospital outpatient clinic care. 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 DHH/OPH Pharmacy Services in New Orleans.

Outpatient Follow-up

Case Priorities:

First: Pulmonary suspect or case with a positive smear.

Second: Pulmonary case with negative smears with positive HIV.

Third: Pulmonary case with negative smear and positive culture.

Fourth: Pulmonary case with a clinical diagnosis.

Follow-up Priorities:

First: Cases delinquent for DOT.

Second: Cases delinquent for sputum collections.

Third: Cases delinquent for medical evaluations.

Cases missing medication appointments should be contacted by phone or field visit before the end of the following work day. Cases missing Directly Observed Therapy appointments are to be reported to the Regional TB Program Manager as soon as possible the same day. Rapid follow-up enhances compliance and reduces the risk of drug resistance.

Cases presenting for drug pickup without sputum should have a specimen collected while in the health unit. If a field visit is necessary for any delinquency, a sputum should be collected if the patient is found. Regular sputum collection is essential for confirming compliance and response to

therapy.

All cases should be medically evaluated at least once every three months. A report of the evaluation for patients seen by private physicians should be obtained by utilizing the TB-9 with the information requested circled in red.

4.4 Suspect Management

- **Definition:** A suspect is any individual for whom the diagnosis of tuberculosis disease should be considered (Class 5).

- Symptomatic individuals should have a PPD skin test by the Mantoux method, have sputum collected for AFB (smear and culture), be X-rayed, and have blood tested for antibodies to HIV. Sputum smear positive individuals should have contact evaluation performed **immediately**.

- **During The Evaluation Process:**

  - If the X-ray does not show evidence of tuberculosis and the tuberculin test is positive, an individual determination should be made by the physician regarding prophylactic treatment (see section on preventive treatment). If the patient is not placed on prophylactic treatment, the patient should be carefully instructed concerning the significance of his tuberculin reaction, the risks of developing tuberculosis, the early symptoms of tuberculosis, and the importance of an early diagnosis. There is no reason to instruct the patient to return for follow up X-ray examinations.

  - If the X-ray is suggestive of pulmonary tuberculosis refer for sputum collection, skin test, and HIV test.

  - If the patient has X-ray evidence suggestive of malignancy (or the radiologist reports "tuberculosis vs. malignancy") the patient should be referred immediately to his family physician, clinic, or hospital for diagnostic study. The physician, clinic, or hospital should be notified by letter of the radiologist's findings, adding that the patient has expressed his intention of seeking medical advice from the doctor, clinic, or a hospital.

  - If the X-ray reveals cardiovascular or any other nontuberculosis chest pathology, the individual should be informed that medical attention is needed. He should be referred to his physician. The physician should be notified of the X-ray findings and the positive tuberculin reaction. The record should remain pending until it is determined whether or not prophylactic treatment is indicated.
  - If the X-ray shows pleural effusion of unknown etiology, tuberculosis should be suspected until diagnostic studies are completed. If tuberculosis is not ruled out, the pleural effusion should be reported and considered a case of tuberculosis (Clinical).

Disposition 90 Days: A definite disposition of tuberculosis suspects should be made within 90 days following the opening of the suspect record. The disposition is to be made according to the information received. If complete information is not obtained after 90 days contact the Regional TB Program Manager for a decision on an individual basis.

Responsibilities: Identification, referral,

and surveillance of the suspects are done by the parish health unit staff. Examination and diagnosis are done by the private physicians, OPH Tuberculosis Medical Clinics, or hospital clinics.

4.5 Contact/Associate Investigation

Purpose: Once a tuberculosis suspect/case has been reported to the health unit, and site of disease and smear results are confirmed, contact investigation must be initiated within 72 hours. The objectives are to:

- Identify the probable source of tuberculosis
- Identify the contacts that have active disease and provide treatment
- Identify the contacts that have been infected and provide LTBI treatment
- Identify contacts exposed but not yet infected and provide prophylaxis.

Definitions - A contact is a person who has "shared air" with an infectious pulmonary or laryngeal tuberculosis case. Usually the contact spends time with the patient after the onset of disease in the same household, at work, or during leisure time. One does not have to be a relative of a TB case or suspect to be a contact. Each case must be individualized from an epidemiologic viewpoint. The daily habits and routines of each patient must be ascertained, and those persons with whom frequent and prolonged association occur should be considered "high risk" contacts. Casual visitors and acquaintances should be listed as "low risk contacts" and pursued only when the high risk contact infection rate exceeds 20%. High or low risk may change as the contact investigation progresses.

An associate is a person who has "shared air" and could be a source case to a child who has tuberculosis infection or disease. When conducting an associate investigation, caution should be exhibited to identify and examine all persons with symptoms of tuberculosis.

4.5.1 Information Gathering

Interviewing the patient and reviewing the history and laboratory tests are the first steps of the investigation. It is imperative to visit the patient's home and (possibly) place of employment to conduct an efficient contact investigation.

- The investigation starts with gathering information about:
  - The suspect/case
  - The environmental factors
  - The contacts exposed.
- The following data should be collected:
  - **Patient factors:** Site of disease, result of smear examination (sputum smear positive cases are the infectious cases), chemotherapy, signs and symptoms, and onset and duration of symptoms.
  - **Environmental factors:** Volume of air shared by contact and patient, ventilation, and recirculation of air.
  - **Contact risk factors:** All persons who have "shared air" with the patient are at some risk of infection. The length of time of association is important; physical proximity, prior infection with tuberculosis, age, and physical conditions should be considered.

4.5.2 Contact Investigation Plan

Plan the program of investigation by establishing priorities and classifying contacts.

- **Set Priorities:** The estimated probability of transmission should influence the priority, rapidity, and thoroughness of the contact investigation.
  Highest priority should be given to contacts of sputum smear positive patients.

- **Classify Contacts**: Contact investigation should proceed in an orderly manner, starting with those who are most likely to be infected.

  The higher risk contacts have shared the same air for long periods of time. Contacts from home, work, and leisure settings should be considered based on the "shared air" concept.

Establish limits for investigation:
Initiate the formal investigation with high-risk contacts. Risk classification should be determined on all contacts. If results show a high proportion of contacts recently infected (20% or above) extend the investigation to the next risk level of contacts. If the results show a very low proportion of infected contacts (less than 20%), consult the Regional TB Program Manager before terminating the contact investigation. This procedure of contact evaluation is much more productive than skin testing of large groups of people (a school population, for example). The occasional reactors naturally occurring in a large population will only confuse the picture if attention is not focused on closest contacts initially. Source case communicability can be determined from results of these skin tests.

4.6 Contact Management

Information about previous tuberculous infection, recent symptoms, previous INH treatment, and other medical conditions should be collected.

- **Initial Examination:** Each contact should receive a PPD Mantoux method tuberculin skin test (unless the contact already has a known positive test or documentation for treatment of TB).

- **High-Risk Contacts:** All high-risk contacts should be referred to a TB medical clinic for X-ray, medical evaluation, and initiation of preventive treatment. INH LTBI treatment is recommended for all high risk contacts to sputum smear positive suspects/cases. Initiation of INH preventive treatment should be determined by the infectiousness of the source case and exposure, regardless of the age of the contact.

  Contacts referred should be accompanied by documentation to allow the clinician to make an informed decision about LTBI treatment. This documentation should include: age, nature, extent and dates of contact, previous and current skin test reading results recorded in millimeters, X-ray findings, if any, and symptoms. **Sputum should be collected immediately on all symptomatic contacts.**

- **Evaluation:**

  - High risk contacts with a reaction of ≥5mm are considered positive and should be medically evaluated.

  - High risk contacts with a reaction of <5mm should be considered not

infected and should be medically evaluated. INH is given to persons exposed to tuberculosis but not yet infected (primary prophylaxis) in an attempt to prevent the establishment of tuberculous infection. With primary prophylaxis, INH is protective only while the person is taking the medication. Contacts with skin test results less than 5mm are considered negative. Negative contacts should remain on treatment of latent tuberculosis infection for 8 weeks after infectious contact has been broken. Contact is considered as broken when physical exposure stops or when sputum smear converts from positive to negative in the source case. Retest with Mantoux PPD tuberculin at this time. If less than 5mm, stop the prophylaxis; if ≥5mm, continue LTBI treatment.

- Low risk contacts with a positive skin test should be medically evaluated.

Contact Classification: After the investigation, is completed contacts may be classified as:

Class 0: No Tuberculosis exposure, not infected.
No action necessary.

Class 1: Tuberculosis exposure, no infection

History suggests definite exposure, but initial skin test is negative. If risk transmission factors suggest high probability of infection or if a high proportion of other similar contacts are positive, the patient should be placed on INH prophylaxis. If the contact does not have a significant skin test and was not at high risk of infection, no further action is necessary.

High-risk contacts should have a repeat the skin test 8 weeks after contact is broken, or following first of successive negative smears. If less than 5mm, stop prophylaxis, no further follow-up is necessary. If ≥5mm continue Treatment of LTBI.

Class 2: Latent tuberculosis infection, no disease. The contact was recently infected (≥5mm) and is at high risk of developing tuberculosis. INH LTBI treatment should be instituted regardless of age unless contraindicated.

Current disease must be ruled out before INH LTBI treatment is initiated. Disease is found in 2 to 3% of high risk contacts.

Class 3: Tuberculosis, clinically active

Class 4: Tuberculosis, not clinically active. History of previous disease.

Class 5: Tuberculosis suspect (diagnosis pending).

4.7 Tuberculosis Register Summary

In order to reach the objectives outlined above, regular management of patient information is necessary. The Regional TB Program Manager will furnish the parish health unit and TB Control office with periodic register information to improve patient follow-up.

Monthly Summary: Every month a Tuberculosis Register Summary listing suspects/cases and treatment of LTBI patients will be printed by the Regional TB Program Manager. This list will be mailed to

the Parish Nursing Supervisor to be checked against the TB-8 Register. If any information has been collected but not reported, that information should be sent with a correct TB-9 immediately to the Regional TB Program Manager.

Register Review: Every month each parish health unit should review the Tuberculosis Register in order to assess individual patient progress and identify problem patients or problem areas. The Regional TB Program Manager or staff from the Tuberculosis Control Section may assist the health units in these reviews.

The Tuberculosis Register Review will consist of:

- Evaluation of each suspect/case under therapy regarding drug pick-ups, bacteriologic examination, medical review, contact follow-up and completion of therapy. This is most easily done by reviewing all TB-8's in the active register.
- Evaluation of each latent tuberculosis infected patient regarding compliance with and completion of therapy. Evaluation of skin tests of negative contacts. This is most easily done by reviewing all TB-8s in the LTBI Veri Visible Register.

4.8 Program Assessment

To plan future activities the Tuberculosis Control Program must continuously assess program operations on a parish, regional and state level.

Program assessment objectives are as follows:

TB Cases:

- Ninety percent of tuberculosis cases starting chemotherapy will complete an adequate course of therapy.
- Seventy-five percent of all positive sputum tuberculosis cases starting chemotherapy will achieve negative bacteriologic status within 3 months.
- Ninety percent of cases will be current on chemotherapy, bacteriology and medical review.
- Ninety-five percent of new cases will have contacts identified.

Contacts To Cases:

- Ninety-five percent of high-risk contacts identified will be medically evaluated.
- Ninety percent of all evaluated contacts will be initiated on chemoprophylaxis.

LTBI Treatment:

- Ninety-five percent of co-infected (HIV positive and PPD positive) patients started on chemoprophylaxis will complete recommended treatment of latent tuberculosis infection.
- Ninety percent of contacts and seventy-five percent of routine reactors started on LTBI treatment will complete the recommended course of treatment of latent tuberculosis infection.

4.9 Bacillus of Calmette and Guerin (BCG)

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, Lille, France. It was first administered to humans in 1921.

The protective effect of BCG vaccine has

been the object of an ongoing controversy, still unresolved today. BCG's mode of action and the immune mechanism in tuberculosis has remained largely obscure. On the basis of sporadic, but impressive vaccination results in small population groups at high risk, BCG mass vaccination programs were launched many years ago. Billions of individuals were immunized. At the same time several strictly controlled clinical trials were started. The results of these trials, after 10 to 15 years of follow-up, were rather contradictory; some showed an 80% level of protection, others 10% or less. Reasons for these discrepancies were numerous (variations among BCG sub-strain, technique, atypical mycobacterial, environment, etc.). No satisfactory conclusion has been reached.

The United States has chosen not to use BCG as a tuberculosis prevention measure since:

- Its efficacy is not proven.
- Use of BCG prevents use of tuberculin skin testing as a screening procedure (after BCG vaccination it is difficult to interpret the tuberculin skin test results). It is felt that case detection, chemotherapy and preventive treatment are sufficient to control tuberculosis.
- Many immigrants and refugees have received BCG immunization in the past; caution has to be taken to interpret their skin test results.
- A few months after BCG administration: 95% of vaccines have a $\geq$10mm reaction, with a mean reaction size of 16mm; only 10% have a reaction >20mm.
- Most vaccines will show a decline in tuberculin skin test reactivity over the years.
- Five years after BCG vaccination: 50% of vaccines have a >10mm reaction, only 10% a >15mm reaction and 2% a >20mm reaction.

Repeated PPD testing at short intervals may recall a positive skin test in some BCG recipients who had become skin test negative.

Recommendations are to assume that any reaction $\geq$10mm, in a person with a history of BCG vaccination is not due to BCG, but is due to *Mycobacterium tuberculosis* infection especially if:

- the person is a recent contact of a person with infectious TB
- there is a family history of TB
- the person comes from an area where TB is common
- chest radiograph findings show evidence of previous TB.

In all circumstances the possibility of tuberculosis infection should be considered as the reason for the positive skin test. **BCG should not be used in HIV positive patients.**

Refer to The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States; *MMWR*, April 26, 1996 / Vol.45 / No. RR-4.

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