

Tuberculosis **E**limination **G**uidelines

Tennessee Department of Health
Communicable and Environmental Disease Services Section
Tuberculosis Elimination

Revised September 2004

TUBERCULOSIS ELIMINATION PROGRAM GUIDELINES



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INTRODUCTION

The 2004 revision of the Tuberculosis Control Program guidelines incorporate state-of-the-art recommendations for an optimal approach to achieving the goal of eliminating tuberculosis in Tennessee. Substantial progress has been made in the last five years. The guidelines represent consensus derived from current literature review, consultation with recognized authorities in tuberculosis management, and discussion among public health practitioners and administrators. Judicious application of the guidelines and good clinical judgment will ensure that the highest standard of care will be met throughout Tennessee.

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We would like to acknowledge Tennessee Department of Health TB Elimination Staff past and present for their many contributions to this document.

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I. RESPONSIBILITY FOR TUBERCULOSIS ELIMINATION

RESPONSIBILITY FOR TUBERCULOSIS ELIMINATION

Tuberculosis services in Tennessee are provided on a cooperative basis by the Department of Health Tuberculosis Elimination Program, regional health offices, county health departments, the private medical sector, and other public agencies. The Department of Health bears the ultimate responsibility for the control of tuberculosis and is accountable for ensuring that these entities work together to implement effective and efficient TB Elimination activities.

I. Responsibility for TB Control and Prevention in Tennessee

A. Central Office Responsibilities:

The Department of Health TB Control Program Central Office is responsible for directing statewide TB control and prevention efforts in Tennessee by performing routine assessment of TB epidemiology and program achievement, identifying areas for improvement, and developing a strategic plan to enhance the quality of patient care and TB Program performance.

Specific Responsibilities include:

1. Provide leadership, guidance, and technical assistance to the Regional Health Offices in assessing local TB program needs, setting objectives, measuring progress, identifying problems, and designing interventions to enhance quality of patient care and TB prevention and control activities.
2. Collaborate with CDC and other state TB control programs to identify new methods to reach the National goal of TB Elimination.
3. Facilitate the technological and methodological transfer of successful TB control and prevention methods among Tennessee's Regional TB programs, e.g., via workshops, conferences, written communications, etc.
4. Establish a Statewide TB Program Evaluation Plan based on Federal expectations and other measurable performance indicators as directed by CDC. Compile and analyze statewide data to identify areas for improvement and develop a strategic plan to meet State and National objectives.
5. Monitor Regional TB program activities and performance to ensure local compliance with State and Federal TB Program

objectives. Provide guidance and assistance to regions in identifying local areas for improvement through various methods including telephone consultation, site visits, quality improvement monitoring and evaluation, and provision of written site visit and QA reports. Provide specific tools, educational materials, training, and technical assistance to enable achievement of State and National TB Program objectives.

6. Provide technical assistance in assessing and prioritizing training and education needs and in planning, implementing and evaluating training and education activities.
7. Develop collaborative relationships with other State departments, agencies, and key stakeholders (i.e. Department of Corrections, Alcohol & Drug Program, American Lung Association, DHS Refugee Health Program, Tennessee Chapter of APIC, etc.) to ensure that their policies and practices are concordant with TB Program objectives.
8. Coordinate cross-program collaborative approaches to HIV, STD and TB prevention and develop effective interventions to reduce the morbidity associated with these conditions.
9. Establish and maintain effective working relationships with the regional TB controller (Health Officer) and public health staff for the purpose of formulating and implementing a local plan for the control and prevention of TB.
10. Provide medical consultation for individuals with TB or LTBI on request.
11. Provide Regional TB Programs with up-to-date information on national recommendations and guidelines for TB diagnosis, treatment, monitoring, and prevention.
12. Provide consultation and assistance to develop, monitor, and improve local surveillance for TB disease and latent TB infection.
13. Support the investigation of TB outbreaks, including on-site assistance with local investigations when indicated.
14. Facilitate resolution of inter-jurisdictional challenges, such as ensuring continuity of case management and treatment of persons with active TB and LTBI who move between Tennessee Health Regions or other States.

15. Ensure that all required TB Program data is collected from Regional TB programs and reported to CDC in an accurate and timely manner.
16. Ensure that requirements for federal or other funding sources are adequately achieved by expected deadlines.

B. Regional TB Control Responsibilities:

The Regional Health Officers are the local TB Control Officers and thus have primary responsibility for establishing and maintaining local TB control & prevention efforts.

Specific Responsibilities include:

1. Review regional epidemiology and apply data to develop and implement a regional strategic plan for the elimination of TB (with Central Office support as needed).
2. Evaluate Regional performance of TB Program activities and progress towards State and National Objectives for TB elimination (local program evaluation); develop methods for monitoring progress and for improving performance.
3. Ensure that regional and local public health staff perform all TB Program activities according to the standards outlined in the TB Guidelines.
4. Ensure that public health staff has adequate knowledge of core competencies regarding TB and LTBI.
5. Manage the Regional TB Clinic and ensure the provision of medical management of patients.
 - a. Ensure the highest quality of medical care for TB cases, contacts and other persons with LTBI according to current State and National standards.
 - b. Ensure client-centered case management for all TB cases and persons with LTBI, regardless of whether the health department is the primary provider.
 - c. Ensure availability of timely and expert medical consultation to other practitioners (private or facility) for persons with TB or LTBI.

- d. Ensure appropriate and state-of-the art diagnostic evaluation for all patients suspected of TB or LTBI.
 - e. Ensure that patients are provided DOT/DOPT according to Health Department protocol and standards.
 - f. Ensure that appropriate monitoring & follow-up is provided for all patients according to State and National guidelines.
 - g. Establish procedures to ensure patient's adherence to a full course of TB or LTBI treatment (i.e. completion of therapy), including the use of incentives & enablers, in-person or phone contact to educate and encourage compliance, and the use of appropriate legal procedures when necessary.
 - h. Ensure that all TB cases and persons treated for LTBI are reviewed by TB clinic physician according to the expected schedule listed in the TB guidelines to identify problems in a timely manner and to follow clinical progress.
 - i. Ensure that effective education and counseling are provided to patients and their family or other sources of support.
 - j. Ensure that all care is provided to patients in their preferred language using a culturally-appropriate approach according to Title VI requirements (i.e. ensure that staff utilize interpreters or telephonic interpretation services when indicated); ensure that children are never used for interpretation and that friends, family or other untrained persons are not utilized as interpreters.
 - k. Ensure that TB/LTBI patients are referred for related non-TB services as indicated (i.e. HIV care, immunization, prenatal care, A&D treatment, etc.)
6. Establish and maintain active surveillance for new TB cases and for persons with LTBI in high-risk settings.
 7. Ensure that efficient & effective contact investigations are conducted for all infectious TB cases so that newly infected contacts can be identified, evaluated and fully treated.
 8. Conduct outbreak investigations in a timely manner in accordance with state guidelines and protocol.

9. Develop collaborative relationships with key stakeholders (e.g. hospitals, nursing homes, community groups, advocacy groups, cultural groups, faith-based clinics, civil surgeons, other medical providers for minority groups).
10. Train and educate non-health department providers and other stakeholders regarding TB screening, evaluation, and management of persons at risk or suspected of TB or LTBI; ensure that providers such as health care facilities, A&D treatment programs, and correctional facilities establish and maintain appropriate TB screening programs and infection control policies and procedures.
11. Perform outreach activities (targeted testing) to prevent TB in high-risk settings (prisons, jails, homeless shelters, A & D centers, etc.), prioritizing these activities based on regional TB epidemiology.
12. Ensure that Regional TB Program reports and data are submitted to Central Office in an accurate and timely manner.

II. Responsibility for Clinical Services

A. Responsibility of Clinical Health Department Staff (physicians, nurses, public health representatives, etc.)

1. Ensure appropriate medical evaluation, treatment and follow-up of all known or suspected TB cases and persons with latent TB infection (LTBI), regardless of whether the Health Department is the primary provider or not.
2. Provide client-centered case management for all TB suspects and cases and patients with LTBI by addressing both clinical and social issues of the patient.
3. Investigate all suspected TB cases and report all new TB cases to the TB Elimination Program Central Office and the Centers for Disease Control and Prevention (CDC).
4. Examine or confirm the examination of contacts to active TB cases.
5. Consult with and give assistance to private physicians who assume responsibility for treating patients with TB or LTBI.

6. Provide TB clinical and epidemiological consultation to other providers of care.
7. Obtain from other providers of care a summary of the patient's current status at one and three months of therapy and at least every three months thereafter to ensure that the patient is on appropriate medication and under current medical supervision.
8. Provide education to the patient and his/her family about TB and LTBI.
9. Enforce, when necessary, TB laws, rules, and regulations to protect the health of the public.
10. Provide education and training regarding TB control standards to public health staff and to other medical providers, agencies or facilities in the community as appropriate.
11. Perform clinical and epidemiologic data collection, analysis, and reporting to enable high quality patient care and to enhance local and statewide TB control efforts.

B. Responsibility of Tuberculosis Clinic Physician

1. Primary Responsibility for treatment of TB/LTBI patients

It is the TB physician's primary responsibility to provide or ensure that appropriate medical care and supervision is provided to all tuberculosis cases and suspects, regardless of whether the Health Department is the primary TB provider. This includes ensuring that cases are reported, classified, placed on the TB register, started on treatment and remain under appropriate medical supervision until they complete a satisfactory course of therapy. **When private physicians or other providers are involved, direct communication must occur between the TB physician and the other medical providers.**

2. Collaboration with the Laboratory

The Tennessee State Laboratory is a critical partner in TB elimination efforts, and plays a key role in early identification and prompt treatment of TB cases. To adequately provide effective clinical TB services to patients, there must be a timely flow of information among laboratorians (State and other labs), clinicians,

and the TB controller. The TB clinic physician should work closely with the Laboratory to ensure that smear, culture and susceptibility results are rapidly obtained and utilized to enhance diagnostic certainty and to decrease delays in reporting cases, initiating of TB treatment, starting or discontinuing isolation, and adjusting TB treatment regimens based on susceptibility results. The TB physician should communicate directly with the laboratory to request special testing (e.g. TB DNA probe testing for patients with AFB-negative smears) when indicated, or to clarify results that do not fit the clinical picture. Discussion of clinical details with laboratory staff enables them to provide better consultation regarding the appropriate tests to consider or the appropriate preliminary diagnosis.

3. Physician Communication

In all situations when a TB case or suspect is reported by other providers or a positive bacteriological specimen or other evidence of TB disease is received from a laboratory or health care facility, direct communication should be made with the patient's primary medical provider (private physician, correctional facility physician, etc.). Contact should be made by a personal telephone call from the TB clinic physician to the physician of record. The physician must ensure that all items included in the physician's checklist (Appendix 1) are addressed (Note: the nurse may collect some of the required information, but the TB physician must confirm it).

4. Documentation

- a. At the conclusion of a telephone conversation, the information discussed should be documented in the patient's TB clinic medical record. Copies of this documentation should be sent to the private physician and to the county health department. Copies may also be sent to other providers as requested by the patient and/or other provider, after the patient's written informed consent has been obtained.
- b. Each call may be followed by a personal letter thanking the provider for his/her cooperation and reiterating pertinent issues discussed and/or roles and responsibilities of the Health Department and other provider (optional, but very useful).
- c. The Health Department Physician should ensure that staff obtains all documentation regarding the information

requested above, and that copies of the patient's relevant medical records are sent to the health department, including clinic notes, hospital admission and discharge summaries, laboratory and radiology reports, etc. Preferably, all records should be sent via fax within 24 hours for immediate sharing of information. In the event that a provider is reluctant to share a patient's medical information, a memo from the TB physician or Health Officer should be sent informing the provider that under public health law all patient records must be released to the health department, regardless of specific patient consent (see Appendix 3).

5. Case review

All TB cases or suspects treated by either the Health Department or another provider should be reviewed by the Rural Regional or Metropolitan Regional TB physician at baseline and *at least* every three months throughout treatment and follow-up. This medical review should include an assessment of the patient's drug regimen, adherence to treatment and tolerance of the medications, evaluation of the patient's clinical progress, an analysis of the most recent sputum smear and culture results, laboratory tests, and x-ray studies (either review of the film itself or the official report), and a determination of the appropriate length of therapy. The completion of the above process must be noted in the patient's chart and all identified problems should be addressed immediately.

6. Education of Other Providers

TB Physicians and Health Officers should educate colleagues in private practice, academics, corrections, and other settings to "Think TB" when evaluating patients with compatible clinical symptoms and to collaborate with the Health Department TB Clinic to appropriately evaluate, treat, and monitor TB suspects and cases according to National and State guidelines. In addition, other practitioners can assist the Health Department with TB control and prevention by ensuring appropriate TB control practices (i.e. immediate isolation and reporting of persons with suspected TB) and by providing TB screening and skin tests for high-risk persons (in particular foreign-born or immunosuppressed/HIV+ persons, substance abusers, and persons with medical conditions with a risk of progression to TB if infected). Education of health care workers and other key stakeholders regarding TB incidence, transmission, risk factors, as well as evaluation and treatment of persons with TB and LTBI will

facilitate achievement of the Health Department's goal of TB Elimination.

C. Responsibility of Private Medical Sector and Other Providers of Care

1. Physicians, hospitals, laboratories, institutions, jails, prisons etc. are required to report all diagnosed and/or suspected TB cases to county or regional health departments by phone within 12 hours. (T.C.A. 68-5-102; Chapter 1200-14-1 of the Rules and Regulations of Communicable Diseases.)
- Appendix 2 is a copy of a memorandum regarding the requirements for reporting persons with known or suspected TB. This memo can be used to educate providers of their responsibility and to encourage compliance with Communicable Disease Rules and Regulations.
2. Hospital and private laboratories are required to submit positive cultures of mycobacterium species to the Tennessee State Laboratory for confirmation and species identification. (TCA 68-29-107; Rules Chapter 1200-6-3-.12).
3. Private physicians and other providers are required to release a TB patient's protected health information, without individual authorization, to public health authorities if requested. The authority to conduct surveillance, which may include examination of medical records, comes from the Communicable Diseases Rules of the Tennessee Code Annotated, Chapter 1200-14-1. "Medical records shall be made available when requested, for inspection and copying of, by a duly authorized representative of the Department while in the course of investigating a reportable disease under these regulations" (1200-14-1-.15).
 - a. Specific patient information includes but is not limited to a report of the patient's current status, including physician's notes, admission and discharge summaries, bacteriology reports, radiology reports, laboratory studies, histopathology reports, and documentation of current drug treatment.
- Appendix 3 is a copy of a memorandum regarding public health reporting and HIPAA authorization.

Physician Communication Checklist

- _____ Is the patient currently on isolation or is he/she considered non-infectious? If patient is infectious, inquire about site and expected duration of patient's isolation.
- _____ Has the patient had a positive sputum smear or culture for TB or other bacteriological evidence of TB? If so, obtain date and specific smear or colony count. Determine where the specimens were sent (i.e. state or other laboratory) and if susceptibility tests have been requested.
- _____ Has patient had any other diagnostic testing (bronchoscopy, biopsy, culture of other specimens such as urine or CSF)? Obtain dates, types of tests and culture *and* histopathology results. If a biopsy was taken, was the specimen placed in formalin? Determine where the specimens were sent (i.e. state or other laboratory) and if susceptibility tests have been requested. Educate providers that specimens can and should be sent to the state lab for mycobacterial culture, susceptibility testing, and genotyping.
- _____ Has the patient had a chest x-ray or other radiographic study? If so, obtain date, type of study and detailed results.
- _____ Has the patient had a tuberculin test? If so, obtain date, type of test, and results in millimeters.
- _____ Has the patient been started on anti-tuberculosis medication? If so, obtain names of drugs, initial dosage and date started. Inquire if any changes have been made in the treatment regimen and the reasons for the changes. Determine if patient has been adherent to treatment. Specifically ask if the patient has been treated with a fluoroquinolone antibiotic prior to or during TB treatment and document the dates and length of this treatment.
- _____ Is the patient receiving treatment under Directly Observed Therapy (DOT)? If not, explain the benefits of DOT and that it is the standard of care in Tennessee and nationally; encourage provider to order this service for the patient.
- _____ Has the provider given the patient prescriptions for TB drugs? Explain that TB medications will be provided by the health department free of charge to the patient. Encourage providers to contact the health department directly with recommendations for the patient's treatment rather than providing a patient with a prescription at hospital discharge or outpatient visit. Explain that patients who get prescriptions filled outside of the health department may not report to the health department and thus may not get adequate case management, evaluation and monitoring, DOT or evaluation for close contacts.

- _____ Will the provider be seeing the patient regularly during the course of therapy and obtain the necessary follow-up chest x-rays, sputum examinations, etc.? Recommend that the health department maintain primary case management and provide the monitoring throughout therapy. Clarify specific services that health department will provide.

- _____ Explain that the Health Department will communicate with them regularly and notify them of the patient's progress and any treatment changes made.

- _____ Has the provider notified the family of the diagnosis and recommended that a contact investigation occur? If so, clarify responsibilities of provider and health department regarding patient/family education and identification and evaluation of potential contacts.

- _____ Was the suspect or case reported to the Health Department in a timely manner (i.e. within 12 hours of being suspected of having TB)? If not, educate provider of current State reporting requirements (T.C.A. 68-5-102; Chapter 1200-14-1 of the Rules and Regulations of Communicable Diseases.)

Note: When communicating with other providers regarding specific patients, Health Department Physicians should take the opportunity to educate them regarding his or her experience and qualifications as a TB Physician and about the specialty TB services that can be provided for patients with TB or LTBI (i.e. clinical or epidemiologic consultation, evaluation and management of patients, and TB/LTBI education and training). Direct physician to physician communication ensures that the patient will receive the highest quality of medical care in a coordinated manner and highlights the Health Department's expertise in TB/LTBI patient management.



STATE OF TENNESSEE
DEPARTMENT OF HEALTH
CORDELL HULL BUILDING
Fourth Floor, CEDSS
425 5th AVENUE NORTH
NASHVILLE, TENNESSEE 37247

August 28, 2004

Dear Colleagues:

I would like to make you aware of new requirements for reporting **tuberculosis (TB)** to the Tennessee Department of Health:

Effective July 1, 2004, all persons with known or suspected TB, including pulmonary and extrapulmonary disease, must be reported to the Tennessee Department of Health within 12 hours by phone (T.C.A. 68-10-101; Chapter 1200-14-1.02 of the Rules and Regulations of Communicable Diseases). This verbal report should include the name, age, sex, race, and address of the patient. Written notification providing the same information must also be submitted within one week, preferably using forms provided by the Department.

Early notification of TB suspects and cases enables the Department of Health to ensure appropriate treatment of TB suspects and cases and to provide all patients with essential services including counseling and education regarding TB disease and treatment, "client-centered" case management, free treatment under directly observed therapy, and monitoring for toxicity and compliance throughout therapy. Early notification also enables the Department of Health to initiate a contact investigation promptly to identify additional persons with active TB or latent TB infection, thus preventing further spread of disease.

Providers should report TB cases and suspects directly to the Regional Health Office TB Clinic designated for the county where the patient resides. Please note that Health Department TB Clinic providers can provide consultation if you are considering the possibility of TB and whether or not to initiate isolation and treatment. For your convenience, a map showing the regional divisions that should be used for reporting purposes is attached, as well as contact names, phone and fax numbers for each Regional

Office. Updated forms for written notification are available on-line at <http://www2.state.tn.us/health/Downloads/ph-1600.pdf>.

New TB reporting requirements

page 2

Please remember to “THINK TB” when evaluating persons with compatible clinical findings, especially those with known TB risk factors such as foreign-birth, HIV, substance abuse, homelessness, immunosuppressive treatment or conditions (i.e. chemotherapy, steroids, or TNF- α blocking agents such as infliximab (Remicade[®]), and residence or employment in correctional facilities or long-term care facilities). A list of TB risk factors and other TB-related resources can be obtained at the following websites:

<http://www2.state.tn.us/health/CEDS/TB/guidelines.htm>.

<http://www.cdc.gov/nchstp/tb/default.htm>.

If you have any questions regarding this notice, please contact your Regional Health Office or the Tennessee Department of Health at (615) 741-7247.

Thank you for working with us to protect the public health.

Sincerely,

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TUBERCULOSIS ELIMINATION PROGRAM
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January 2004

To Whom It May Concern:

Re: Public Health Reporting and HIPAA

The Tuberculosis (TB) Elimination Program, as part of the Communicable and Environmental Disease Services Section of the Tennessee Department of Health, conducts surveillance for tuberculosis in its capacity as a public health authority as defined by the Health Insurance Portability and Accountability Act (HIPAA), Standards for Privacy of Individually Identifiable Health Information: Final Rule (Privacy Rule) [45 CFR §164.501].

Pursuant to 45 CFR § 164.512(b) of the Privacy Rule, covered entities such as your organization may disclose, without individual authorization, protected health information to public health authorities "...authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, including, but not limited to, the reporting of disease, injury, vital events such as birth or death, and the conduct of public surveillance, public health investigations, and public health interventions...".

The authority to conduct surveillance, which may include examination of medical records, comes from the Communicable Diseases Rules of the Tennessee Code Annotated, Chapter 1200-14-1. "Medical records shall be made available when requested, for inspection and copying of, by a duly authorized representative of the Department while in the course of investigating a reportable disease under these regulations." (1200-14-1-.15)

The Privacy Rule provides that covered entities "... may rely, if such reliance is reasonable under the circumstances, on a requested disclosure as the minimum necessary for the stated purposes when making disclosures to public officials that are permitted under 45 CFR §164.512, if the public official represents that the information requested is the minimum necessary for the stated purpose(s)." The information being requested

represents the minimum necessary to carry out the public health purposes of the TB Elimination Program pursuant to 45 CFR §1643514(d) of the Privacy Rule.

The requirement to provide the Tennessee Department of Health with information regarding notifiable diseases, and the authority to do so without patient authorization, does not release covered entities from the requirement to account for those disclosures. The Centers for Disease Control (CDC) published in the April 11, 2003 MMWR provisions covering "Accounting for Public Health Disclosures", which states "where the covered entity has, during the accounting period, made multiple disclosures to the same recipient for the same purpose, the Privacy Rule provides for a simplified means of accounting. In such cases, the covered entity need only identify the recipient of such repetitive disclosures, the purpose of the disclosure, and describe the PHI routinely disclosed. The date of each disclosure need not be tracked. Rather, the accounting may include the date of the first and last such disclosure during the accounting period, and a description of the frequency or periodicity of such disclosures." A copy of this CDC MMWR publication is enclosed for your information and reference.

Thank you and your institution for continuing to work so diligently with the Tennessee Department of Health TB Elimination Program to ensure the safety and health of all Tennesseans. If you have any questions, please feel free to call the TB Elimination Program at 615-741-7247.

Sincerely,

Connie Haley, M.D., M.P.H.
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II. TUBERCULIN SKIN TESTING

TUBERCULIN SKIN TESTING

I. BASIC PRINCIPLES

A. Description of the Tuberculin Skin Test

The tuberculin skin test (TST) is currently the only test available for detecting infection with *M. tuberculosis*. The reactivity of the test is based on a delayed hypersensitivity response to tuberculin antigens contained in the purified protein derivative (PPD). The injection of tuberculin (mycobacterial antigens) intradermally into a person previously infected with *M. tuberculosis* will result in accumulation of previously sensitized inflammatory cells at the site of injection resulting in edema and erythema. The TST results can be determined by measuring the size of induration at the injection site 48-72 hours after administration of the test.

Tuberculin skin testing with intermediate strength (5 TU) PPD, administered by the Mantoux intradermal technique is the only currently recommended method; Multiple puncture tests should never be used.

B. Usefulness of the TST

The tuberculin skin test (TST) is primarily useful in three situations:

1. As a diagnostic aid in establishing whether an individual has active TB disease.
2. To determine whether an individual has latent tuberculosis infection for the purpose of administering treatment to prevent TB disease.
3. As a tool for epidemiologic assessment of the prevalence of *M. tuberculosis* infection within groups or regions (e.g. to determine the proportion infected in a specific targeted testing setting or among contacts to a TB case).

C. When to Place a TST

Unless the individual is a documented previous tuberculin reactor (in mm's), a TST test should be given in all diagnostic situations, such as the evaluation of:

1. All TB suspects and cases.
2. All contacts to newly diagnosed cases

3. Individuals who are identified as high-risk for TB infection using the TB/LTBI Risk Assessment Tool (PH-3714).

D. Who Should be Skin Tested

Tuberculin skin testing should be reserved for persons who meet some or all of the following criteria:

1. Are at high risk for TB infection
2. If infected, are at high risk of developing active TB
3. If infected, would be a candidate for treatment to prevent active TB or
4. Have symptoms or other evidence of active TB

High-Risk Persons:

- Close contacts of active TB cases or suspects
- Foreign-born persons from high-prevalence countries (excluding Canada, Western Europe, Australia, New Zealand and Japan)
- Persons working or residing in congregate settings known to be associated with TB transmission (homeless shelters, jails/prisons, alcohol and drug rehabilitation centers, long-term care facilities, residential facilities for patients with AIDS)
- Persons working in health care facilities where known TB cases exist, and other cases are suspected or likely
- Mycobacterial laboratory personnel
- Persons with certain medical conditions associated with progression to active TB:
 - ⇒ HIV infection, silicosis, diabetes mellitus, chronic renal failure/hemodialysis, gastrectomy, jejunum-ileal bypass, carcinoma of the head and neck or lung, hematologic conditions such as leukemia, lymphoma, being more than 10% underweight, and immunosuppression from organ transplant or medications (equivalent of prednisone >15mg/d for 3 or more weeks, infliximab (Remicade®) or other anti-TNF-alpha drugs, etc.)
- Injection drug users
- Children who meet any of these criteria or who have been in regular contact with high-risk adults
- Persons with frequent or prolonged travel to high-prevalence countries (see above)
- Other persons at high-risk for TB/LTBI as locally defined

Testing for High-Risk Employment

- Persons who are otherwise low-risk but require a baseline skin test prior to initial employment in a high risk setting (hospital,

correctional facility, long-term care facility, alcohol and drug centers, homeless shelters, etc.) may also be tested.

- Persons who are already employed in such settings and require repeat skin testing are considered high-risk and can be tested.

Note: The health department is not required to perform TST on any low or high-risk persons who require testing for employment, and these persons should be referred to other providers or their employer for testing. These persons should be charged for their TST, if they cannot be referred elsewhere and are tested at the health department.

Low-Risk Testing:

Testing of low-risk persons is generally not recommended (except to establish a baseline prior to high-risk employment as noted above). A substantial proportion of TST-positive persons without any TB risk factor will have a false-positive result. Identification of a positive TST in a low-risk person will lead to potentially unnecessary testing and difficult treatment decisions. Low-risk persons requesting a TST should be counseled regarding their risk of TB disease and the potential risk of unnecessary testing and treatment. **The Public Health Department is not required to perform testing on any low-risk person**, and those who insist on being tested can be referred to another provider.

Retesting When Previous TST Results are Questionable

- There is no benefit in retesting persons who have already been treated for TB or LTBI.
- In general, persons with documented positive skin test results in mm do not need to be retested.
- Retesting can safely be performed in most persons for whom the TST results are questionable if further evaluation for TB disease or possible LTBI treatment is being considered. Questionable results include a history of a positive TST without a documented result in millimeters or when there is suspicion of improper testing technique or measurement (i.e. of redness rather than induration).
- There is no contraindication to repeating the tuberculin test for persons with a prior “positive” result unless a significant adverse reaction to the test has previously occurred (i.e. significant allergic reaction, blistering/vesiculating reaction or skin sloughing).

II. INTERPRETING THE RESULTS

The TST is subject to variability and must be read by a trained health care worker.

A. Definition of a Positive Skin Test Result

There are 3 cut-offs for a positive TST: ≥ 5 mm, ≥ 10 mm, ≥ 15 mm, depending on the risk of TB infection or disease in the individual or population being tested, as follows:

5 mm or greater TST induration:

- HIV-infected persons
- Immunosuppressed persons (organ transplants, steroid use, etc.)
- Recent contacts of TB case
- Persons with fibrotic changes on chest X-ray consistent with old healed TB

10 mm or greater TST induration:

- Foreign-born persons from high-prevalence countries
- Persons with frequent, prolonged travel to high-prevalence countries
- Employees and residents of high-risk congregate settings (shelters, jails/prisons, etc.)
- Injection drug users
- Health care workers and volunteers
- Mycobacteriology laboratory personnel
- Children <4 years with a risk factor, or children and adolescents exposed to adults in high-risk categories
- Persons with high-risk medical conditions (silicosis, diabetes mellitus, chronic renal failure/hemodialysis, gastrectomy, jejunio-ileal bypass, carcinoma of the head and neck or lung, leukemia, lymphoma, and being more than 10% underweight.)

15 mm or greater TST induration:

- Persons with no risk factors for TB/LTBI (i.e. Low-risk; includes persons previously at low-risk requiring TST prior to initial employment in a high-risk setting)

B. Other Considerations:

1. The TST is an imprecise tool that can be affected greatly by biological variability. All clinicians should use clinical judgment as well as skin test results in deciding whether or not a patient has become infected with *M. tuberculosis*.

2. A positive test can support the diagnosis of active TB disease in the absence of a positive culture (**Note:** a positive test is part of the CDC criteria required for reporting a TB case using a “clinical diagnosis”).
3. A negative skin test does not rule out active TB disease or latent TB infection.

C. Skin Test Conversion vs. Reaction

- A skin test “reactor” is anyone who has a positive TST, according to the appropriate cut point for their risk category.
- Skin test “conversion” is defined as a person with a documented negative TST who either 1) develops a positive reaction based on the criteria above for each specific risk group or 2) has an increase in induration of ≥ 10 mm within a period of two years.

D. Causes of Falsely Negative Skin Tests

Factors related to the person being tested

- ◆ Viral Infections (measles, mumps, chicken pox, HIV)
- ◆ Bacterial Infections (typhoid fever, brucellosis, typhus, leprosy, peruses, overwhelming tuberculosis, pleurisy)
- ◆ Fungal Infections (South American blast mycosis)
- ◆ Live virus vaccinations (measles, mumps, polio, varicella)
- ◆ Metabolic derangements (chronic renal failure)
- ◆ Low protein states (severe protein depletion, afibrinogenemia)
- ◆ Diseases affecting lymphoid organs (Hodgkin’s disease, lymphoma, chronic leukemia, sarcoidosis)
- ◆ Drugs (corticosteroids and many other immunosuppressive agents)
- ◆ Age (newborns, elderly patients with “waned” immune responses)
- ◆ Stress (surgery, burns, mental illness, graft-versus-host reactions)
- ◆ Acute illness or generalized dermatitis

Factors related to the tuberculin antigen used

- ◆ Improper storage (exposure to light and heat)
- ◆ Improper dilutions
- ◆ Chemical denaturation
- ◆ Contamination
- ◆ Adsorption (partially controlled by adding Tween 80)

Factors related to the method of administration

- ◆ Injection of too little antigen
- ◆ Subcutaneous injection (injecting PPD solution too deep)
- ◆ Delayed administration after drawing into syringe
- ◆ Injection too close to other skin tests
- ◆ Bleeding at injection site

- ◆ Pressure on injection site may extrude antigen

Factors related to reading the test and recording results

- ◆ Inexperienced reader
- ◆ Conscious or unconscious bias

E. Boosted Reactions

In most individuals, PPD skin test sensitivity persists throughout life. However, in some persons the size of the TST reaction may decrease and even may disappear over time. If PPD is administered to infected individuals whose sensitivity has waned, the reaction of the initial test may be small or absent; however, there may be an accentuation of response on repeated testing. This is called the “booster effect” and can be misinterpreted as a new skin test conversion. Boosted reactions also are common in individuals exposed to other mycobacteria or who have been vaccinated with Bacille Calmette-Guerin (BCG).

F. Two-step testing

Two-step testing is a technique used to distinguish between boosted reactions and reactions due to new infections. Two-step testing should be used for the initial skin testing of adults who will be skin tested periodically, such as health care workers and residents/staff of correctional facilities and long-term care facilities. In this method, persons who have a negative initial PPD skin test undergo a second tuberculin test 1-3 weeks after the first. The results from the second test should be considered to be the “correct” result, i.e., those individuals with a positive reaction on the second test should be considered to be previously infected, and those with a negative reaction on the second test should be considered uninfected. In these uninfected persons, a positive result on any future PPD skin test should be interpreted as a new skin test conversion. Repeated skin testing with tuberculin will not induce a positive skin test reaction in individuals who have no cellular immunity to the antigens in PPD.

III. SPECIAL CONSIDERATIONS FOR CERTAIN GROUPS

A. Tuberculin Skin Test Recommendations for Infants, Children, and Adolescents

The American Academy of Pediatrics recommends a TST only for children who are at increased risk of acquiring TB infection and disease. **Children without TB/LTBI risk factors should not be tested.**

When a child is found to have a positive tuberculin skin test, especially a child <5 years, a thorough investigation of his/her close contacts should be made to identify the source of the child's infection. A source case investigation should be done for children ages 5 to 18 with a positive skin test, as time and resources permit.

Children for whom immediate TST is indicated:

- Contacts of persons with confirmed or suspected tuberculosis (contact investigation)
- Children with radiographic or clinical findings suggesting tuberculosis disease
- Children immigrating from TB-endemic countries (includes all countries except Canada, Japan, Australia, New Zealand and those in Western Europe)
- Children with travel histories to TB-endemic countries and/or significant contact with indigenous persons from such countries

Children who should have annual TST*

- Children infected with HIV or living in household with HIV-infected persons
- Incarcerated adolescents

Some experts recommend that certain children should be tested every 2-3 years*:

- Children with ongoing exposure to the following people: HIV-infected, homeless, residents of nursing homes, institutionalized adolescents or adults, illicit drug users, incarcerated adolescents or adults, and migrant farm workers; foster children with exposure to adults in the preceding high-risk groups are included.

Some experts recommend that certain children should be tested at 4-6 and 11-16 years of age:

- Children whose parents immigrated (with unknown TST status) from regions of the world with a high prevalence of tuberculosis; continued potential exposure by travel to the endemic areas and/or household contact with persons from the endemic areas (with unknown TST status) should be an indication for repeated TST
- Children without specific risk factors who reside in high TB-prevalence areas (based on local epidemiology)

Children with certain medical conditions

- Children with certain medical conditions are at increased risk of progression to TB disease if infected, including diabetes mellitus, chronic renal failure, malnutrition (being below 10% of ideal body weight), and congenital or acquired immunodeficiencies from organ transplant or immunosuppressive treatments, leukemia, lymphomas and

other malignancies. Without recent exposure, these people are not at increased risk of acquiring tuberculosis infection. Underlying immune deficiencies associated with these conditions theoretically would enhance the possibility for progression to severe disease. Initial histories of potential exposure to TB should be included for all of these patients. If these histories or local epidemiologic factors suggest a possibility of exposure, immediate and periodic TST should be considered. An initial TST should be performed before initiation of immunosuppressive therapy, including prolonged steroid administration, for any child with an underlying condition that necessitates immunosuppressive therapy.

***Note: Initial TST should be given when risk factor identified, beginning at 3 months of age.**

B. Pregnancy

Pregnancy is not a contraindication to tuberculin testing.

C. Prior BCG Vaccination

Bacille Calmette-Guerin (BCG) is a live, attenuated strain of *M. bovis* that is administered to more than 80% of children in the world as part of the Extended Program on Immunization. The vaccine is given primarily in countries with high rates of TB infection, therefore many persons who have previously received BCG may also have TB infection. The efficacy of BCG in preventing TB infection and disease is variable and controversial. Thus, **persons who have received BCG should be tested for TB infection**, unless otherwise contraindicated.

The size of tuberculin skin test reactions caused by BCG vaccination (i.e., post-vaccination sensitivity) is also highly variable and tends to wane over time. After BCG vaccination, it is not possible to distinguish between a positive reaction caused by true TB infection and a positive result from the vaccination itself. **A positive TST result in a vaccinated person should be assumed to be due to infection with *M. tuberculosis***, not BCG, and treatment of TB or LTBI should be considered as for any other person with a positive TST.

D. Anergy Testing

Persons with HIV infection or other conditions or treatment resulting in significant immunosuppression may have a compromised ability to react to tuberculin skin tests because of cutaneous anergy. However, the usefulness of anergy testing in determining tuberculin-negative persons who might benefit from treatment of LTBI has not been demonstrated. Thus, anergy testing is no longer recommended.

E. HIV Infection

All persons with HIV or AIDS should be given a TST at diagnosis. If previous tests are negative, retesting should be performed annually if the patient has other risk factors for TB and with immune reconstitution (CD4 > 200 cells/ μ l).

IV. PROCEDURES

A. Procedure for Mantoux Tuberculin Test

Prior to placing a tuberculin skin test, all persons should be assessed using the TB/LTBI Risk Assessment Tool (PH-3714, RDA-150).

Supplies and Equipment

1. PPD Antigen, Tween-Stabilized (Tubersol® or Aplisol®). Purified Protein Derivative is light and heat sensitive and when not in use it should be protected from light and stored in the refrigerator at 2°C to 8°C (35°F to 46°F). The expiration date must be strictly adhered to. Discard unused portion of opened vials after 30 days.
2. Tuberculin syringe, vanish point retractable 1.0 or 1/2 cc., with 25 gauge needle, disposable (one for each patient tested). The type of syringe utilized may change as new syringe/needle units become available.
3. Antiseptic (alcohol) and millimeter ruler.

Procedure:

1. Follow universal recommendations for infection control. Gloves should be worn during the procedure and care should be taken to avoid contact with the patient's blood. Do not recap, bend or break needles, or remove needles from the syringe.
2. The test is given in the flexor surface of the forearm (usually on the left arm) 2 to 4 inches below the elbow.
3. Cleanse injection site with alcohol sponge.
4. Cleanse vial stopper of antigen with a new alcohol sponge and insert needle into inverted bottle.

5. Withdraw 0.1 ml (excluding air bubbles) of 5 tuberculin units (TU) of PPD and have the lumen of the needle filled.
6. Never transfer tuberculin antigen from one container to another. Skin tests should be given immediately after the syringe has been filled.
7. Hold syringe horizontal to arm with the bevel of the needle pointing upward.
8. Before injecting, the skin can be tightened by grasping the underpart of the forearm and exerting pressure downward.
9. Insert needle tip between layers of the skin, with the needle bevel upward. Inject antigen. A discrete, pale elevation of the skin, i.e. a tense, white wheal 6-10 mm in diameter, should be produced when the prescribed amount of antigen (0.1 ml) is correctly injected intradermally.
10. If a discrete wheal is not produced, it is likely that the antigen was given subcutaneously rather than intradermally. Repeat the test at a different site (Note this information in the medical record).
11. Do not use Band-aids. Instruct the patient not to rub or scratch the site.
12. Give appointment for reading in 48-72 hours (tests should not be placed on a Thursday unless the test results can be measured over the weekend by a qualified/trained person).

Reading:

1. Tests should be read between 48 and 72 hours after injection, when the induration is maximal.
 - a. Tests read after 72 hours tend to underestimate the true size of induration, thus patients with a negative reaction beyond this time frame must be retested.
 - b. However, a reaction that meets the criteria for TST positivity detected after 72 hours may still be considered positive.
2. Reading should be performed in a good light, with the forearm slightly flexed at the elbow.
3. The basis of reading is the presence or absence of induration, which may be determined by inspection (from a side view against the light as well

as by direct light) and by palpation. For standardization, the diameter of induration should be measured transversely to the long axis of the forearm. Observer variability may be decreased by using the ball-point pen method to measure induration (drawing until pen stops at induration).

Note: Erythema alone is not indicative of a positive test and should not be measured or recorded.

Recording:

1. Record the manufacturer and lot number of tuberculin used. The person administering the test should record the date the test was placed and sign his/her initials next to this.
2. TST results should be recorded only in millimeters of induration. The absence of induration should be recorded as “0 mm,” not “negative.”
3. The person reading the test should record the date the test was read and initial next to the results.

B. Procedure for Two-Step Method

Two-step testing is done to detect waning sensitivity to infection with *Mycobacterium tuberculosis*. This method is used in initial skin testing of adults who will be tested periodically, such as health care workers.

1. Administer a Mantoux Tuberculin Test using 5 TU (0.1 ml) PPD in the left forearm as described above.
2. Read the test within 48-72 hours.
 - a. If reading is negative repeat the skin test one week from the first test. If positive, do not precede to second test.
 - b. If second test has no significant induration, consider it negative, depending on clinical situation. Record measurement.
3. Two-step skin testing should never be repeated, once a base line is established. All subsequent TST should be given in the left forearm and read in 48 to 72 hours.

V. QUANTIFERON TEST

Recently, CDC has published recommendations for the use of a new and licensed blood test for detecting infection with *M. tuberculosis*, the quantiFERON® test. At this time, the TDOH TB Elimination Program does not recommend this test for routine public health use, and the Tennessee State Laboratory is not currently conducting this test.

Table 1. Summary of TST Recommendations		
TST Cut-point	Risk Group	Testing Frequency
≥ 5 mm	HIV infection	At diagnosis; with immune reconstitution (CD4 > 200 cells/ μ l; annually if person has other risk factors or TB exposures.
	Recent contacts to active TB	Baseline, and if negative repeat 10-12 weeks after exposure ended.
	Radiographic or clinical findings consistent with active TB	Immediately
	Fibrotic changes on CXR suggestive of prior TB	At time of CXR
	Immunosuppression from disease, transplant or treatment with steroids, infliximab (Remicade®), etc.	Two-step testing prior to transplant, treatment or at initial diagnosis of condition; repeat only if new exposures or TB risk factors occur.
≥ 10 mm	Foreign-born persons	Upon arrival or as identified; repeat only if other risk factors including travel to high risk areas.
	Injection drug users	Initially and if risk factors change or new exposure occurs
	Resident of A&D facilities	At intake
	Inmates in correctional facilities (jail/prison)	Upon intake (two-step recommended) and annually
	Residents of long term care facilities	Two-step testing at baseline only
	Employees of congregate settings (jails/prisons, LTCF, health care facilities, residential facilities for AIDS patients, homeless shelters)	Two-step testing at baseline*, then periodically based on risk assessment of setting** (usually annually).
	Mycobacteriology lab personnel	Two-step baseline and every 6 months.
	Medical conditions associated with increased risk of progression to active TB	At diagnosis. Repeat only if new exposures or TB risk factors occur.
	Children exposed to high-risk adults	Test every 2-3 years, as indicated* (*Refer to <u>Red Book</u>)
≥ 15 mm	Low-risk adults and children $\geq 5^*$ years old	Not recommended
<p>*Use a cut-point of 15 mm if person is otherwise low-risk prior to employment in HR setting. **CDC Guidelines for Preventing the Transmission of <i>M. tuberculosis</i> in Health care Facilities; MMWR, October 1994, Vol. 43, No. RR-13. Note: For high-risk children <5 years use a cut-point of 10mm.</p>		

III. TARGETED TESTING

TARGETED TUBERCULIN TESTING GUIDELINES

I. TARGETED TUBERCULIN TESTING INITIATIVE: OVERVIEW

As the rate of active tuberculosis (TB) in the United States has decreased, the identification and treatment of persons with latent TB infection (LTBI) who are at high risk for active TB has become an essential component of TB elimination. Pursuant to such strategies, Tennessee's TB Elimination Program began to implement its Targeted Tuberculin Testing Initiative (TTI) in July 2001.

Although Tennessee's TB Elimination Program is committed to identifying and treating LTBI in all high-risk populations, the state provided a funding increase in Fiscal Year 01-02 to develop and implement a targeted tuberculin testing and treatment initiative of foreign-born persons (immigrants, refugees and residents from high-incidence countries) in Tennessee. Tennessee's TB Elimination Program considers this the priority high-risk group for targeted testing efforts based on local trends in the epidemiology of TB. The TTI policies, procedures and infrastructure currently established will lay the groundwork for future focused targeted testing efforts in other high-risk groups.

To achieve a high rate of acceptance of TB/LTBI screening, tuberculin skin testing and completion of LTBI treatment in our high-risk groups, Tennessee's TTI places much emphasis on working within high-risk communities to create educational materials and messages that are culturally and linguistically appropriate. In addition, a major TTI strategy is to conduct TB/LTBI screening and tuberculin testing services at community sites in conjunction with immigrant and refugee leaders, community advocates, faith-based entities, various non-profit organizations and employers of high-risk persons across the state. Such a collaborative effort between local health departments, community sites, and members of foreign-born and other high-risk communities will prove to be critical to TB elimination in the state of Tennessee.

II. LATENT TUBERCULOSIS INFECTION

Latent tuberculosis infection is an asymptomatic state in persons who are infected with *Mycobacterium tuberculosis*. LTBI is detected as a result of skin testing among persons with risk factors for TB. For persons with untreated latent TB infection with intact immunity, the estimated risk of developing symptomatic tuberculosis disease is up to 10% over a lifetime, with about half of that risk occurring during the first year or two after infection. For persons who are immunocompromised by HIV co-infection, the risk of developing disease increases to approximately 10% per year.

Finding persons with LTBI provides an opportunity to treat and prevent progression to active disease (reactivation). Studies have shown that LTBI treatment can prevent TB reactivation with 60%-80% efficacy. Due to relatively low TB prevalence in the United States, treatment of LTBI is considered an important public health strategy to achieve TB elimination.

III. PURPOSE OF TARGETED TUBERCULIN TESTING*

The purpose of such an initiative is to identify persons at high risk for TB who would benefit by treatment of LTBI. Following this principle, targeted tuberculin testing programs should be conducted among groups at risk for recent infection with *M. tuberculosis* and those who, regardless of duration of infection, are at increased risk for progression to active TB. With the exception of initial testing of persons at low risk whose future activity will place them at increased risk of exposure (e.g., employment in a setting where TB transmission may occur), screening of low-risk persons is discouraged because it diverts resources from activities of higher priority. In addition, a substantial proportion of tuberculin test-positive persons from low-risk populations may have false-positive skin tests.

*MMWR, Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, June 9, 2000, Vol. 49/No. RR-6.

IV. ROLE OF THE PUBLIC HEALTH DEPARTMENT

In TTI's community-based approach to high-risk tuberculin testing and treatment of LTBI, the health department TB Elimination Program should be instrumental in planning, coordinating and overseeing quality of service. The health department is responsible for assessing the community's TB problem, identifying communities of high-risk populations based on local TB epidemiology, and ascertaining the sites of most convenient access to these groups by conducting an assessment of community organizations and resources in the local health department service area. In addition, the health department should assume responsibility for organizing the community-based approach, educating the community and other health professionals about TB, motivating them to institute targeted tuberculin testing and treatment programs, and recruiting other health professionals to collaborate in the implementation of targeted tuberculin testing programs and community education. **Consideration should be given to recruiting health department employees or contractual workers from within high-risk groups** (e.g., local immigrant, refugee and foreign-born resident communities) in order to facilitate health department efforts to provide culturally and linguistically appropriate and competent services.

With Tennessee's TTI, the roles of the Central Office and rural/metropolitan regional health department TB Elimination Programs are as follows:

1. Serve as advisor, consultant, and facilitator to community providers and institutions that conduct testing and treatment programs.
2. Provide screening, evaluation and treatment for LTBI as appropriate.
3. Provide staff in-service training on targeted tuberculin testing and LTBI treatment.
4. Develop written protocols for targeted testing activities, including patient tracking codes and procedures, nursing protocols, and systems of care.
5. Provide staff in-services on providing both care and educational messages and materials that are culturally and linguistically appropriate.
6. Be responsible for providing or facilitating the ongoing evaluation of community-based targeted testing and treatment programs, including development and monitoring of program indicators (e.g., proportion of tests read that are positive, initiation and completion rates of treatment, etc.).
7. The Central Office TB Elimination Program will collect and review data to determine yield and relative effectiveness of targeted testing and treatment of LTBI in the community.

High-risk patients should not be expected to pay directly for public health interventions (e.g., testing, evaluation, and treatment of LTBI). The more convenient and culturally and linguistically appropriate the process of evaluation and treatment, the more likely it is that patients will adhere to therapy – especially as high-risk tuberculin testing and treatment of LTBI are extended beyond the province of public health TB clinics to both community sites and sites where primary health care is delivered.

V. DECISION TO TEST IS DECISION TO TREAT

The decision to administer a TST should be a decision to assess the patient, to consider treatment of LTBI if the person has a positive TST result, and to have the ability to follow-through with the patient to therapy completion. Testing is therefore discouraged unless a plan is in place to complete a course of treatment in persons found to have LTBI. Such planning should include arrangements for medical evaluation (e.g., chest radiographs) of persons with positive skin tests and medical supervision during the course of treatment. It is important to consider potential barriers to completing treatment before initiating LTBI therapy. For example, a person not planning to be in the U.S. for at least four to nine months should not be treated (refer to Section IV, *Treatment for Latent Tuberculosis Infection*). **Maximum efforts must be made to ensure that all persons initiated on LTBI therapy complete a full course.**

VI. INDIVIDUAL RISK ASSESSMENT FOR TB/LTBI

The Tennessee TB Elimination Program has developed a TB/LTBI Risk Assessment Tool (RAT) (PH-3714) and standardized screening procedure to determine whether individuals are at high or low risk for TB. The RAT is used in county health departments, regional health departments, and at community sites. It should be used as a guide to educate the patient about key issues concerning TB/LTBI, as a flow sheet to determine a patient's risk of TB/LTBI, as documentation that the counseling and risk assessment for TB/LTBI are done, and as a way to report the findings from the assessment.

The initial priority high-risk group for Targeted Tuberculin Testing in Tennessee is the foreign-born (i.e. immigrants, refugees and residents from high-incidence countries). In the local health department, such persons should be screened for TB/LTBI using the RAT. In addition, the RAT should be used prior to tuberculin testing to assess all suspects and cases, contacts or any person suspected to have risk for TB infection or disease. High-risk persons may present to any health department program such as HIV/STD clinics, WIC clinics, women's health, etc., and all health department personnel should be trained to either screen these persons using the RAT or to refer them to the health department TB Clinic for screening. In addition, this form should be used to screen any person (at health department or community site) to whom a health department employee is considering offering a PPD. At employer-based community sites, health department staff may need to screen all employees using the RAT, due to employers' requests to avoid discrimination. In these situations, educate the employers that only those employees determined to be high-risk are advised to receive a skin test. **A skin test is not necessary and should not be given to employees determined to be low-risk.**

Note: The Risk Assessment Tool is not to be used for screening Department of Health employees.

VII. TESTING FOR TB INFECTION

- Refer to Section II, Tuberculin Skin Testing, for details regarding test procedure and interpretation of results

VIII. LOW-RISK GROUPS

Routine tuberculin testing is not recommended for populations at low risk for TB/LTBI. Mandated skin-testing programs (e.g., those formerly conducted among teachers and food handlers) should be discouraged unless the groups contain substantial proportions of high-risk persons. The Tennessee Department of Health has worked with the following Agencies involving Low Risk Groups to discontinue

the practice of required tuberculin testing for administrative purposes (contact the TB Program Central Office for the most recent list of groups):

- Tennessee Department of Education
- Tennessee Department of Human Services
- Tennessee Commission on Health and Aging and Tennessee Department of Mental Health and Developmental Disabilities regarding Providers of personal support services in individual homes (**Note:** staff providing personal support in facilities will be required to have TST placed per facility licensure rules).

Note: Certain individuals within low-risk groups may be identified as having a risk factor or medical condition associated with increased risk of TB/LTBI. If such high-risk persons are identified, skin testing is indicated. However, Risk Assessment screening of these groups to identify high-risk individuals is not an efficient use of resources and thus should not be performed. For low-risk persons who are skin tested (e.g., at entry into a work site where exposure to TB is anticipated and a longitudinal tuberculin testing program is in place), a cut off of ≥ 15 mm is recommended.

IX. RETESTING HIGH-RISK PERSONS FOR TB INFECTION

Only those persons with ongoing risk of new exposure to TB should be retested. For example, it is reasonable to retest a foreign-born person if he/she has developed new risk factors for TB, such as return travel to a high-incidence country.

By definition, low-risk persons testing less than 15 mm induration are not considered TB-infected, and should be retested only if their risk status changes.

X. EVALUATION FOR ACTIVE TB

Persons who should be referred for immediate evaluation for active TB, regardless of TST result:

- Persons with symptoms of active TB
 - Child <5 years with recent contact to active TB
 - HIV-infected with recent contact to active TB
 - Immunosuppressed with recent contact to active TB
- Refer to sections on diagnosis, LTBI and TB treatment for specific management guidelines.



TUBERCULOSIS ELIMINATION PROGRAM
STATE OF TENNESSEE
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TUBERCULIN SKIN TESTING POLICY

April 2004

While tuberculosis (TB) remains a serious public health threat, the incidence of TB in the United States and Tennessee has decreased to an all-time low. In addition, the epidemiology of TB has dramatically changed in that TB disease now occurs predominantly among groups with certain risk factors. These risk factors include birth or residence in a country where TB is common, HIV infection, homelessness, residence or employment at a correctional facility, residence or employment in a long term care facility, and use of injection drugs.

In 2000, the Centers for Disease Control and Prevention (CDC) changed its approach to tuberculosis (TB) screening and testing. The previous TB “screen-all” strategies have been replaced by targeted tuberculin testing of high risk persons who would benefit from treatment to prevent this disease. Targeted tuberculin testing of high-risk populations is an effective TB control strategy that focuses TB screening and prevention efforts on groups in greatest need for these services. Under these new CDC guidelines, testing of low-risk occupational groups for administrative purposes (i.e. school teachers and bus drivers, childcare workers, adult day home workers, food handlers) is discouraged. Tuberculin testing of persons without a specified TB risk factor is low yield and may result in a falsely positive test result that could lead to the inappropriate treatment with potentially toxic TB medications.

Based on the above current CDC recommendations, the Tennessee Department of Health has instituted a policy that targeted tuberculin testing of high-risk persons should be performed statewide, and that tuberculin testing of low-risk groups be discouraged. Under this policy, tuberculin testing should only be performed for the following persons at higher risk for exposure to or infection with TB:

- Close contacts of a person known or suspected to have TB
- Foreign-born persons from areas where TB is common^{*}
- Health care workers who serve high-risk clients
- Mycobacterial laboratory workers
- Persons with HIV infection or AIDS
- Persons with medical conditions that place them at high-risk[†]
- Persons who inject illegal drugs
- Residents and staff or volunteer workers in high-risk congregate settings (alcohol and drug rehabilitation or methadone maintenance centers, homeless shelters, correctional facilities, mental health facilities, and long-term care facilities)
- Children under 18 years of age exposed to adults in high risk categories
- Homeless persons
- Persons with radiographic or clinical findings suggesting TB disease
- Residence or prolonged travel in a country where TB is common
- Other high-risk populations as locally defined by the Department of Health[‡]

If you have any questions regarding this policy, please contact the Tennessee Department of Health's Tuberculosis Elimination Program at 615-741-7247.

^{*}Includes all countries except Canada, Western Europe, Japan, Australia, and New Zealand.

[†]Includes diabetes, silicosis, end-stage renal disease, certain malignancies, immunosuppressive condition or treatment, intestinal bypass surgery or gastrectomy, chronic malabsorption syndromes, or body weight less than 10% ideal.

[‡]Designation as a locally defined high-risk population will be based on the incidence of TB disease and infection for that specific area or population; may include some medically underserved populations (i.e. US-born Asians and Pacific Islanders, Hispanics, Native Americans, or migrant farm workers).

IV. TREATMENT FOR LATENT TUBERCULOSIS INFECTION

TREATMENT OF LATENT TUBERCULOSIS INFECTION

I. GROUPS RECOMMENDED FOR LTBI TREATMENT

A. Anyone at high-risk for TB who has a positive test for latent infection is a candidate for treatment if they also fulfill the following criteria:

- No symptoms, signs, or radiographic evidence of active TB
- Willing and able to complete a full course of therapy
- Available to be clinically monitored during the full course of treatment (that is, not about to leave the country, etc.)
- Adherence to the full treatment course is likely*
- No medical contraindications to treatment, such as severe liver disease or drug hypersensitivity

**If a patient is at high-risk of developing active TB but there are medical or social conditions that make adherence unlikely (i.e., mental illness or substance abuse), directly observed preventive therapy (DOPT) can be used to facilitate treatment completion.*

B. HIV-positive or other immunosuppressed persons and children <5 years old who are contacts to active TB cases should be placed on “window period” LTBI therapy.

II. PRE-TREATMENT MEDICAL EVALUATION

A. Patient History

1. Determine the patient’s primary language and communicate through an interpreter, as indicated.
2. Review the patient’s TB/LTBI Risk Assessment Tool for any pertinent data including medical conditions that promote the development of active TB, prior treatment of TB/LTBI, HIV risk factors or symptoms suggestive of TB.
3. Determine if patient has any current symptoms of active TB disease (fever, cough, fatigue, weight loss, malaise etc.).
4. Determine if patient has any current symptoms suggestive of liver disease (anorexia, dark urine, jaundice, scleral icterus, etc.) or

- underlying neurological disease (numbness or tingling of hands or feet, dizziness, confusion, etc.)
5. Obtain a thorough review of systems, considering the possibility of extra-pulmonary TB or other symptoms that could affect LTBI treatment or adherence.
 6. Ask specifically about conditions associated with chronic or previous liver disease such as viral hepatitis or cirrhosis.
 7. Ask female patients about possible pregnancy.
 8. Inquire about diseases that run in the family, especially chronic liver or kidney disease.
 9. Record all medications that patient takes on a regular basis as well as medications he/she may take occasionally.
 - a. Ask specifically about over-the-counter medications, herbal supplements, home or native remedies.
 10. Record all allergies, and ask for details about any history of adverse reactions to medications.
 11. Obtain a social history that focuses on issues that may affect your ability to contact or monitor the patient (i.e., phone and transportation) or other barriers that may affect the patient's ability to adhere to treatment (i.e., work schedules, frequent or anticipated travel or unstable residence).
 12. Ask patient if they have any current or past substance abuse.
 - a. Ask specifically about both injection and non-injection drug use.
 - b. Ask about the number of alcoholic drinks per day/week and drinking binges (assume patient's use of alcohol is greater than they claim).
 13. After reassuring patient about confidentiality, inquire about risk factors for HIV or viral hepatitis.
 - a. These include male-male sex, multiple partners, sex with a high-risk partner (prostitute, HIV+ etc), injection drug use, non-sterile tattoos, etc.
 - b. Counsel patient about importance of protecting themselves and others from these infections and how to change high-risk behaviors.

14. Refer LTBI patients to other programs, as appropriate (HIV/STD, mental health, prenatal care, WIC, A&D programs, etc.).

B. Physical Exam

1. A *focused* physical exam should be performed on all LTBI patients including *at least*:
 - Patient's weight
 - Skin for jaundice, eyes for icterus (yellow)
 - Lymph nodes for adenopathy (swollen or tender)
 - Heart and lung exam
 - Abdomen for tenderness, liver abnormalities, or ascites (fluid)
 - Extremities for edema (swelling)
 - Other stigmata of chronic liver disease (spider angiomas, palmar erythema, gynecomastia, etc.)
2. Consider the possibility of extra-pulmonary TB and expand exam if indicated, especially in children and HIV-infected persons.

C. Further Testing

1. Obtain a chest radiograph of all patients to rule out active pulmonary TB.
 - a. Adults can have a screening Posterior-Anterior (PA) film or both PA and lateral views.
 - b. Children <5 years should have both a PA and lateral radiograph.
 - c. Because of the risk for progressive and/or congenital TB, pregnant women who have a positive tuberculin skin test should have chest radiographs (with appropriate shielding) as soon as feasible, even during the first trimester of pregnancy.
2. Sputum examination is not indicated for most persons being considered for treatment of LTBI.
3. Persons with radiographic findings suggestive of prior TB should have three consecutive sputum samples, obtained on different days, submitted for AFB smear and culture.
 - a. Examples of radiographic evidence of prior TB include:
 - 1) Dense pulmonary nodules, with or without visible calcification, in the upper lobes

- 2) Smaller nodules, with or without fibrotic scars, in the upper lobes, frequently accompanied by upper lobe volume loss
 - 3) Nodules or fibrotic lesions with well-demarcated, sharp margins
- b. Most persons with radiographs that show only pleural thickening or isolated calcified pulmonary nodules do not require sputum AFB smear or culture.
4. HIV-infected persons with respiratory symptoms who are being considered for LTBI treatment should also have sputum specimens submitted for AFB smear and culture, even if the chest radiograph is normal.
 5. **If sputum culture is indicated as above, treatment for LTBI should be deferred until the final culture results are reported as negative.**
 6. Obtain HIV testing for all persons with LTBI.
 - a. Most patients will accept HIV testing if it is encouraged and presented as a critical part of their evaluation and as the routine standard of care.
 - b. Written consent is required.
 - c. Report LTBI patients with a positive HIV test to Central Office and the Regional HIV Surveillance Representative.
 7. Obtain pregnancy test for females, if indicated.

D. Documentation

1. Details of the patient's history and evaluation must be recorded in the medical record according to established Current Procedural Terminology (CPT) documentation requirements.

III. CONSIDERATIONS BEFORE BEGINNING THERAPY

A. Medical considerations

1. Do not start treatment for LTBI unless active TB, including extra-pulmonary disease, has been ruled out.

2. History of BCG vaccination should not affect the decision to treat a high-risk person with a positive TST (i.e., ignore BCG history if from a high-risk country).
3. Consider the risk of treatment toxicity in all patients (substance abuse, liver disease, other medications that may affect the liver, etc).
4. Consider potential drug interactions, especially with rifampin/rifabutin and medications for HIV or concurrent use of dilantin and INH.

B. Age

1. Children <5 years of age who are close contacts to a TB case should have “window period” treatment for LTBI initiated, even if initial TST is negative (unless first TST was placed more than 10-12 weeks after exposure to TB ended). Treatment can be discontinued if the child is >6 months *and* the second TST performed at least 10 weeks after TB exposure is negative.

C. HIV

1. HIV-infected or other immunosuppressed **close contacts** to a TB case should be treated for LTBI after TB is ruled out, regardless of TST results.
2. HIV-infected persons who are re-exposed to an infectious TB case should be re-treated for LTBI, even if they completed a course of therapy previously (they do not develop sufficient immunity after initial exposure or treatment).

D. Pregnancy

1. For pregnant women at high risk for progression of LTBI to disease, especially those with HIV or who have been infected recently, initiation of therapy should not be delayed on the basis of pregnancy alone, even during the first trimester.
2. For women whose risk of progression to active TB is lower, some experts recommend deferring treatment until after delivery.

E. Prior BCG Vaccination

1. Children from high-TB incidence areas with a positive TST should be considered for treatment regardless of BCG since the consequences of developing active TB are potentially severe.

F. Logistical considerations

1. Determine if patient can complete treatment course (i.e., stable residence, no plans to travel out of the area).
2. Determine if patient has appropriate access and resources to enable timely communication of potential complications (phone, etc.).
3. Provide information on how patient can get help after clinic hours (i.e., the closest ER).

G. Patient education and choice

1. The patient will be informed and documentation should be made in the patient's record that the patient has been made aware:
 - a. Of signs and symptoms of possible drug toxicity
 - b. That the patient will stop LTBI medications and immediately contact the health department nurse if symptoms of toxicity or other problems occur
 - c. That the patient, parent, or legal guardian acknowledges he/she has been informed of and understands the risk/benefit ratio of LTBI treatment and agrees either to take or see that the medication is taken
 - d. That the patient will be given only a one month's supply of anti-tuberculosis drugs
 - e. That the patient is to return to the Health Department and/or TB clinic for monthly visits
 - f. That the patient should contact the health department nurse and inform them of plans to move or travel from the area

H. Provider considerations

1. When an individual is considered for LTBI treatment and does not have a personal physician, the Rural or Metropolitan Regional TB Physician should write orders to dispense prescribed treatment in the dose, frequency, and length of treatment indicated and for the appropriate laboratory clinical monitoring.

2. If a patient for whom LTBI treatment is recommended has a personal physician, that physician should be notified by the clinic physician or public health nurse, and:
 - a. Advise the physician **by phone** of the recommendation for treatment of LTBI and the appropriate TB risk factor or justification.
 - b. If the physician accepts the recommendation, make arrangements for the medicine to be dispensed. Obtain prescription from physician or obtain permission for health department physician to manage patient's LTBI treatment.
 - c. If the patient's physician does not concur with the recommendation, this should be documented in the record and brought to the attention of the Rural or Metropolitan Regional TB Physician. The Health Department physician should discuss his/her recommendations directly with the other provider to ensure that the patient receives optimal LTBI care.

IV. RECOMMENDED TREATMENTS FOR LTBI

A. Treatment of Persons Likely Infected with Drug-sensitive *M. tuberculosis*

1. Details of the treatment plan must be recorded in the medical record, including regimen, doses, duration and how it will be administered (DOPT or self-administered), and the clinical and laboratory monitoring schedule.
2. The preferred treatment for LTBI is **9 months of isoniazid (INH)** daily or twice-weekly, regardless of HIV status. Twice-weekly INH can only be given as DOPT.
 - a. Pregnant women should be treated with 9 months of INH, daily or twice-weekly.
 - b. Children and adolescents should be treated with 9 months of INH. Twice-weekly DOPT is strongly recommended as the standard of care for all children in Tennessee. Patients will be allowed to self-administer if parents refuse DOPT. (DOPT can be provided by a trained school nurse to enhance patient convenience).
 - c. For persons with fibrotic lesions on chest X-ray consistent with previous TB, INH should be given for 9 months instead of 12.

3. **6 months of INH** is acceptable if patient is unable to complete longer course.
4. **4 months of daily RIF** is an acceptable alternative to 9 months or 6 months of INH.
 - a. For persons likely to be infected with INH-resistant TB, 4 months of RIF can be used.
 - b. Rifampin may be useful to enhance compliance in targeted testing setting or for other high-risk adults who are unlikely to complete 6-9 months of INH.
 - c. HIV status should be determined prior to use of Rifampin, and HIV-positive patients with LTBI should be prescribed this regimen only if strict adherence to therapy is likely (poor adherence could lead to rifampin resistance which would be a significant problem if the patient developed active TB disease).
 - d. **4 months of Rifabutin (RBT)** can be substituted for RIF if drug interactions are present.

Note: The 2-month RIF-PZA (2RZ) regimen for LTBI should not be used.

B. Treatment of Persons Likely Infected with Drug-resistant *M. tuberculosis*

1. For contacts of MDR-TB (INH- and RIF-resistant), PZA and EMB or PZA and a fluoroquinolone (Levaquin, moxifloxacin or gatifloxacin) for 6-12 months is recommended.

Note: Consultation from the Medical Director of the TB Elimination Program should be obtained.

2. There is a high prevalence of INH-resistant tuberculosis in Vietnam, Haiti and the Philippines. Some providers recommend that persons from these countries should be treated with a rifampin-based regimen. The Regional TB Clinic Physician should determine the appropriate treatment regimen by considering the specific characteristics of each individual LTBI case (other medical problems, medication interactions, etc.).

C. Other Treatment Considerations

1. Active hepatitis and end-stage liver disease are relative contraindications to the use of INH or PZA.

2. TB suspects who have been on four-drug therapy for 6 weeks and are ruled out as cases may complete LTBI therapy with 2 additional weeks of Isoniazid, Rifampin and Pyrazinamide. Alternatively, LTBI therapy can be completed with 2.5 additional months of Rifampin or 7.5 additional months of INH.
3. Some providers recommend that low risk persons with a positive (≥ 15 mm) TST should not be treated for LTBI after TB is ruled out. The TB clinic physician should consider each individual's risk from treatment compared to the possibly lower benefits of LTBI treatment (and the possibility that the positive TST is a false-positive result).

V. MONITORING PATIENTS ON LTBI THERAPY

A. General Recommendations

- Table 6 under "Treatment of TB Disease" includes a list of treatment side effects and monitoring recommendations.
- 1. At least monthly, all patients on any LTBI therapy should have *clinical* monitoring for signs and symptoms of possible adverse effects, with prompt evaluation and changes in treatment, as indicated.
- 2. Signs and symptoms to monitor monthly include:
 - Loss of appetite
 - Fever/malaise/fatigue or weakness for longer than 3 days.
 - Nausea/vomiting
 - Jaundice/scleral icterus
 - Dark urine
 - Abdominal tenderness (especially right upper quadrant discomfort)
 - Rash
 - Dizziness/unsteadiness
 - Numbness/tingling of extremities (hands or feet).
 - Joint pains/rheumatic-like symptoms
 - Any marked behavioral change
 - Visual disturbances
 - Other signs and symptoms patient reports

3. Only a one month supply of medicine should be given to patients at each visit.

B. 9 mos. INH/ 6 mos. INH

1. Baseline and follow-up laboratory monitoring is *not* routinely indicated for most patients.
 - a. Patients whose initial evaluation suggests a liver disorder (hepatitis B or C, or cirrhosis) should have baseline hepatic measurements of ALT, AST and bilirubin at the beginning of treatment.
 - b. Baseline testing is also recommended in patients with HIV infection, pregnant women and those within 3 months post-partum, persons with chronic liver disease, and those who use alcohol regularly.
 - c. Baseline monitoring is not routinely indicated in older persons, but may be considered on an individual basis and in those taking other medications for chronic medical conditions.
2. Routine laboratory monitoring during therapy is only indicated in persons whose baseline measurements are abnormal or other persons at risk for liver disease.
3. Laboratory monitoring may be indicated for the evaluation of potential adverse effects that occur during the course of treatment.
4. Asymptomatic mild elevations of serum aminotransaminases (AT) are expected with INH use and do not require treatment to be stopped.
5. Consider withholding therapy if AT increase to ≥ 3 times the upper limit of normal, if associated with symptoms, or ≥ 5 times the upper limit of normal if the patient is asymptomatic.
6. If liver enzymes increase on therapy, ask patient about concurrent use of alcohol or other medications or substances that may be contributing.
7. Decisions to restart INH should be made carefully.

C. 4 mos. RIF/RBT

1. Baseline and follow-up laboratory monitoring is not routinely indicated for most patients but may be ordered at the provider's discretion (as per INH above).

2. Measurement of baseline AT should be considered in persons with risk factors for liver disease.
3. A complete blood count and platelet should be considered in persons with a history of low platelets or other hematologic diseases.
4. Laboratory monitoring during treatment may be indicated if patient has symptoms of an adverse reaction.
5. Rifamycin therapy should be withheld if adverse events occur (as per INH). Decisions to restart therapy should be made individually by the TB clinic physician.

D. Documentation

The following information should be documented in the medical record each month:

1. Monitoring for signs and symptoms suggestive of hepatotoxicity. Report all cases of drug induced Hepatitis on FDA Form 3500. Send a copy to MEDWATCH and a copy to Central Office TB Elimination Program.
2. Medication provided to patient, including name of medications, milligrams per pill and per dose, number of bottles, number of pills per bottle and length of supply (i.e., 1 month's supply).
3. Date and time of return appointment.
4. Any new recommendations or counseling provided to the patient.

VI. RECOMMENDATIONS FOR COMPLETION OF LTBI TREATMENT

Completion of a full course of LTBI treatment is the only way to ensure that the patient will not develop active TB and to prevent community transmission of TB.

A. Completion of LTBI Therapy

1. Completion of therapy should be based on the actual number of doses taken (Table 1).
 - a. 9-month course of INH: 270 daily doses should be given within 12 months (or 76 doses if twice-weekly DOPT given).

- b. 6-month course of INH: 180 daily doses should be given within 9 months, if longer duration of INH (9 mo.) cannot be completed.
- c. 4 months of Rifampin: 120 daily doses should be given within 6 months for adults; 180 daily doses should be given within 9 months for children.

B. Treatment Interruptions

1. If the LTBI treatment interruption is less than 2 months, patients may be restarted on therapy by the Public Health Nurse (PHN) *in consultation with the Regional TB Physician* after carefully monitoring for signs or symptoms of active tuberculosis.
2. Any patient who fails to receive his/her medicine for more than two months should be referred back to the physician for reassessment of possible TB disease (exam and CXR). If TB is again ruled out and the interruption is less than 2 months, LTBI therapy can be restarted to complete the remaining amount of doses.
3. LTBI therapy should be restarted if treatment interruption is greater than 3 months. Patient must be reevaluated for active TB by a physician and chest radiograph should be repeated prior to restarting therapy.
4. If patient fails to pick up medications, contact should be made with the patient to encourage compliance and completion of therapy. Contact can be made either in person (preferred) or by phone call.

C. Deferral of LTBI Treatment

1. If LTBI therapy is deferred for more than 2 months for any reason (i.e., until after pregnancy or rehab is complete, or patient returns from travel), a full evaluation in TB Clinic, including chest x-ray, must be repeated before LTBI therapy can be provided.

D. Follow-up for Patients who will not or cannot take LTBI Treatment

1. Patients who cannot or will not take treatment for LTBI are generally not followed clinically for reactivation of TB. Periodic clinical exams and periodic CXRs have not been shown to be effective in detecting TB reactivation before symptoms develop and are not recommended for most patients. **Annual follow-up CXR for LTBI patients will not be provided by the Health Department**, even if required for employment.
2. Patients should keep a record of their positive TST and understand its significance.

3. Patients should be instructed to seek medical care if they develop any unexplained, persistent symptoms, and to remind their provider of their TST+ status.
4. Patients who complete a course of treatment for LTBI require no further follow-up unless TB symptoms or other evidence of active disease are present.

Table 1. Treatment Regimens for Latent Tuberculosis Infection in Adults				
Drug Regimen	Dose	Completion of treatment (total minimum doses)	Adverse effects	Monitoring
Isoniazid, 9 mo	Daily: 5 mg/kg body weight (maximum, 300mg)	270 doses within 12 mo	Hepatic enzyme elevation Hepatitis Rash Peripheral neuropathy Mild CNS effects	Clinical monitoring monthly. Measurement of liver enzymes at baseline in people with risk factors for hepatitis; during treatment if patient has symptoms of adverse reactions
	Twice-weekly [†] : 15 mg/kg body weight (max. 900 mg)	76 doses within 12 mo		
Isoniazid, 6 mo	Daily: As above	180 doses within 9 mo	As above	As above
	Twice-weekly [†] : As above	52 doses within 9 mo		
Rifampin, 4 mo	Daily: 10 mg/kg body weight (max. 600mg)	120 doses within 6 mo	Hepatitis Rash Fever Thrombocytopenia Flu-like symptoms Orange-colored body fluids	Clinical monitoring monthly. Measurement of liver enzymes at baseline in people with risk factors for hepatitis; during treatment if patient has symptoms of adverse reactions
Rifabutin, 4 mo	Daily: 5 mg/kg body weight (max. 300 mg)	120 doses within 6 mo	Hepatitis, Rash, Fever, Thrombocytopenia, Flu-like symptoms Orange-colored body fluids With increased levels: Severe arthralgias Uveitis, Leukopenia Leukopenia	Clinical monitoring monthly. Measurement of liver enzymes at baseline in people with risk factors for hepatitis; during treatment if patient has symptoms of adverse reactions

[†] *Twice-weekly dosing schedule should be administered by DOPT only*

V. CLASSIFICATION AND CASE REGISTRIES

CASE DEFINITIONS FOR PUBLIC HEALTH SURVEILLANCE

I. Clinical case definition

- A. A case that meets all of the following criteria:
 - 1. A positive tuberculin skin test; and
 - 2. Other signs and symptoms compatible with tuberculosis, such as an abnormal, unstable [i.e., worsening or improving] chest radiograph, or clinical evidence of current disease; and
 - 3. Treatment with two or more antituberculosis medications; and
 - 4. Completed diagnostic evaluation.

II. Laboratory criteria for diagnosis

- A. Isolation of *M. tuberculosis* from a clinical specimen; or
- B. Demonstration of *M. tuberculosis* from a clinical specimen by nucleic acid amplification test; or
- C. Demonstration of acid-fast bacilli in a clinical specimen when a culture has not been or cannot be obtained

III. Case definitions

- A. Confirmed: a case that meets the clinical case definition or is laboratory confirmed
- B. Provider diagnosis: Patient does not meet bacteriological confirmation criteria or the clinical case definition, but the physician feels strongly that the diagnosis is *M. tuberculosis*.

Note: All cases classified as “Provider Diagnosis” must be reviewed and confirmed by the Tennessee Department of Health Tuberculosis Control Officer prior to submission in TIMS as a counted case.

CLASSIFICATION OF PERSONS EXPOSED TO AND/OR INFECTED WITH *M. TUBERCULOSIS*

IV. CLASSIFICATIONS OF TUBERCULOSIS DISEASE

- A. Class 0 - No tuberculosis exposure, not infected. No history of exposure, negative tuberculin skin test.
- B. Class 1 - Tuberculosis exposure, no evidence of infection. History of exposure, negative tuberculin skin test.
- C. Class 2 - Tuberculosis infection, no disease. Positive (significant) tuberculin skin test, negative bacteriological studies (if done), no x-ray findings compatible with tuberculosis, no symptoms due to tuberculosis.
- D. Class 3 - Tuberculosis: Clinically Active. The current status of patient's tuberculosis is described by three characteristics: location of the disease, bacteriological status, and chemotherapy status. For some patients, additional characteristics - x-ray findings and tuberculin skin test reaction - would be included.
- E. Class 4 - Tuberculosis: Not Clinically Active. History of past tuberculosis or abnormal stable x-ray findings in a person with a positive (significant) tuberculin skin test; negative bacteriological studies (if done); no clinical and/or x-ray evidence of current disease.
- F. Class 5 - Tuberculosis suspect (diagnosis pending). No confirmation or verification of tuberculosis disease or diagnostic procedures not complete. Persons not to remain in this classification more than 3 months.

V. TUBERCULOSIS CASE REGISTERS

Registers for tuberculosis patients must be maintained in the regional health offices and the metropolitan health departments. These registers assist in improving patient care, ensuring treatment, contact investigation and in assessing the magnitude and characteristics of the tuberculosis problem in the community. They are used to measure progress in meeting the Minimum Program Standards for Tuberculosis Elimination and they are required by the TB Control Act of 1971.

VI. DIAGNOSIS

DIAGNOSIS

Tuberculosis is an infectious disease that is usually symptomatic before it is suspected or diagnosed. However, in asymptomatic patients and patients with unusual manifestations, (especially extrapulmonary disease) the best diagnostic skills of the physician may be challenged. Identification of tuberculosis in these difficult cases is often possible only after an extensive diagnostic evaluation.

A definite diagnosis requires the identification of *Mycobacterium tuberculosis* by culture. Identification of the DNA of *M. tuberculosis* in a specimen by genetic probe or HPLC analysis may also be considered diagnostic. It is appropriate in some cases to make a clinical diagnosis of TB on the basis of a positive skin test and other findings, such as hilar adenopathy in a young child with a positive skin test and recent significant contact to infectious tuberculosis.

I. DIAGNOSTIC PROCESS

A. Obtain a medical history which includes the patient's exposure to tuberculosis. The history of exposure may be remote or unknown to the patient who develops clinical TB disease. The TB/LTBI Risk Assessment Tool can be used to identify:

1. Specific risk factors for TB infection
2. Clinical conditions associated with progression to TB disease once infected
3. The presence of symptoms of TB disease (pulmonary and extrapulmonary)

B. Identify other clinical findings compatible with the disease.

1. A documented positive tuberculin skin test (**Note:** a negative test does not exclude a diagnosis of tuberculosis)
2. Radiographic abnormalities compatible with tuberculosis
3. Biopsy material revealing histopathologic findings compatible with the diagnosis

C. Obtain laboratory confirmation of TB disease.

1. The growth of *Mycobacterium tuberculosis* from the appropriate specimen (including sputum, urine, spinal fluid, biopsy specimens etc.) or the identification of *M. tuberculosis* genetic material in a specimen

II. SIGNS AND SYMPTOMS

A. Generalized or Systemic

1. Fatigue, anorexia, weight loss, irregular menses, night sweats and/or low grade fever persisting for weeks or months.
2. Acute febrile illness and influenza - like symptoms, which may persist or be superimposed on a more chronic pattern

B. Pulmonary Signs and Symptoms

1. Cough, slowly progressive over weeks, productive of mucoid or mucopurulent sputum
2. Pleural pain
3. Hemoptysis
4. Shortness of breath or wheezing

C. Extrapulmonary Tuberculosis

1. Tuberculosis can occur in sites other than the lungs; extrapulmonary tuberculosis can occur with or without pulmonary disease. Tuberculosis can affect nearly any other organ in the body, with the most common extrapulmonary sites being the lymph nodes, genitourinary tract, bones and joints, meninges, and the pleural and peritoneal spaces. The tubercle bacillus is spread to these sites from the lungs, primarily via the bloodstream; this spread may be the result of either a recent or a remote infection.
2. Extrapulmonary TB can be manifested by any clinical symptom, depending on where the disease is located.
3. The diagnosis of extrapulmonary tuberculosis may require a multi-disciplinary approach, depending on the site involved. This may include obtaining special radiographic tests or performing diagnostic procedures to obtain specimens for culture.
4. All cases of extrapulmonary tuberculosis should be evaluated for pulmonary involvement with a chest radiograph and sputum sample collection.

VII. CHEST RADIOGRAPH

CHEST RADIOGRAPHS

Diagnostic radiographic procedures are among the most valuable of all the tools of modern medicine. However, there is an element of risk in human exposure to ionizing radiation. To improve utilization and reduce unnecessary x-ray exposure and expense, priorities for performing chest radiographs for specific groups of individuals have been established.

I. PERSONS WHO SHOULD HAVE A CHEST RADIOGRAPH

- A.** All known cases of pulmonary tuberculosis should receive a chest x-ray at the beginning and completion of TB therapy; chest radiographs may also be obtained during treatment to assess interim improvement or failure to improve/relapse, as determined by the clinic physician. *Initial CXR should include both PA and lateral views, but subsequent CXR can be either one or two views.*
- B.** All persons with extra-pulmonary TB should receive a PA and lateral chest x-ray at diagnosis to exclude the presence of pulmonary disease.
- C.** All individuals with pulmonary symptoms suspicious of TB (TB suspects) should receive a PA and lateral chest x-ray.
- D.** All contacts who are skin test-positive should receive a chest x-ray (1 or 2 views) to rule out pulmonary TB; those who are skin test negative but who are at particular risk of TB (e.g., children and HIV positive patients) should also receive a chest x-ray.
- E.** Because of the risk for progressive and/or congenital TB, pregnant women who have a positive tuberculin skin test or who have negative skin-test results but who are recent contacts of persons with infectious TB disease should have chest radiographs (1 or 2 views, with appropriate shielding) as soon as feasible, even during the first trimester of pregnancy.
- F.** All recent tuberculin reactors should receive a chest x-ray (1 or 2 views).
- G.** All persons being considered for treatment of LTBI should receive a chest x-ray (1 or 2 views) to exclude pulmonary TB.
- H.** All children <5 years of age with a positive skin test, a negative skin test as a contact to a case, or as a TB suspect should receive a PA and lateral chest x-ray.

II. PERSONS WHO SHOULD NOT HAVE A CHEST RADIOGRAPH

- A. Individuals requesting a routine chest x-ray with no other indication.
- B. Individuals who have completed a recommended course of treatment for LTBI.
- C. Individuals who have had tuberculosis in the past, who have had an adequate course of drug therapy and are considered to be cured.

These persons, if asymptomatic, should be instructed that they do not require routine screening for tuberculosis but should contact a private physician or health department at once for evaluation if pulmonary symptoms develop.

Periodic CXRs are not recommended for persons with prior positive TST who require routine evaluation for employment, unless the patient is being considered for LTBI treatment.

III. PRECAUTIONS FOR PATIENTS AND STAFF DURING RADIOGRAPHIC EXAMINATION

- A. Limit the field of exposure to the area above the diaphragm. Special precautions to accomplish this should be taken in young children and all women of childbearing age. This includes the use of proper lead shielding.
- B. Check the machine to assure proper collimation, at periodic intervals.
- C. Staff should not hold patients for x-rays. A family member, wearing a lead apron, should be asked to assist the patient.
- D. Film badges must be worn at all times by staff members while taking x-rays.

Only x-ray operators certified by the Board of Professions of the Healing Arts of the Tennessee Department of Health or registered x-ray technicians shall perform x-ray examinations at health department clinics.

VIII. BACTERIOLOGY

BACTERIOLOGY

Specimens are to be collected from all new or suspected cases of tuberculosis, preferably prior to initiation of TB treatment. Specimens should be collected during the first visit with a health department provider even if already obtained by another provider. Specimen containers (postage paid and pre-addressed) are available at all county health departments and should be used for mailing specimens to the State Laboratory.

I. PULMONARY SPECIMENS

A. Sputum

1. Spontaneously expectorated (natural) sputum is preferred.
2. A series of three single, early morning specimens on consecutive days (one per day) should be collected and mailed promptly after each daily collection. Subsequent spontaneously produced specimens may be collected at home, in the sputum induction booth at the clinic, or outdoors with precautions to avoid transmission to other persons. Preferably, at least one should be observed and collected by health department staff during a patient encounter (home or health department).
3. When more than one specimen is required and the first specimen is collected at the rural regional or metropolitan regional TB clinic, give the patient additional containers to take home with instructions for collecting and mailing the specimens.

B. Gastric Lavage

1. Overnight, respiratory specimens are swallowed and pool in the stomach. Mycobacterial culture can be performed on gastric fluid if collected early in the morning before the patient has eaten. Usually gastric lavage is performed in a hospital setting. Contact the State Laboratory and/or the Rural Regional or Metropolitan Regional Tuberculosis Physician for specific instructions on specimen collection and processing.

II. EXTRAPULMONARY SPECIMENS

- A. Urine.** A mid-stream specimen voided in the early morning should be submitted. It may be collected and mailed in a tightly sealed sputum container (24 hour pooled specimen is not required). Specimen bottle one-half full is adequate.

- B. Other Specimens.** These include aseptically collected specimens such as tissue, blood, pleural fluid, bronchial washing, pus, joint fluid, and laryngeal swab. Instructions regarding the collection of these specimens may be given by the TB physician/nurse or the State Mycobacteriology Laboratory.

III. LABORATORY EXAMINATION OF SPECIMENS

- A.** All sputum smears and cultures are prepared from the submitted specimens. Cultures are examined at scheduled times, for a period of six weeks.
- B.** Results of smears are available by 2:00 P.M. the day of receipt by the Lab.
1. First time positive smears (i.e., first recording by State Lab) are reported to the Provider by phone call.
 2. If requested, the Lab will phone negative smear results for special situations, such as when results will impact release from isolation or hospital discharge.
- C.** For all new patients, the first smear-positive sputum sample will be directly tested using the MTD test for *M. tuberculosis complex*. By special request, the Lab can perform the MTD test directly on smear-negative samples.
- D.** At the state lab, rapid identification of *Mycobacteria tuberculosis* and certain other species has been enhanced by the following methodologies:
1. DNA Probe: A nucleic acid hybridization test that detects ribosomal RNA
 2. High Pressure Liquid Chromatography (HPLC): Detects characteristic mycolic acid
 3. Mycobacterium Tuberculosis Direct test (MTD): A target-amplified nucleic acid probe test that detects Ribosomal Ribo-Nucleic Acid (rRNA) of *M. Tuberculosis*

IV. INTERPRETATION OF SMEAR AND CULTURE REPORTS

- A.** Microscopic observation of acid-fast bacilli (AFB) in stained smears of clinical secretions, though helpful, is not sufficient alone for a definitive diagnosis of Mycobacterial infections. A definitive diagnosis is made only

when *M. tuberculosis complex* is identified by genetic, biochemical (Nitrate test, urease) or HPLC techniques.

- B.** Quantification of the number of organisms on clinical acid fast smears is useful in evaluating early response, or lack of response, to drug therapy in the early stage of treatment. AFB smears are quantified as the number of organisms/microscopic per high power field. The following quantitative terminology is used by the state lab:

Less than 1 per HPF

1-10 per HPF

10+ per HPF

- C.** Some reports may quantify culture colonies as follows:

Less than 50 colonies - the actual colony count

50-100 colonies is 1+

100-200 colonies is 2+

200-500 colonies is 3+

More than 500 colonies is 4+

V. DRUG SENSITIVITY TESTING

Drug susceptibility testing is performed at the State Lab on all initial isolates of *M. tuberculosis complex* using the MGIT, fluorescent method. As of Spring 2004, isolates will be tested for sensitivity to: streptomycin, isoniazid, rifampin, ethambutol and pyrazinamide. Results are reportable as early as 7 to 12 days after the organism has been identified as *M. tuberculosis complex*. If after the appropriate length of time there is decreased growth or no growth in the drug medium the organism is reported as “sensitive”. Growth of the organism in drug medium indicates resistance, and is reported as “resistant”. The following is a table of the drugs used and the final concentration in the broth medium.

Streptomycin	1.0 mcg/ml
Isoniazid	0.1 mcg/ml
Rifampin	1.0 mcg/ml
Ethambutol	5.0 mcg/ml
Pyrazinamide	100 mcg/ml

- A.** The State Laboratory will automatically perform susceptibility testing for first-line drugs on all initial isolates of *M. tuberculosis complex*. Other commercial laboratories require a specific physician’s order for susceptibility

testing. **Ensure that culture and sensitivity have been ordered for any patient whose initial specimens were not submitted to the State Lab.**

- B.** Isolates requiring testing for sensitivity to second-line drug will be referred to the Center for Disease Control and Prevention (CDC) in Atlanta, Georgia.
- C.** Initial isolates of *M. tuberculosis complex* are stored by the state lab for a period of at least 5 years. Subsequent isolates of *M. tuberculosis* and other acid fast isolates (i.e., *M. kansasii*, *M. avium complex*, *M. gordonae*, *M. scrofulaceum*, *M. fortuitum* and *M. xenopi*) are held for four (4) weeks.
- D.** If susceptibility studies are required on an atypical organism, clinical information should be furnished and a specific request in writing should be submitted. These isolates are referred by the state lab to CDC for drug susceptibility studies. The CDC does not perform susceptibility studies of *M. avium complex*; these isolates are sent to National Jewish Hospital in Denver, Colorado for susceptibility testing if necessary at request of the provider.

VI. STRAIN IDENTIFICATION-UNIVERSAL FINGERPRINTING

DNA fingerprinting is used to determine whether or not individuals have been infected by the same strain of *M. tuberculosis complex*. As of January 1, 2004, fingerprinting will be automatically performed on the initial isolate for all TB cases. Specific tests used will include Restriction Fragment Length Polymorphism (RFLP), Spoligotyping, and Mycobacterial Interspersed Repetitive Units (MIRU).

Universal Fingerprinting will enhance TB Elimination efforts in several ways.

1. To identify or confirm outbreaks
2. To detect unsuspected transmission between cases
3. To identify potential laboratory contamination

If two or more cases have the same strain they are considered “clustered”, and transmission between these cases may have occurred. Local epidemiology must be used to determine a possible connection between clustered cases (i.e., determine if the cases know each other or have been in the same locations where possible transmission could have occurred). Laboratory contamination can be confirmed by fingerprinting when there is a patient with a positive TB culture but a negative AFB smear and a clinical picture inconsistent with TB. In these situations, the fingerprint may match that of another TB patient who underwent testing on the same day.

VII. INSTRUCTIONS FOR COLLECTING SPECIMENS

A. Natural Sputum Collection

Health department staff should complete the label for each specimen container, prior to providing these to the patient. The box marked “natural sputum” should be checked on the laboratory slip. The lab will not perform testing on specimens with improper or missing labels.

Instructions to Patient:

1. Collect specimen in the early morning, if possible.
2. The mouth should be rinsed with water prior to specimen collection.
3. Sputum should be coughed from deep in the chest and placed in the sterile, 50 ml. plastic tube provided.
4. A hot drink or breathing deeply over a steam kettle may help raise sputum.
5. A specimen of 2 to 10 ml volume is adequate; container should not be more than half full, 1/3 - 1/2 full container is ideal.
6. Clean the outside of the bottle before placing it in the mailing container.
7. Be sure the top is placed securely on the specimen container and each of the metal containers.
8. Do not remove the pre-dated lab slip from the container. Leave the numbered tear strip on the specimen container.
9. Mail one specimen each day. (Pooled specimens should be discouraged because of the contamination rate).
10. Place the addressed, post-paid container in the mailbox.
11. Notify the Health Department when the specimens have been submitted so the nurse can obtain the results for you in a timely manner.

B. Procedures for the collection of induced sputum specimens

Getting Started

1. Obtain permission from the physician prior to induction of sputum in young children and debilitated adults.

2. The ultraviolet light and exhaust fans should be turned on at the beginning of clinic and may be turned off at the conclusion of the clinic.
3. Assemble and prepare the nebulizer for use according to the operator's manual.
4. Materials needed
 - "Kleenex" tissue.
 - Specimen bottle and lab slip.
 - Small waste-basket lined with plastic bag in booth for disposal of tissue.
 - Liquid detergent. "NEVER USE SOAP."
 - 4" x 4" gauze squares (soft lint free cloth).
 - 2 percent glutaraldehyde
 - Distilled water - to rinse nebulizer chamber after soaking in 2% glutaraldehyde.
 - Sterile distilled water to be used in nebulizer chamber.
 - Accordion disposable plastic tubing.
 - T-adaptor and mouthpiece.
 - Rubber gloves - to immerse and remove nebulizer chamber from 2% glutaraldehyde.

Instructions to Patient

1. The patient should be seated in the booth.
2. Do not look directly at the ultraviolet light.
3. Open mouth and inhale the aerosol mist deeply several times.
4. Remove mouthpiece on exhalation or cough.
5. Cough and expectorate into specimen bottle.
6. Put lid on specimen bottle, and wipe off with tissue.

Instructions to Operate Sputum Induction Unit

1. Staff members should not remain in the sputum booth with the patient, however, the patient shall be observed through the window of the booth at all times. Staff members should not enter sputum booth for 10-20 minutes after induction. If situation warrants staff member entering the booth, wear appropriate personal protective equipment (N-95 mask).

2. It may take 10 to 15 minutes to produce an induced specimen. However, the procedure should be terminated if the patient is unable to produce a specimen in 20 minutes. The patient should be given a sputum container as he leaves the booth, since he may be able to produce a spontaneous specimen 30 minutes to several hours after the induction process is terminated. The patient should be instructed to mail such a specimen to the laboratory.
3. A new mouthpiece, T-tube, and accordion tubing are to be used for each patient and should be discarded following use.
4. Induced specimens are watery therefore, laboratory slips should be checked as "Induced Sputum."
5. At the end of each day's use the nebulizer should be disassembled and cleaned according to the operator's manual.
 - a. Nebulizer parts should be immersed in 2% glutaraldehyde for at least 20 minutes but overnight immersion is preferred.
 - b. After immersion in 2% glutaraldehyde, nebulizer parts should be rinsed thoroughly in distilled water and allowed to air dry.
 - c. Use rubber gloves during this process and avoid contact with skin and eyes.
 - d. Discard prepared glutaraldehyde solution after 14 days.

Note: The proper use of the ultrasonic nebulizer aids in the production of adequate specimens. Adherence to the above instructions minimizes the danger of iatrogenic infection.

6. The ultraviolet light should be dusted at least every 30 days. The ultraviolet light bulb should be replaced at least every two years, and the date the bulb replaced recorded in a log.

IX. TREATMENT OF TUBERCULOSIS



STATE OF TENNESSEE
DEPARTMENT OF HEALTH
CORDELL HULL BLDG.
425 5TH AVENUE NORTH
NASHVILLE TENNESSEE 37247

PHIL BREDESEN
GOVERNOR

KENNETH S. ROBINSON, M.D.
COMMISSIONER

June 1, 2004

Dear Doctor:

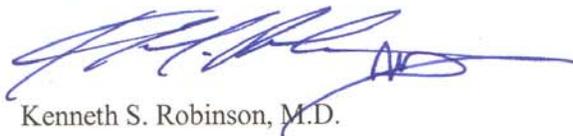
Despite the high potential for cure of tuberculosis (TB) with available therapeutic regimens, actual achievement of such cure in practice is far less certain. The nature of the treatment regimen itself poses special challenges for patients and for their health care providers. Successful treatment typically requires multiple drugs taken together on a daily, twice weekly or thrice weekly schedule continually for at least 6 months. Treatment failure generally occurs, either through premature cessation of all drugs, or through erratic drug taking. Inappropriate therapeutic prescription types or combinations of anti-TB drugs can also cause treatment failure and the development of drug resistance.

In order to enhance Tennessee's TB elimination efforts, the Tennessee Department of Health has adopted directly observed therapy (DOT) as the standard of care for the treatment of active TB. This strategy is also recommended by the Centers for Disease Control and Prevention (CDC). With DOT, a health care provider or some other trained and responsible person (not related to the patient) observes the patient swallowing each dose of anti-TB medication. DOT may be administered with daily or intermittent regimens and may be given to patients in an office or clinic setting or in the patient's home, place of employment, school, or other mutually agreed upon site. All county health departments in Tennessee provide this service upon request.

Additionally, the Department of Health has adopted and recommends the utilization of a 6 month regimen. The initial regimen should consist of Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB). PZA may be discontinued after 2 months. EMB may be discontinued when the results of the drug susceptibility studies are available.

Your assistance with using the 4 drug regimen for treating suspected and/or confirmed active TB disease and encouraging and educating patients about DOT will contribute greatly toward the effort to eliminate TB in Tennessee. If you have any questions or need assistance, please contact the Tennessee TB Elimination Program at (615) 741-7247 or your county health department. Your consideration is greatly appreciated.

Sincerely,



Kenneth S. Robinson, M.D.
Commissioner

TREATMENT OF TUBERCULOSIS

I. RESPONSIBILITY FOR SUCCESSFUL TREATMENT

A. The overall goals for treatment of tuberculosis are:

- To cure the individual patient,
 - To prevent the development of resistance, and
 - To minimize the transmission of *Mycobacterium tuberculosis* to other persons.
1. The prescribing physician, whether in the public or private sector, is carrying out a public health function with responsibility for:
 - a. prescribing an appropriate regimen
 - b. ensuring successful completion of therapy
 - c. monitoring adherence and toxicity throughout treatment.
 2. Oversight of treatment may be shared between a public health program and other providers and organizations including private physicians, community health centers, migrant health centers, correctional facilities, hospitals, hospices, long-term care facilities and homeless shelters.
 3. Regardless of the means of providing treatment, the ultimate legal authority for assuring patient completion of therapy rests with the public health system.
 4. **For all TB cases and suspects, the Health Department TB provider or Health Officer should communicate directly with the patient's other medical care providers to ensure that responsibility for all aspects of the patient's treatment and management are clearly established.** Given the expertise of Department of Health TB physicians, other providers should be encouraged to allow the TDOH physicians to manage all cases.

II. ORGANIZATION AND SUPERVISION OF TREATMENT

A. **Patient-Centered Care:** “a comprehensive framework that addresses both clinical and social issues of relevance to the patient”. Treatment is tailored to each individual patient and is based on the patient's clinical and social circumstances.

1. Patient-centered care should be the management strategy for all TB cases and suspects, regardless of whether the primary TB provider is the health department or a private provider. This strategy should also be used for TB

patients in corrections, long-term care facilities or other settings where the health department may not provide day-to-day care.

2. For all TB cases and suspects, the health department is ultimately responsible for ensuring that adequate, appropriate diagnostic and treatment services are provided, and for monitoring the results of therapy.
3. The *TB Clinical Pathway* (PH 3742) should be utilized to ensure appropriate and timely evaluation, treatment, monitoring and follow-up for all TB cases and suspects.
4. A public health nurse should be assigned responsibility as case manager for each TB case or suspect. This entails frequently reviewing the patient's TB Clinical Pathway and other medical records to ensure that appropriate management is provided and treatment is completed in a timely manner according to CDC and TDOH TB Program standards.
5. **Patient-centered care should include an adherence plan emphasizing directly observed therapy (DOT).**
6. Each patient's management plan should be individualized to incorporate other measures that facilitate adherence to the drug regimen. Such measures may include social service support, treatment incentives and enablers, housing assistance, referral for treatment of substance abuse, provision of other medical services like immunizations or prenatal care, assistance with enrollment in TennCare or obtaining other financial assistance, and coordination of tuberculosis services with those of other providers.
 - Possible components of a multifaceted, patient-centered treatment strategy are listed in Table 1.

III. DIRECTLY OBSERVED THERAPY AND ADHERENCE TO THERAPY

- A. Under DOT, patients are observed ingesting each dose of anti-tuberculosis medications, in order to maximize the likelihood of completion of therapy.
 - Specific guidelines for DOT are included in Section XI.
1. **DOT is the *National* standard of care for treatment of tuberculosis and should be utilized for all TB cases and suspects in Tennessee.** (Although all patients should be provided this service, priority situations for the use of DOT are listed in Section XI. Central Office should be notified by the Health Officer if a Rural or Metropolitan Regional TB Program cannot deliver DOT to all cases and suspects).

2. DOT enables early identification of non-adherence, adverse drug reactions, and clinical worsening of tuberculosis.
3. DOT provides a close connection to the health-care system for patients at high risk of other adverse health events and, thus, should facilitate identification and management of other conditions that may impact or result from TB treatment.
4. DOT cannot be limited merely to passive observation of medication ingestion. **There must be aggressive interventions when patients miss doses.**
5. Using DOT in conjunction with intensive educational efforts and fixed-dose combination preparations of medications may improve patient adherence and completion of therapy.
6. The use of DOT does not guarantee ingestion of all doses of every medication. Patients may miss appointments, may not actually swallow the pills, or may deliberately regurgitate the medications. Consequently, **all patients, including those who are being treated using DOT, should continue to be monitored for signs of treatment failure.**
7. If a patient continues to exhibit non-adherence to treatment recommendations, clinic appointments or other aspects of TB management, legal action such as a Health Directive, court-ordered DOT, or legal detainment should be pursued to ensure completion of therapy and maximal protection of the public.

B. Detecting and Preventing Non-adherence

Patient non-adherence is the primary reason for treatment failures and relapses. Non-adherence is found in patients of all ages.

Predicting which patients will be non-adherent is a difficult task. Therefore, *every patient should be considered a potential defaulter.*

1. Non-adherence Indicators:
 - a. Patient will not accept that he/she has TB and will not accept that it can harm him/her.
 - b. Patient has undue concern about possible side effects of the drugs.
 - c. Patient has extreme fears or misconceptions about TB, the health department, etc.
 - d. Parent indicates concern about child on TB drugs who has difficulty taking medicine, or parent refuses medication for child.

- e. Patient complains about clinic or staff.
- f. Patient is elderly, on other medication and/or seems confused about medication.
- g. Patient indicates you do not trust him/her.
- h. Patient is homeless
- i. Patient abuses alcohol or drugs.
- j. Patient does not keep appointments after being reminded.
- k. Patient is late for first 2 appointments.
- l. Sputum doesn't convert within 2 months, or patient fails to send in sputum specimen.
- m. Chest-x-ray doesn't improve.
- n. Patient has a history of non-adherence to treatment of LTBI or other medical conditions.
- o. Communication barriers exist.
- p. Cultural or religious barriers to treatment exist.

2. How to Detect Non-adherence:

- a. Identify patients who fail to keep appointments.
- b. Identify patients who have not converted their sputum to negative within the expected time frame.
- c. Ask in a non-threatening manner if patient is taking medication.
- d. Identify patients with prior history of low adherence.
- e. Use tests for measuring levels of tuberculosis drugs and their metabolites for patients suspected of not taking their medication.
- f. Conduct a pill count at each home or clinic visit.
- g. Evaluate urine sample for orange discoloration if taking rifampin.
- h. Patients on PZA usually have elevated uric acid levels.

3. How to Improve Adherence:

- a. Directly observed therapy.
- b. Improve staff-patient rapport, especially communication, written instructions and patient education.
- c. Promptly contact patients who miss appointments and assist the patient in solving problems affecting adherence (providing transportation, reminding of appointment).
- d. Tailor the taking of TB medications with the patient's daily habits, e.g., having morning coffee or meals, including the use of reminders.
- e. Simplify the treatment as much as possible. Use combination drugs (rifamate®, rifater®) and intermittent treatment (2-3 times per week).
- f. Negotiate with the patient regarding clinic appointments, medication schedule, etc.
- g. Educate and engage other friends or family members who can encourage adherence (avoid persons with adverse influence).

- h. Provide clear verbal and written instructions for taking medication in appropriate language.
- i. Provide information to patients about therapeutic response to treatment and test results.
- j. Encourage and praise patient when possible.
- k. Provide closer supervision including home visits for counseling, monitoring, collection of sputum and lab specimens, and DOT.
- l. Do not take an “either/or” position with patients, especially with alcohol users.
- m. Tell the patient the drugs cannot be used for other illnesses. Some patients will save expensive medicine for another illness.
- n. If possible, prevent long waits to see physician.

Note: One study showed only 31% adherence for patients waiting more than one hour to see physician; 57% adherence if waiting period was less than one-half hour.

- o. Send patients Christmas, birthday, and get well cards when hospitalized.
- p. Have patient see physician frequently.
- q. Fear-arousing health messages including quarantine and confinement of patients for failure to comply should be reserved until all other strategies have failed.

IV. DRUGS USED FOR TREATING TUBERCULOSIS

➤ The drugs currently recommended for treatment of TB disease are listed in Table 2.

A. First-line antituberculosis agents:

1. Isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA) form the core of initial treatment regimens.
2. Rifabutin and rifapentine may also be considered as first-line agents under specific situations.
 - a. Rifabutin is useful for treating tuberculosis in patients concurrently taking drugs that have unacceptable interactions with other rifamycins. Rifabutin is not FDA approved for treatment of TB.
 - b. Rifapentine can be substituted for RIF and used in a once-weekly regimen with INH during continuation phase of treatment if all of the following criteria are met:

- 1) Pulmonary disease with no cavity on the initial CXR
- 2) Culture conversion to negative (on 2 consecutive months) must be documented within 2 months of starting treatment.
- 3) Patient must have documentation of negative HIV status.
- 4) Organism sensitive to INH, RIF and PZA
- 5) Not Pregnant

B. Second-line antituberculosis agents:

1. Streptomycin (SM) was formerly used as a first-line agent and in some instances is still used in initial treatment; however, concern with increasing rates of resistance to SM in many parts of the world has decreased its overall usefulness.
2. Ethionamide, cycloserine, para-aminosalicylic acid (PAS), amikacin/kanamycin, and capreomycin are reserved for special situations such as drug intolerance or resistance (see this section, XII C, “Drug Resistance”).
3. Fluoroquinolones are commonly used to treat tuberculosis caused by drug-resistant organisms or for patients who are intolerant of some of the first-line drugs. Levofloxacin is the preferred FQ, given its good safety profile with long-term use. While Moxifloxacin and gatifloxacin have the best activity against *M. tuberculosis*, there is limited data on the long-term safety and tolerability of these drugs. Ciprofloxacin and ofloxacin are not recommended for TB treatment.
4. Amikacin and kanamycin are nearly identical aminoglycoside drugs used in treating patients with tuberculosis caused by drug-resistant organisms. There is no cross-resistance between SM and amikacin or kanamycin (although resistance to all may occur as independent events); however, cross-resistance between amikacin and kanamycin is universal.
5. Fluoroquinolones, amikacin and kanamycin are not FDA approved for treatment of TB.
6. Drugs available at the Regional Pharmacy include: isoniazid, rifampin, rifamate (combination INH and RIF), pyrazinamide, ethambutol, streptomycin, capreomycin, cycloserine, and ethionamide. Amikacin, kanamycin, and levofloxacin can be supplied on an individual basis. Paraminosalicylic acid (PAS) is available from the CDC
 - Doses of antituberculosis drugs are listed in Table 3.
 - Suggested Doses of pyrazinamide and ethambutol using whole tablets for adults weighing 40-90 Kg are listed in Tables 4 and 5, respectively.

- Tables 6 and 7 provide specific information regarding medication side effects and recommendations for monitoring.
- Table 8 outlines instruction for giving streptomycin and other injectable TB drugs.

C. Pyridoxine (B6)

1. Pyridoxine is not required for all patients taking INH for TB (or LTBI). However, B6 should be used for patients with HIV infection, diabetes, neuropathy, alcoholism, cancer, chronic liver disease, pregnancy (up to 3 months post-partum), and malnourishment (more than 10% underweight).
2. B6 should also be given to breast feeding infants whose mothers are taking INH.
3. B6 can be used to treat persons who develop paresthesia during INH treatment.
4. Recommended dose for B6 is 25mg for each 300mg of INH daily or 50mg for twice or thrice weekly therapy. Pregnant women should take 50mg daily.
5. B6 should be used at a dose of 50mg for each 250mg of cycloserine up to a maximum of 200mg daily.

V. RECOMMENDED TREATMENT REGIMENS

Currently recommended treatment regimens are largely based on evidence from clinical trials and rated using a system developed by the United States Public Health Service and the Infectious Disease Society of America. The rating system includes a letter (A [best], B, C, D, or E) that indicates the strength of the recommendation and a Roman numeral (I [best], II, or III) that indicates the quality of evidence supporting the recommendation (Table 10).

There are four recommended regimens for treating patients with tuberculosis caused by drug-susceptible organisms (Table 11). Although these regimens are broadly applicable, there are modifications that should be made under specified circumstances (MMWR 2003;52,RR-11:1-77). Each regimen has an *initial phase* of 2 months followed by a choice of several options for the *continuation phase* of either 4 months or 7 months. The initial phases are denoted by a number (1-4), and the continuation phases that relate to the initial phase are denoted by the number plus a letter designation (a,b,c).

- The general approach to treatment is summarized in Figure 1.

- Recommended regimens together with the number of doses specified for the regimen are described in Table 11.

A. Initial Phase:

1. Because of the relatively high proportion of adult patients with TB caused by organisms that are resistant to INH, **4 drugs are necessary in the *initial phase* for the 6-month regimen to be maximally effective.**
 - a. In most circumstances, the treatment regimen for all adults with previously untreated tuberculosis should consist of a 2-month *initial phase* of isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) (Table 11).
 - b. In children whose visual acuity cannot be monitored, EMB is usually not recommended except when there is an increased likelihood of the disease being caused by INH-resistant organisms (Table 12).
 - c. If PZA cannot be included in the *initial phase* of treatment, or if the isolate is resistant to PZA (an unusual circumstance), the *initial phase* should consist of INH, RIF and EMB given daily for 2 months (regimen 4). Examples of circumstances in which PZA may be withheld include severe liver disease, active gout, and during pregnancy. EMB should be included in the *initial phase* of regimen 4 until drug susceptibility is determined.
2. The *initial phase* may be given daily throughout (regimens 1 and 4) or daily for 2 weeks then twice weekly for 6 weeks (regimen 2). While current CDC/ATS/IDSA guidelines recommend that treatment can be given 3 times weekly throughout (regimen 3, given a “B” rating), TDOH recommends that this regimen should generally be used only for select patients, such as those who are not initially infectious (under isolation) and patients with end stage renal disease who receive therapy after dialysis.
3. For patients receiving daily therapy, EMB can be discontinued as soon as the results of drug susceptibility studies demonstrate that the isolate is susceptible to INH and RIF. When the patient is receiving less than daily drug administration, expert opinion suggests that EMB can be discontinued safely in less than 2 months (i.e., when susceptibility test results are known), but there is no evidence to support this approach.
4. Although clinical trials have shown that the efficacy of streptomycin (SM) is approximately equal to that of EMB in the *initial phase* of treatment, the increasing frequency of resistance to SM globally has made the drug less useful currently. Thus, SM is not recommended as being interchangeable

with EMB unless the organism is known to be susceptible to the drug or the patient is from a population in which SM resistance is very unlikely.

B. Continuation Phase

1. The *continuation phase* (Table 11) of treatment should consist of INH and RIF given for either 4 months or 7 months.
 - a. The 4-month *continuation phase* should be used in the large majority of patients.
 - b. The 7-month *continuation phase* is recommended only for two groups:
 - 1) Patients with cavitary pulmonary tuberculosis, caused by drug-susceptible organisms, whose sputum cultures are positive at the time of completion of 2 months of treatment; and
 - 2) Patients whose *initial phase* of treatment did not include PZA.
 - c. In some circumstances the continuation phase may be extended beyond 7 months, such as for TB meningitis.
2. The *continuation phase* may be given daily (regimens 1-a and 4-a), 2 times weekly by DOT (regimens 1b, 2a, and 4b), or 3 times weekly by DOT (regimen 3a).
 - a. For HIV-seronegative patients with non-cavitary pulmonary tuberculosis (as determined by standard chest radiography) and negative sputum smears at completion of 2 months of treatment, the *continuation phase* may consist of **rifapentine and INH** given once-weekly for 4 months by DOT (regimens 1c and 2b) (Figure 1).
 - 1) If the 2-month *culture* is positive the continuation phase should be extended to 7 months.
3. All of the 6-month regimens, except the INH-Rifapentine once-weekly continuation phase for persons with HIV infection, are rated as AI or AII, or BI or BII in both HIV-infected and uninfected patients.
 - a. The once weekly continuation phase is contraindicated (rating E I) in patients with HIV infection because of an unacceptable rate of failure/relapse, often with rifamycin-resistant organisms.
 - b. For the same reason twice weekly treatment, either as part of the *initial phase* (regimen 2) or *continuation phase* (regimens 1b and 2a) is not

recommended for HIV-infected patients with CD4 cell counts < 100 cells/ml. These patients should receive therapy either daily or 3 times weekly during treatment. Regimen 4 (and 4a/4b) is rated CI for patients without HIV infection and CII for those with HIV infection.

C. Alternative Regimens

1. If INH cannot be used (resistance or intolerance), a 6 month regimen using RIF, PZA and EMB throughout treatment is nearly as efficacious as an INH-containing regimen (rating BI).
2. Alternatively, RIF and EMB for 12 months may be used, preferably with PZA during at least the initial 2 months (rating BIII).
3. If RIF cannot be used, INH, EMB and a fluoroquinolone should be given for a minimum of 12-18 months supplemented with PZA during at least the first 2 months (rating BIII).
4. An injectable agent may also be included for the initial 2-3 months for patients with extensive disease or to shorten the duration (e.g. to 12 months).
5. Levofloxacin, moxifloxacin, and gatifloxacin may be useful in alternative regimens, but the potential role of a fluoroquinolone and the optimal length of therapy have not been defined.
6. In situations where multiple first line agents cannot be used because of intolerance, regimens based on the principles described for treating MDR-TB should be used (XII-C, "Drug Resistance" found in this "Treatment Section").

VI. DECIDING TO INITIATE TREATMENT

- A. The decision to initiate combination antituberculosis chemotherapy should be based on epidemiologic information, clinical, pathological, and radiographic findings, and the results of microscopic examination of acid-fast (AFB) stained sputum (smears) (as well as other appropriately collected diagnostic specimens) and cultures for mycobacteria.
 1. A positive AFB smear provides strong inferential evidence for the diagnosis of tuberculosis.
 - a. **A negative PPD-tuberculin skin test does not exclude the diagnosis of active tuberculosis.**

- b. However, a positive PPD-tuberculin skin test supports the diagnosis of culture-negative pulmonary TB.
2. If the suspicion of tuberculosis is high or the patient is seriously ill with a disorder that is thought to be TB, either pulmonary or extrapulmonary, **combination chemotherapy using one of the recommended regimens should be initiated promptly**, often before AFB smear results are known and usually before mycobacterial culture results have been obtained.
3. If the diagnosis is confirmed by isolation of *M. tuberculosis* or a positive rapid amplification test, treatment can be continued to complete a standard course of therapy (Figure 1).
4. When the initial AFB smears *and* cultures are negative, a diagnosis other than tuberculosis should be considered and appropriate evaluations undertaken.
 - a. If no other diagnosis is established and the PPD-tuberculin skin test is positive (5 mm or greater induration), empiric combination chemotherapy should be initiated.
 - b. If there is a clinical or radiographic response within 2 months of initiation of therapy, a diagnosis of culture-negative pulmonary tuberculosis can be made and treatment continued with an additional two months of INH and RIF to complete a total of 4 months of treatment, an adequate regimen for culture-negative pulmonary tuberculosis.
 - c. If there is no clinical or radiographic response by 2 months, treatment can be stopped and other diagnoses including inactive TB should be considered.
5. If suspicion for active tuberculosis is low, treatment can be deferred until the results of sputum AFB smears and mycobacterial cultures are known and a comparison chest radiograph is available (usually within 2 months) (Figure 2).
 - a. In low-suspicion patients not initially being treated, if cultures remain negative, the PPD-tuberculin skin test is positive (5 mm or greater induration), and the chest radiograph is unchanged after 2 months, the two regimens recommended for the treatment of latent tuberculosis infection could be used (see Section IV, “Latent TB Infection”).
 - 1) INH for a total of 9 months, or
 - 2) RIF with or without INH for a total of 4 months.

Note: RIF and PZA for 2 months should not be used.

6. Reporting in TIMS

- a. Culture-confirmed case: diagnosis is confirmed by isolation of *M. tuberculosis* or a positive rapid amplification test.
- b. Clinical case: AFB cultures are negative, *and* TST is positive (>5mm), *and* patient has a clinically compatible syndrome, *and* CXR is abnormal and improves with adequate therapy, *and* patient is receiving treatment for active TB disease.
- c. Provider-verified: Any patient with disease clinically compatible with active pulmonary tuberculosis that responds to appropriate antituberculosis therapy but fails to meet the criteria of both a culture-confirmed and clinical case. **Provider-verified cases must be submitted to Central Office for review and approval prior to counting these cases in TIMS.**

VII. BASELINE AND FOLLOW-UP EVALUATIONS

- Table 7 contains comprehensive recommendations regarding baseline and follow-up monitoring for specific medications.

A. Recommended time frames

1. Contact suspects or cases within 24 hours of notification and make arrangements for a visit.
2. A TB nurse should assess all new suspects or cases within 3 working days of notification.
 - a. Patients at home:
 - 1) The nurse should telephone the patient within 24 hours of notification and make arrangements for a home visit to evaluate the patient for infectiousness, obtain a medical history, identify sites where medical records may be obtained (primary physician's office, hospitals, consultant's offices, etc.), obtain sputum or other lab samples, provide education regarding TB to the patient and their family, and initiate contact investigation if indicated.
 - 2) The nurse should determine if urgent medical treatment is indicated (i.e. patient appears very ill, patient cannot be isolated at home, etc.).

- 3) The nurse should obtain the appropriate medical records for the patient within 24 hours of notification (admission summary, clinic notes, sputum and lab results, current medication lists with dosages and dates of treatment, radiology reports, pathology or microbiology reports, etc.).
 - 4) All medical information regarding the case should be discussed with the TB clinic physician or Health Officer within 24 hours of notification of the case/suspect.
 - 5) The nursing assessment should be discussed with the TB clinic physician or Health Officer within 24 hours of evaluating the patient.
- b. Patients in the hospital
- 1) The nurse should obtain the appropriate medical records for the patient within 24 hours of notification (admission summary, clinic notes, sputum and lab results, current medication lists with dosages and dates of treatment, radiology reports, pathology or microbiology reports, etc.).
 - 2) All medical information regarding the case should be discussed with the TB clinic physician or Health Officer **within 24 hours of notification of the case/suspect**.
 - 3) Nurse should telephone the patient within 24 hours of notification and make arrangements for a hospital visit within 3 working days to assess the patient's needs and begin discharge planning.
 - 4) The assessment, including discharge planning, should be discussed with the TB clinic physician or Health Officer within 24 hours of evaluating the patient.
3. The TB clinic physician or Health Officer should determine whether the patient needs immediate evaluation by a TB physician or can be safely seen in the next scheduled TB clinic (within one week).
- a. Patients who have already been evaluated by another provider and have received adequate management may be scheduled for TB clinic at the discretion of the TB physician or Health Officer.
 - b. Patients who are managed solely by a private provider may not require any evaluation in TB clinic.

B. Baseline Evaluation

1. A physician or nurse clinician should conduct a thorough medical history and physical exam on all TB suspects or cases. Consideration should be given to whether the patient may have pulmonary TB, extra-pulmonary TB or both.
2. Chest radiograph should be performed for all patients suspected of having either pulmonary or extra-pulmonary TB.
3. Patients suspected of having tuberculosis should have appropriate specimens (sputum, urine, bronchoscopy washing, biopsy etc.) collected for microscopic examination and mycobacterial (AFB) culture, preferably prior to initiation of therapy.
4. When the lung is the site of disease, three early morning sputum specimens should be obtained on consecutive days. Sputum induction with hypertonic saline may be necessary to obtain specimens and bronchoscopy may be considered for patients who are unable to produce sputum, depending on the clinical circumstances.
5. For extra-pulmonary disease, cultures should be obtained from appropriate body fluids or tissue.
 - a. Specimens should not be collected in formalin, as it may inhibit growth of *M. tuberculosis*.
 - b. Sputum specimens to evaluate for co-existing pulmonary disease should also be collected.
6. Susceptibility testing for INH, RIF, and EMB (\pm SM) should be performed on a positive initial culture, regardless of the source of the specimen. Second-line drug susceptibility testing should be done only in reference laboratories and should be limited to specimens from patients who have had prior therapy, who are contacts of patients with drug-resistant tuberculosis, who have demonstrated resistance to rifampin or to other first-line drugs, or who have positive cultures after more than 3 months of treatment.
7. **It is recommended that *all* patients with tuberculosis have counseling and testing for HIV infection, at least by the time treatment is initiated, if not earlier.**
8. Patients with risk factors for hepatitis B or C (e.g., injection drug use, foreign birth in Asia or Africa, HIV infection) should have serological tests for these viruses. Hepatitis serology should also be considered for persons

with abnormal liver enzymes at baseline or who give a history of previous liver disease.

9. Baseline measurements of serum aminotransferases (AST, ALT), bilirubin, alkaline phosphatase, and serum creatinine and a platelet count should be obtained for all patients. Measurement of uric acid is not generally necessary.
10. Baseline testing of visual acuity and red-green color discrimination should be obtained when EMB is to be used. For visual acuity, use the Snellen chart to test each eye separately and jointly (Table 9). For children, only visual acuity and color perception tests are necessary.
11. Baseline audiogram, vestibular testing, Romberg testing and serum creatinine should be obtained when streptomycin is to be used. To screen for auditory dysfunction, ask patient to discriminate a whispered voice at 20 feet or watch ticking at 1-3 inches from the ear. Test each ear separately and where appropriate, do audiogram. Question the patient about tinnitus. For the Romberg test, have the patient stand with their feet close together and their eyes closed and evaluate for swaying of the body or falling). Inquire about a history of dizziness or unsteadiness of gait, especially when patient is in the dark or their eyes are closed.

C. Follow-up evaluation

1. A nurse or physician should perform a **clinical evaluation** for all TB patients at least monthly to identify possible adverse effects of the antituberculosis medications and to assess for adherence.
 - Table 6 contains specific recommendations regarding monitoring for each medication.
 - Table 7 contains a monitoring schedule for TB patients throughout therapy.
 - The Drug Screening and Monitoring Record (Form PH-2040) should be used to monitor patients for signs and symptoms suggestive of toxicity to specific drugs.
2. For patients with pulmonary TB, a **sputum specimen** for AFB smear and culture should be obtained at a minimum of monthly intervals until sputums are negative on *culture for 2 consecutive months*. More frequent AFB smears may be useful to assess the early response to treatment and to provide an indication of infectiousness. For patients with extrapulmonary TB, the frequency and kinds of evaluations will depend on the site involved.

3. **Drug susceptibility tests** should be repeated on isolates from patients who have positive cultures after 3 months of treatment.
4. **Chest Radiography**
 - a. For patients with positive cultures at diagnosis, a repeat chest radiograph at completion of 2 months of treatment may be useful but is not essential. A chest radiograph at completion of therapy should be done to provide a baseline against which subsequent examinations can be compared.
 - b. For patients with culture-negative pulmonary TB, a chest radiograph should be done at completion of 2 months of treatment and at completion of therapy to assess clinical improvement.
 - c. Chest radiography can be obtained to monitor progress or evaluate problems at any point during therapy at the provider's discretion.
5. **Laboratory monitoring:** Routine measurements of hepatic and renal function and platelet count are not necessary during treatment unless patients have baseline abnormalities or are at increased risk of hepatotoxicity (e.g., hepatitis B or C infection, alcohol abuse).
6. **Vision monitoring:** Patients taking EMB should be questioned every month about possible visual disturbances including blurred vision or scotomata; monthly testing of visual acuity (using the Snellen chart) and color discrimination is recommended for patients taking doses that on a mg/kg basis are greater than those listed in Table 5 and for patients receiving the drug for longer than 2 months. The physician should do gross visual field examinations and ophthalmological examinations if changes in visual acuity are suspected or known to be occurring. Referral for a formal evaluation by an ophthalmologist may be indicated if changes are significant.
7. **Auditory and Vestibular monitoring:** Patients taking aminoglycosides should be questioned every month about possible auditory dysfunction, including hearing loss or tinnitus. Have the patient discriminate a whispered voice at 20 feet or watch ticking 1-3 inches from the ear to screen for auditory deficits; acoustic testing should be recommended if problems have been noted. Monitoring of vestibular function can be performed using the Romberg test as described in VII-B-11 in this "Treatment Section". **Follow-up after completion of therapy** is not generally required, but patients should be instructed to seek care promptly if signs or symptoms recur.

VIII. IDENTIFICATION AND MANAGEMENT OF PATIENTS AT INCREASED RISK OF TREATMENT FAILURE AND RELAPSE

For patients with pulmonary TB, the two most significant risk factors for adverse outcome (treatment failure or relapse) are:

- A. The presence of cavitation on the initial chest radiograph, *and*
- B. Having a positive sputum *culture* 2 months after initiation of appropriate treatment.
 - 1. Sputum must be collected for smear and culture at 2 months after initiation of treatment (Figure 1).

Note: Approximately 80% of patients with pulmonary tuberculosis caused by drug-susceptible organisms who are started on standard four-drug therapy will have negative sputum cultures at this time.

- 2. Patients with positive cultures after 2 months of treatment should undergo careful evaluation to determine the cause.
 - a. Non-adherence is the most common reason, if DOT has not been used.
 - b. Other possibilities include extensive cavitory disease at the time of diagnosis, drug-resistance, malabsorption of drugs, laboratory error, and biologic variation in response.
- 3. For patients who have cavitation on the initial chest radiograph and a positive culture at 2 months, treatment should be extended to a minimum of 9 months (a total of 112 - 252 doses depending on whether the drugs are given daily or intermittently) (Figure 1).
- 4. For patients who have *either* cavitation on the initial film *or* a positive culture after completing the initial phase of treatment (i.e. at 2 months), the decision to extend therapy should be made on an individual basis. Follow-up clinical assessment at 3-6 month intervals for 1 year after completion of therapy is recommended.

IX. COMPLETION OF TREATMENT

A. General Concepts

- 1. Completion of treatment is determined by the **total number of doses taken** and the **duration of therapy**.

- a. For example, the “6-month” daily regimen should consist of at least 182 doses of INH and RIF, and 56 doses of PZA. Thus, 6 months is the minimum duration of treatment and accurately indicates the amount of time the drugs are given *only* if there are no interruptions in drug administration.
2. In some cases, either because of drug toxicity or non-adherence to the treatment regimen, the specified number of doses cannot be administered within the targeted period. In such cases the goal is to deliver the specified number of doses within a recommended maximum time.
 - a. For example, for a 6-month daily regimen the 182 doses should be administered within 9 months of beginning treatment. If treatment is not completed within this period, the patient should be assessed to determine the appropriate action to take – continuing treatment for a longer duration or restarting treatment from the beginning.
3. Interruptions in treatment may have a significant effect on the duration of therapy.
 - a. Reinstitution of treatment must take into account the **bacillary load** of the patient, the point in time when the interruption occurred, and the **duration of the interruption**.
 - b. In general, the earlier in treatment and the longer the duration of the interruption, the more serious the effect and the greater the need to restart therapy from the beginning. Figure 3 represents a flow chart on management of treatment interruptions.
4. Clinical experience suggests that patients being managed using DOT administered 5 days a week have a rate of successful therapy equivalent to those being given drugs 7 days a week.
 - a. “Daily therapy” may be interpreted to mean DOT 5 days a week and the required number of doses adjusted accordingly.
 - b. For the 6-month "daily" regimen given 5 days a week, the planned total number of doses is 130.
 - c. As an option, patients might be given the medications to take without DOT on weekends.

Note: TDOH strongly recommends that all patients be given DOT 7 out of 7 days during the initial 2 weeks of therapy, or longer if patient is on prolonged isolation. This practice will ensure the highest

quality of care by facilitating close monitoring for problems during initial therapy, ensuring adherence to isolation, providing early opportunity to perform contact investigation, and enhance initial patient reassurance, education and trust.

5. Missed DOT doses should be added to the end of therapy to ensure the total number of required doses is provided. If patient is allowed to self-administer any required doses, consideration should be given to adding those doses to the end of treatment.

B. Counting Doses

1. Determine the appropriate length of treatment for each individual patient (6 months, 9 months, etc.).
2. Determine how many weeks should be included in that time period.
 - a. 4 month regimens require 18 weeks
 - b. 6 month regimens require 26 weeks
 - c. 9 month regimens require 39 weeks
 - d. 12 month regimens require 52 weeks
3. Count a week as complete if the following doses were taken in the Sunday to Saturday period:
 - a. Patient took 5-7 daily treatment doses by DOT
 - b. Patient took 2 of 2 twice weekly doses by DOT
 - c. Patient took 3 of 3 thrice weekly doses by DOT
4. Count the total number of completed weeks and the number of incomplete weeks.
5. If the number of completed weeks is less than the total number required for your patient (see 1. above), determine how many doses *and what type of doses* (daily, twice weekly or thrice weekly) were missed and add these to the end.
6. One daily dose is not equivalent to one twice or thrice weekly dose. For example, if 3 twice weekly doses are missed during therapy, the equivalent of one and a half weeks should be added to the end either as 10 daily doses, 3 twice weekly doses or 5 thrice weekly doses. *An intermittent dose should not be replaced by one daily dose.*

a. Example 1:

Patient had culture positive pan-susceptible non-cavitary pulmonary TB (requires 6 months total treatment).

- 1) Patient was on isolation for 3 weeks and received 21 days of daily DOT.

- 2) Patient was then switched to biweekly treatment for the remainder of the initial phase (5 weeks) and the continuation phase (18 weeks).
 - 3) Total number of expected doses should be: 3 weeks daily (21 doses) + 5 weeks biweekly intermittent doses in initial phase (10 doses) + 18 weeks biweekly doses in continuation phase (36 doses) = 67 total doses expected.
- b. Example 2:
- 1) Same patient as above missed 3 doses of daily therapy (half of a week) during the initial phase and 5 biweekly doses (2 and a half weeks total) during the continuation phase.
 - 2) Patient should have 3 weeks added to the end of treatment. These added doses can be given as daily or intermittent doses as long as the equivalent of 3 weeks is taken.
- c. Example 3:
- 1) Same patient as above travels out of town for a 4-day weekend during the continuation phase, misses one biweekly dose, and is allowed to self-administer 4 daily doses while he is away.
 - 2) Consideration should be given to add one biweekly dose to the end of therapy. This will ensure that the patient has completed a full course of strict DOT.

X. PRACTICAL ASPECTS OF PATIENT MANAGEMENT DURING TREATMENT

A. Drug Administration

1. The first-line antituberculosis medications should be administered together; split dosing should be avoided.
2. Although ingestion with food delays or moderately decreases the absorption of antituberculosis drugs, the effects of food are of little clinical significance. Thus, if patients have epigastric distress or nausea with the first-line drugs, dosing with meals or changing the hour of dosing is recommended. *Administration with food is preferable to splitting a dose or changing to a second-line drug.*

3. Although the absorption of INH can be substantially decreased when the drug is ingested with glucose or lactose, administration of crushed INH tablets in a food with relatively low concentrations of glucose, such as applesauce has been used successfully by many providers.
4. The commercial preparation of INH elixir uses sorbitol for flavor, which can cause diarrhea, limiting the acceptability of this form of INH.
5. Antacids have minimal effects on the absorption of the first line antituberculosis drugs.
 - a. However, antacids and other medications containing divalent cations markedly decrease the absorption of the **fluoroquinolones** and may be associated with failure of antibiotic therapy. Therefore, any fluoroquinolone should not be administered within 2 hours of a dose of antacids, the chewable tablet form of didanosine (DDI), sucralfate (carafate), iron, magnesium, calcium, zinc, vitamins or dietary supplements (e.g., Ensure, Sustacal) containing a significant amount of these cations.
6. There is little information regarding the effect of food and antacids on the other second line antituberculosis drugs, therefore it is preferable to administer these drugs on an empty stomach if they are tolerated.
7. Parenteral therapy is indicated for severely ill patients who cannot take oral therapy and may be useful for the uncommon patient for whom poor absorption has been documented. Preparations of INH, RIF, the aminoglycosides, capreomycin, and most fluoroquinolones are available for intravenous administration

B. Fixed-dose Combination Preparations

1. Fixed-dose combination preparations may be administered more easily than single drug tablets and may decrease the risk of acquired drug resistance and medication errors.
2. Fixed-dose combinations may be used when DOT is given daily and are especially useful when DOT is not possible, but they are not formulated for use with intermittent dosing. Also, the number of pills is not decreased when used in intermittent regimens.
3. There are two combination formulations approved for use in the United States, **Rifamate®** (INH and RIF), and **Rifater®** (INH, RIF, and PZA).
 - a. Rifamate®: contains 150mg of INH and 300mg of RIF.

- 1) 2 tablets of Rifamate® provide conventional daily doses of both INH (300 mg) and RIF (600 mg).
- b. Rifater®: contains INH (50 mg), RIF (120 mg) and PZA (300 mg).
 - 1) 6 tablets of Rifater® would provide INH (300 mg) RIF (720 mg) and PZA (1800 mg).
 - 2) The RIF dose is higher than is used typically in the United States because RIF is less bioavailable in this formulation.
 - 3) For patients weighing more than 74 kg, the dose of PZA in the three-drug combination is insufficient and additional PZA tablets are necessary.

C. Management of Common Side Effects

Adverse effects, especially gastrointestinal upset, are relatively common in the first few weeks of antituberculosis therapy; however, **first-line antituberculosis drugs, particularly RIF, must not be discontinued because of minor side effects.** Mild adverse effects can generally be managed with symptomatic therapy, whereas with more severe effects the offending drug or drugs must be discontinued. A comprehensive list of reported adverse reactions and their frequency is described in Table 6.

1. *Gastrointestinal upset; nausea, vomiting, poor appetite, abdominal pain:*
 - a. Gastrointestinal reactions are common, particularly in the first few weeks of therapy.
 - b. If gastrointestinal symptoms occur, serum AST and bilirubin should be measured.
 - 1) If the AST is less than 3 times the upper limit of normal, the symptoms are not likely due to hepatic toxicity.
 - 2) However, if the AST is ≥ 3 times the upper limit of normal the symptoms should be assumed to represent hepatic toxicity, and the patient should be evaluated as described below.
 - 3) The initial approach to gastrointestinal intolerance not associated with hepatic toxicity is to change the hour of drug administration and/or to administer the drugs with food.

2. *Rash:*

- a. All drugs used in treating tuberculosis can cause a rash.
 - 1) If the rash is minor, affecting a limited area or being predominantly manifested as itching, anti-histamines should be given for symptomatic relief, but all antituberculosis medications can be continued.
 - 2) A petechial rash may suggest thrombocytopenia in patients taking a rifamycin. The platelet count should be checked and, if low, rifamycin hypersensitivity should be presumed. Rifamycin should be stopped and the platelet count should be monitored until it returns to baseline. *Rifamycin should not be restarted in this situation.*
 - 3) If there is a generalized erythematous rash, especially if it is associated with fever and/or mucus membrane involvement, *all drugs should be stopped immediately.* If the patient has severe TB, three new drugs (for example, an aminoglycoside and two oral agents) should be started. When the rash is substantially improved the medications can be restarted one by one, at intervals of 2-3 days. RIF should be restarted first (because it is the least likely to cause rash, and it is the most important agent), followed by INH, then EMB or PZA. If the rash recurs the last drug added should be stopped. If no rash appears after the first three drugs have been restarted, the fourth drug should not be restarted unless the rash was relatively mild and the fourth drug is considered essential for therapy.

3. *Drug fever:*

- a. Recurrence of fever in a patient who has been receiving therapy for several weeks should suggest drug fever, especially if the patient is showing microbiologic and radiographic improvement.
 - 1) The clinical hallmark of drug fever is that the patient looks and feels well despite having a high fever (often greater than 39° C); Eosinophilia may or may not be present.
- b. The first step in management of a possible drug fever is to ensure that there is no superinfection or worsening of TB.
 - 1) Fever from tuberculosis may persist for as long as 2 months after therapy has been initiated.

- 2) Fever may also be a manifestation of a paradoxical reaction, especially in patients with HIV infection and immune reconstitution as discussed in this section, XI- A- 7- a.
- c. If other potential causes of fever are excluded, all drugs should be stopped.
 - 1) Drug-related fever usually will resolve within 24 hours.
 - 2) Patients with severe TB should be given at least three new drugs in the interim.
 - 3) Once the fever has resolved, the same protocol as described above for restarting drugs in the presence of a rash should be followed.

4. *Hepatitis:*

- a. Management of patients with baseline abnormal liver function is described in this section, XI- G.
- b. Increases in serum AST during TB therapy:
 - 1) An asymptomatic increase in AST concentration occurs in nearly 20% of patients treated with the standard 4-drug regimen, and in most patients it resolves spontaneously. *In the absence of symptoms, therapy should NOT be altered because of modest asymptomatic elevations of AST, but the frequency of clinical and laboratory monitoring should be increased.*
 - 2) However, if AST levels are > 5 times the upper limit of normal (ULN) with or without symptoms or > 3 times ULN in the presence of symptoms, hepatotoxic drugs should be stopped immediately and the patient evaluated carefully.
 - 3) A significant increase in bilirubin and/or alkaline phosphatase is cause for a prompt evaluation.
- c. Management of hepatitis occurring during TB treatment:
 - 1) INH, RIF, and PZA, all potential causes of hepatic injury, should be stopped immediately.
 - 2) The patient should be questioned carefully regarding symptoms suggestive of biliary tract disease and exposures to other potential hepatotoxins, particularly alcohol and hepatotoxic

medications (consider over the counter preparations and home remedies as well).

- 3) Serologic testing for hepatitis viruses A, B, and C (if not done at baseline) and HIV should be performed.

Note: All cases of drug-induced hepatitis must be reported to MedWatch on Form FDA 3500 A. Send a copy to MedWatch and a copy to the TB Program Central Office immediately following the diagnosis.

d. Continuing TB therapy in patients with hepatitis:

- 1) Two or more antituberculosis medications without hepatotoxicity, such as EMB, SM, amikacin/kanamycin, capreomycin, or a fluoroquinolone (levofloxacin, moxifloxacin or gatifloxacin), may be used until the cause of the hepatitis is identified.
- 2) Once the AST decreases to < 2 times ULN and symptoms have significantly improved, the first-line medications should be restarted in sequential fashion. (In patients with elevated baseline AST from pre-existing liver disease, drugs should be restarted when the AST returns to near baseline levels).
- 3) Because RIF is much less likely to cause hepatotoxicity than is INH or PZA and is the most effective agent, it should be restarted first.
- 4) If there is no increase in AST after approximately 1 week, INH may be restarted.
- 5) PZA can be started 1 week after INH if the AST does not increase.
- 6) If symptoms recur or AST increases the last drug added should be stopped.
- 7) If RIF and INH are tolerated, and hepatitis was severe, PZA should be assumed to be responsible and should be discontinued. In this last circumstance, depending on the number of doses of PZA taken, severity of disease, and bacteriologic status, therapy might be extended to 9 months.

- e. Close monitoring, with repeat measurements of serum AST and bilirubin and symptom review, is essential in managing TB patients who developed hepatitis during treatment.

D. Serum Drug Concentration Measurements

Note: There are limited data on the usefulness of measuring serum drug concentrations and this practice is not recommended for routine management of TB patients.

Clinical situations in which therapeutic drug monitoring may be helpful:

- Patients with treatment failure that is not explained by non-adherence or drug resistance.
 - Persons with medical conditions that may result in very abnormal pharmacokinetics of the first-line drugs (HIV infection).
 - In the management of multidrug-resistant tuberculosis using **second-line drugs**.
1. Therapeutic drug monitoring for the **first-line drugs** should only be used for patients who are having an inadequate response to DOT (that is not due to non-adherence or drug resistance) or evidence of severe gastrointestinal or metabolic abnormalities.
 - a. Examples of such circumstances include severe gastroparesis, short-bowel syndrome, chronic diarrhea with malabsorption, and renal insufficiency.
 - b. Patients with HIV-related tuberculosis may have an increased incidence of malabsorption of antituberculosis drugs (although some studies have contrary findings). Even if true, this tendency for lower drug concentrations among patients with HIV-related tuberculosis is not sufficient to warrant routine therapeutic drug monitoring in this population (i.e. obtain only in situations listed above).
 2. Drug levels should be obtained through National Jewish Medical Center. Rural Regions must obtain prior approval from Central Office TB Elimination Program for payment. The order form will be sent from Central Office, after prior approval. Metropolitan Regions can order and pay for this service directly.

E. Drug Interactions

The drugs used to treat tuberculosis affect the metabolism of many other drugs, and can result in the lack of efficacy (interactions with the rifamycins) or toxicity (interactions with isoniazid and the fluoroquinolones).

1. Drug interactions due to the rifamycins:

- A list of clinically significant drug-drug interactions involving the rifamycins is listed in Table 13.
- a. Some drug-drug interactions can be managed with close clinical or laboratory monitoring and dose increases of the medication(s) affected by the rifamycins.
- b. In other cases, the magnitude of the decrease in concentrations of a concomitant medication may be such that serum concentrations cannot be restored by a dose increase.
- c. If the dose of a medication is increased to compensate for the effect of a rifamycin, it is critical to remember that the dose of this drug will probably need to be decreased within the two weeks after the rifamycin is discontinued and its inductive effect resolves.
- d. **Rifabutin** can sometimes be used in place of rifampin, if there is an unacceptable drug-drug interaction between rifampin and another drug, such as cyclosporine and most of the HIV-1 protease-inhibitors.
- e. All the rifamycins may cause unacceptable decreases in the serum concentrations of certain drugs, such as delavirdine, ketoconazole and itraconazole.

2. Drug interactions due to isoniazid:

- a. Isoniazid can increase concentrations of some drugs to the point of toxicity, (e.g. phenytoin and carbamazepine), and serum levels of these drugs should be monitored during treatment with INH.
- b. Isoniazid also increases concentrations of benzodiazepines such as diazepam and triazolam, but not oxazepam.

Note: Rifampin has the opposite effect on the serum concentrations of many of these drugs. The overall effect of combined therapy with rifampin and isoniazid is a decrease in the concentrations of drugs such as phenytoin and diazepam.

- c. Isoniazid may increase toxicity of other drugs – acetaminophen, valproate, serotonergic antidepressants, disulfiram, warfarin, and theophylline – but these potential interactions have not been well studied.

3. Drug interactions due to the fluoroquinolones:

- a. Ciprofloxacin inhibits the metabolism of theophylline and can cause clinical theophylline toxicity. However, levofloxacin, gatifloxacin, and moxifloxacin do not affect theophylline metabolism.

XI. TREATMENT IN SPECIAL SITUATIONS

A. HIV Infection

1. Recommendations for the treatment of tuberculosis in HIV-infected adults are, with a few exceptions, the same as those for HIV-uninfected adults.
 - a. Prior to the initiation of therapy, HIV-infected TB patients and suspects should be carefully evaluated for underlying liver disease, substance abuse, psychiatric disorders or other factors that may influence non-adherence or intolerance/toxicity of therapy.
 - b. When the disease is caused by organisms that are known or presumed to be susceptible to the first-line agents, an initial phase of INH, RIF, PZA, and EMB given for 2 months followed by INH and RIF for the continuation phase should be used ([Table 11](#)).
 - c. Six months should be considered the minimum duration of treatment for HIV+ adults, even for patients with culture-negative tuberculosis.
 - d. Patients with both a cavity on baseline chest x-ray and positive cultures despite 2 months of adequate therapy and good adherence should be treated for a minimum of 9 months to prevent treatment failure or relapse.
 - e. If there is evidence of a slow or suboptimal response (e.g., cultures are still positive after 2 months of therapy), prolongation of the *continuation phase* to 7 months (a total of 9 months treatment) should be considered, even if there was no cavity at baseline.
2. DOT and other adherence promoting strategies should be used for all HIV+ TB patients.
3. The American Academy of Pediatrics recommends that HIV-infected children with TB receive a minimum of 9 months of treatment.
4. Because HIV-infected patients are often taking numerous medications, some of which interact with antituberculosis medications, and because these patients often have other significant co-morbid conditions, it is strongly

encouraged that experts in the treatment of HIV-related tuberculosis be consulted (Tuberculosis Control Officer can provide this consultation).

5. All HIV-positive patients should be evaluated for possible drug-interactions if they are being treated with anti-retroviral agents or medications to treat other co-existent conditions/opportunistic infections (Table 13):
 - a. Rifampin can be used for the treatment of tuberculosis with certain combinations of antiretroviral agents.
 - b. Rifabutin, which has fewer problematic drug interactions, may also be used in place of rifampin and appears to be equally effective although the doses of rifabutin and antiretroviral agents may require adjustment (MMWR 2000;49:185-189).
 - c. A new website has been established to provide current recommendations for treatment of TB in HIV-positive persons, http://www.cdc.gov/nchstp/tb/tb_hiv_drugs/toc.htm
6. Contraindicated regimens:
 - a. **The INH-Rifapentine once weekly continuation phase** (Regimens 1c and 2b) is contraindicated in HIV-infected patients because of an unacceptably high rate of relapse and acquired resistance to rifamycins.
 - b. The development of acquired rifampin resistance has also been noted among HIV-infected patients with advanced immunosuppression treated with twice weekly rifampin or rifabutin-based regimens. Consequently, patients with **CD4 cell counts < 100/ml** should receive daily or thrice weekly treatment. (Table 11, Regimen 1/1a or Regimen 3/3a).
7. Immune reconstitution syndromes:
 - a. Occasionally, patients with HIV-related tuberculosis may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations of TB while receiving antituberculosis treatment. This clinical or radiographic worsening (paradoxical reaction) occurs in HIV-infected patients with active tuberculosis and is thought to be the result of immune reconstitution as a consequence of effective antiretroviral therapy. Symptoms and signs may include high fevers, lymphadenopathy, expanding central nervous system lesions, and worsening of chest radiographic findings.

- b. The diagnosis of a paradoxical reaction should be made only after a thorough evaluation has excluded other etiologies, particularly tuberculosis treatment failure.
 - c. Nonsteroidal anti-inflammatory agents may be useful for symptomatic relief. For severe paradoxical reactions, prednisone (1-2 mg/kg/day for 1-2 weeks then in gradually decreasing doses) may be used, although there are no data from controlled trials to support this approach (Rating CIII).
8. All patients with tuberculosis should be encouraged to undergo voluntary HIV counseling, testing, and referral (MMWR 2001;50(no.RR19):1-57).
- a. Informed written consent must be obtained prior to HIV testing.
 - b. Efforts should be made to engage all patients with a new diagnosis of HIV infection in HIV care during their treatment for tuberculosis.
 - c. Patients with HIV risk factors (IV drug use, unprotected male-male sex, use of prostitutes, multiple partners, etc.) should be counseled about risk of acquiring HIV and risk behavior modification.
 - d. HIV counseling, testing and referral provided should be documented in the medical record.
9. **Patients with unknown HIV status should not be put on once or twice-weekly treatment regimens.**

B. Children

In general, the regimens recommended for adults are also the regimens of choice for infants, children and adolescents with tuberculosis.

1. Because tuberculosis in infants and young children is more likely to disseminate, **treatment should be started as soon as the diagnosis is suspected.** In Tennessee this is to be implemented for children < 5 years of age. Asymptomatic children with a positive PPD-tuberculin skin test and an abnormal chest radiograph (atelectasis, parenchymal infiltrate or nodules, or hilar adenopathy) should also receive combination chemotherapy immediately.
2. Most children should be treated with three (rather than four) drugs in the *initial phase*, usually INH, RIF and PZA, since many infants and children cannot tolerate the pill burden required by four oral drugs. In addition, because there is a lower bacillary burden in childhood-type tuberculosis there is less concern with the development of acquired drug resistance.

However, children and adolescents with adult-type pulmonary tuberculosis should be started on the four-drug regimen.

3. Ethambutol is not used routinely in children whose visual acuity cannot be easily assessed. When epidemiological circumstances (Table 12) suggest an increased probability of INH resistance, EMB can be used safely at a dose of 15 mg/kg/day, even in children too young for routine eye testing. Streptomycin, kanamycin, or amikacin also can be used as the fourth drug, when necessary.
4. Most studies of treatment in children have used 6 months of INH and RIF supplemented during the first 2 months with PZA.
5. DOT should always be used in treating children.
6. Pyridoxine is recommended only for children and adolescents who are being treated with INH and who have nutritional deficiencies, symptomatic HIV infection, or who are breastfeeding.
7. Because it is difficult to isolate *M. tuberculosis* from a child with pulmonary tuberculosis, it is frequently necessary to rely on the results of drug susceptibility tests of the organisms isolated from the presumed source case to guide the choice of drugs for the child. In cases of suspected drug-resistant tuberculosis in a child or when a source case isolate is not available, specimens for microbiologic evaluation should be obtained via early morning gastric aspiration, bronchoalveolar lavage, or biopsy.
8. In general, extrapulmonary tuberculosis in children can be treated with the same regimens as pulmonary disease. **Exceptions are disseminated tuberculosis and tuberculous meningitis, for which 9-12 month durations are recommended.**
9. The American Academy of Pediatrics recommends that initial therapy of pulmonary tuberculosis in children and adolescents with HIV infection should always include at least three drugs, and the total duration of therapy should be at least 9 months.

C. Extrapulmonary Tuberculosis

Confirmed extrapulmonary TB without pulmonary disease is not considered a direct public health threat. However, the primary goal of the TB Program is to provide effective treatment and case management of all TB cases, regardless of infectiousness or site of involvement. By ensuring completion of an adequate course of TB treatment, the TB Program can prevent extrapulmonary tuberculosis from hematogenously becoming pulmonary (and potentially infectious) tuberculosis, and the individual patient's morbidity and mortality will be greatly reduced.

The basic principles that underlie the treatment of pulmonary tuberculosis also apply to extrapulmonary forms of the disease.

1. Duration of treatment: For most forms of extrapulmonary tuberculosis, a 6-month regimen that includes 2 months of INH, RIF, PZA, and EMB followed by 4 months of INH and RIF is recommended as initial therapy unless the organisms are known or strongly suspected of being resistant to the first-line drugs.
 - a. If PZA cannot be used in the *initial phase*, the *continuation phase* must be increased to 7 months, as described for pulmonary tuberculosis.
 - b. Prolongation of therapy also should be considered for patients with tuberculosis in any site that is slow to respond.
2. TB of the lymph nodes: The affected nodes may enlarge while patients are receiving appropriate therapy or after the end of treatment without any evidence of bacteriological relapse. On occasion, new nodes can appear during or after treatment as well. Therapeutic lymph node excision is not indicated except in unusual circumstances. For large lymph nodes that are fluctuant and appear to be about to drain spontaneously, aspiration or incision and drainage appears to be beneficial, although this approach has not been examined systematically (Table 11, Rating B III).
3. **TB meningitis:** treatment should be increased to 9-12 months. Consider repeat lumbar puncture 1-2 months after initiation of therapy to evaluate improvement.
4. **Bone and joint tuberculosis:** Treated with standard regimens, 6-9 months is usually sufficient.
 - a. In general, there is no additional benefit of surgical debridement or radical operation (resection of the spinal focus and bone grafting) in combination with chemotherapy compared with chemotherapy alone, and myelopathy with or without functional impairment most often responds to chemotherapy.
 - b. However, surgery appears to be beneficial and may be indicated in certain situations such as failure to respond to chemotherapy with evidence of ongoing infection, the relief of cord compression in patients with persistence or recurrence of neurological deficits, or instability of the spine.

5. Corticosteroids: The addition of steroids is recommended for patients with tuberculous pericarditis and tuberculous meningitis.
 - a. For adults the dose is 60 mg/day of prednisone (or the equivalent dose of prednisolone) given for 4 weeks, followed by 30 mg/day for 4 weeks, 15 mg/day for 2 weeks, and finally 5 mg/day for the 11th and final week.
 - b. Children should be treated with doses proportionate to their weight, beginning with approximately 1 mg/kg body weight and decreasing the dose as described for adults.

D. Culture-Negative Pulmonary Tuberculosis

Failure to isolate *M. tuberculosis* from persons suspected of having pulmonary tuberculosis based on clinical features and chest radiographic examination does not exclude a diagnosis of active tuberculosis. Alternative diagnoses should be considered carefully and further appropriate diagnostic studies undertaken in persons with apparent culture-negative tuberculosis. The general approach to management is shown in Figure 2.

1. A diagnosis of tuberculosis can be strongly inferred by the clinical and radiographic response to antituberculosis treatment.
 - a. Careful clinical re-evaluation should be performed after 2 months of effective therapy to determine if there has been a response attributable to antituberculosis treatment.
 - b. PA and lateral chest radiographs should be repeated 2 months after treatment was initiated.
2. If either clinical or radiographic improvement is noted and no other etiology is identified, treatment should be continued for active tuberculosis. Treatment regimens in this circumstance include one of the standard 6-month chemotherapy regimens or INH, RIF, PZA, and EMB for 2 months followed by INH and RIF for 2 additional months (4 months total).
3. If there has been no clinical or radiographic improvement, further evaluation for other diagnoses should be made and discontinuation of therapy may be indicated. *Ensure that failure to improve cannot be attributed to non-adherence, inadequate therapy, or the development of resistance prior to stopping therapy.*
4. Occasionally, patients who are being evaluated for pulmonary tuberculosis will be found to have positive AFB smears but negative cultures. There are several potential explanations for this occurrence, including the possibilities that the acid-fast organisms are non-tuberculous and difficult to culture, that they are nonviable tubercle bacilli, and that they are the result of laboratory

or processing error (specimen put in formalin). The approach taken in such cases should be individualized, based on clinical and radiographic findings. If suspicion of tuberculosis is high and the patient has positive AFB smears, even with negative cultures, he/she should be treated as if the culture is positive using one of the recommended regimens.

E. Radiographic Evidence of Prior Pulmonary Tuberculosis

1. Persons with a positive tuberculin skin test who have radiographic evidence of prior tuberculosis (e.g., upper lobe fibronodular infiltrations) but who have not received adequate therapy are at increased risk for the subsequent development of tuberculosis.
2. Sputum examination (using sputum induction if necessary) should be performed to assess the possibility of active tuberculosis being present.
3. If the patient has symptoms of tuberculosis related to an extrapulmonary site, an appropriate evaluation should be undertaken prior to starting LTBI therapy.
4. Once active tuberculosis has been excluded (i.e., by negative cultures and a stable chest radiograph), treatment for latent tuberculosis infection should be started ([Table 14](#), and Section IV, “Treatment of Latent TB Infection”)

F. Renal Insufficiency and End-Stage Renal Disease

- Specific dosing guidelines for patients with renal insufficiency and end-stage renal disease are provided in [Table 15](#).
1. For patients undergoing hemodialysis, administration of all drugs after dialysis is preferred to facilitate DOT and to avoid premature removal of drugs such as PZA and cycloserine.
 2. In order to avoid toxicity it is important to monitor serum drug concentrations in persons with renal failure who are taking cycloserine or EMB.
 3. RIF and INH are metabolized by the liver, so conventional dosing may be used in the setting of renal insufficiency.
 4. A longer interval between doses is recommended for PZA and EMB.

G. Liver Disease

INH, RIF, and PZA all can cause hepatitis that may result in additional liver damage in patients with preexisting liver disease. However, because of the effectiveness of these

drugs (particularly INH and RIF), they should be used if at all possible, even in the presence of preexisting liver disease.

1. If serum AST is more than three times normal prior to the initiation of treatment (and the abnormalities are not thought to be caused by tuberculosis), several treatment options exist.
 - a. One option is to treat with RIF, EMB, and PZA for 6 months, avoiding INH.
 - b. A second option is to treat with INH and RIF for 9 months, supplemented by EMB until INH and RIF susceptibility are demonstrated, thereby avoiding PZA.
2. For patients with severe liver disease, a regimen with only one hepatotoxic agent, generally RIF plus EMB, could be given for 12-18 months depending on the extent of the disease and response. This regimen should preferably be used with another agent, such as a fluoroquinolone, for the first 2 months; however, there are no data to support this recommendation.
3. In the setting of severe unstable liver disease, a regimen with no hepatotoxic agents might be necessary. Such a regimen might include SM, EMB, a fluoroquinolone and another second-line oral drug. There are no data that provide guidance as to the choice of agents or the duration of treatment or that indicate the effectiveness of such a regimen. Expert opinion suggests that a regimen of this sort should be given for 18-24 months (rating C III).
4. In all patients with preexisting liver disease, frequent clinical and laboratory monitoring should be performed to detect drug-induced hepatic injury.
5. Recommendations regarding management of hepatotoxicity that develops during TB therapy are discussed in this section, X-C-4.

H. Pregnancy and Breastfeeding

Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease. Therefore, treatment of tuberculosis in pregnant women should be initiated whenever the probability of maternal disease is moderate to high.

- Refer to Table 6 for specific recommendations regarding medication safety in pregnancy.
 1. The initial treatment regimen should consist of INH, RIF, and EMB. Although all of these drugs cross the placenta, they do not appear to have teratogenic effects.

2. In the U.S., PZA is generally not used except under special circumstances (e.g. MDR-TB or mother is critically ill). Although detailed teratogenicity data are not available, PZA can probably be used safely during pregnancy and is recommended by the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD). If PZA is not included in the initial treatment regimen, the minimum duration of therapy is 9 months.
3. Streptomycin is the only antituberculosis drug documented to have harmful effects on the human fetus (congenital deafness) and should not be used (kanamycin, amikacin, and capreomycin presumably share this toxic potential).
4. The fluoroquinolones have been associated with arthropathies in young animals; therefore, they should be avoided if possible in pregnant women.
5. There are not enough data to adequately determine the risk of other second line agents.
6. **Breast-feeding should not be discouraged for women being treated with the first-line antituberculosis agents** (unless they are HIV+) because the small concentrations of these drugs in breast milk do not produce toxicity in the nursing newborn.
 - a. Conversely, drugs in breast milk should not be considered to serve as effective treatment for tuberculosis or for latent tuberculosis infection in a nursing infant.
 - b. Pyridoxine supplementation (50mg daily) is recommended for all women taking INH who are either pregnant or breastfeeding. The amount of pyridoxine in multivitamins is variable but generally less than the needed amount.

XII. MANAGEMENT OF RELAPSE, TREATMENT FAILURE, AND DRUG RESISTANCE

Note: Consultation can be obtained from the Tuberculosis Control Officer for recommendations on management for any patient with treatment relapse or failure.

A. Relapse

Relapse: A patient becomes and remains culture-negative while receiving therapy but, at some point after completion of therapy, either becomes culture-positive again or has clinical or radiographic deterioration that is consistent with active tuberculosis.

1. If relapse is suspected, rigorous efforts should be made to establish a diagnosis and to obtain microbiologic confirmation of the relapse to enable testing for drug resistance.
2. Most relapses occur within the first 6-12 months after completion of therapy.
3. In nearly all patients treated with rifamycin-containing regimens using DOT, relapses occur with organisms having the same drug-susceptibility pattern as the pretreatment isolate.
4. However, in patients who received self-administered therapy or a non-rifamycin based regimen and who have a relapse, the risk of acquired drug-resistance is substantial.
5. The selection of empirical treatment for patients with relapse should be based on the prior treatment scheme and severity of disease.
 - a. For patients with tuberculosis that was caused by drug-susceptible organisms, who were treated under DOT, and who have early relapses, initiation of the standard four-drug regimen is appropriate until the results of drug susceptibility tests are available.
 - b. However, for patients who have life-threatening forms of tuberculosis at least three additional agents to which the organisms are likely to be susceptible should be included.
 - c. For patients with relapse who did not receive DOT, who were not treated with a rifamycin-based regimen, or who are known or presumed to have had irregular treatment, it is prudent to infer that drug resistance is present and to begin an expanded regimen with INH, RIF, PZA plus an additional two or three agents based on the probability of *in vitro* susceptibility.
 - d. Usual agents to be employed would include a fluoroquinolone (levofloxacin, moxifloxacin, or gatifloxacin), an injectable agent such as SM (if not used previously and susceptibility to SM had been established), amikacin, kanamycin, or capreomycin, with or without an additional oral drug (PAS, cycloserine, ethionamide).

B. Treatment failure

Treatment failure: Continued or recurrently positive cultures *during the course of antituberculosis therapy*.

1. Patients with positive cultures after 3 months of what should be effective treatment must be evaluated carefully in order to identify the cause of the delayed conversion. Patients whose sputum cultures remain positive after 4 months of treatment should be deemed treatment failures.
2. Possible reasons for treatment failure in patients receiving appropriate regimens include non-adherence to the drug regimen (the most common reason), drug-resistance, malabsorption of drugs, laboratory error, and extreme biologic variation in response.
3. A fundamental principle in managing patients with treatment failure is **never to add a single drug to a failing regimen**. This could lead to acquired resistance to the new drug. Instead, at least two, and preferably three, new drugs to which susceptibility could logically be inferred should be added in order to lessen the probability of further acquired resistance.
4. If failure is likely due to drug-resistance and the patient is not seriously ill, an empirical re-treatment regimen could be started or administration of an altered regimen could be deferred until results of drug-susceptibility testing from a recent isolate are available.
5. If the patient is seriously ill, an empirical regimen should be started immediately and continued until susceptibility tests are available.
6. For patients who have treatment failure, *M. tuberculosis* isolates should be sent promptly to the State laboratory with a request for drug susceptibility testing to both first and second line agents.
7. Empirical re-treatment regimens might include a fluoroquinolone, an injectable agent such as SM (if not used previously and the patient is not from an area of the world having high rates of SM resistance), amikacin, kanamycin, or capreomycin, and an additional oral agent such as PAS, cycloserine, or ethionamide.
8. Once drug-susceptibility test results are available, the regimen should be adjusted according to the results.
9. **Isolation must be maintained until the patient is no longer infectious.** Central Office can assist with arrangements (housing or other special needs) for patients requiring prolonged isolation.

C. Drug Resistance

Patients having tuberculosis caused by strains of *M. tuberculosis* resistant to at least INH and RIF (multidrug-resistant [MDR]) are at high risk for treatment failure and further acquired drug resistance. **Such patients should be immediately reported to the Tuberculosis Control Officer.**

- Table 16 contains treatment regimens suggested for use in patients with various patterns of drug-resistant tuberculosis (all are rated AIII).

Note: Definitive randomized or controlled studies have not been performed to establish optimum regimens for treating patients with the various patterns of drug-resistant TB, thus, treatment recommendations are based on expert opinion.

1. When initiating or revising therapy, always attempt to employ **at least three previously unused drugs to which there is in vitro susceptibility**. One of these should be an injectable agent.
2. Do not limit the regimen to three agents if other previously unused, likely to be active drugs are available. In patients with MDR organisms in whom there is resistance to first-line agents in addition to INH and RIF, regimens employing 4-6 medications appear to be associated with better results.
3. Patients with MDR-TB should receive either hospital-based or domiciliary DOT. The implications of treatment failure and further acquired resistance are such that these cases should receive highest priority for DOT.
4. Intermittent therapy should not be used in treating tuberculosis caused by drug-resistant organisms, except perhaps for injectable agents after an initial period (usually 2-3 months) of daily therapy.
5. The use of drugs to which there is demonstrated in vitro resistance is not encouraged because there is little or no efficacy of these drugs (assuming the test results are accurate), and, usually, alternative medications are available. However, the clinical significance and effectiveness of the use of INH in the setting of low-level INH resistance is unclear.

Note: The use of INH in patients with the strain-W variety of MDR-TB that was susceptible to higher concentrations of INH was associated with better survival rates.

6. Resistance to rifampin is associated in nearly all instances with cross-resistance to rifabutin and rifapentine. Rare strains with RIF resistance retain susceptibility to rifabutin. However, unless in vitro susceptibility to rifabutin is demonstrated, this agent should not be employed in cases with

RIF resistance. Cross-resistance between RIF and rifapentine appears almost universal.

7. There is no cross-resistance between SM and the other injectable agents, amikacin, kanamycin, and capreomycin (although resistance to all may occur as independent events); however, cross-resistance between amikacin and kanamycin is universal. Simultaneous use of two injectable agents is not recommended due to the absence of proof of efficacy and potential amplification of drug toxicity.
8. Determination of resistance to PZA is technically problematic and, thus, is not done in many laboratories. However, resistance to PZA is uncommon in the absence of resistance to other first-line drugs. If monoresistance to PZA is observed, consideration must be given to the possibility that the etiologic agent is *M. bovis*, not *M. tuberculosis* (*M. bovis* is genotypically resistant to PZA and is not distinguished from *M. tuberculosis* by nucleic acid hybridization-probe assays that are commonly used for identification).
9. Surgical Treatment of MDR TB: The role of resectional surgery in the management of patients with extensive pulmonary MDR tuberculosis has not been established. If surgery is to be done, it should only be performed after several months of intensive chemotherapy to lessen the risk of operative complications, the anticipation of extended chemotherapy post-operatively (1-2 years) to prevent relapse, and by surgeons with demonstrated skill in these extremely challenging cases. All cases that are being considered for surgical intervention should be discussed with the Tuberculosis Control Officer.

XIII. INCENTIVES AND ENABLERS

The TB Elimination Program is currently working with the Bureau of Health to develop a plan for providing incentives and enablers for TB patients under the care of the Tennessee Department of Health. An addendum will be sent to all Rural Regional TB Programs when this plan has been approved and is ready for implementation. Possible components of this plan may be found in Table 1 on the following page.

TABLE 1. POSSIBLE COMPONENTS OF A MULTIFACETED, PATIENT-CENTERED TREATMENT STRATEGY

Enablers: *Interventions to assist the patient in completing therapy* *

A. Transportation vouchers

- Child care
- Convenient clinic hours and locations
- Clinic personnel who speak the languages of the populations served
- Reminder systems and follow-up of missed appointments
- Social service assistance (*referrals for substance abuse treatment and counseling, housing, and other services*) **
- Outreach workers (*bilingual/bicultural as needed; can provide many services related to maintaining patient adherence, including provision of DOT, follow up on missed appointments, monthly monitoring, transportation, sputum collection, social service assistance, and educational reinforcement*)
- Integration of care for tuberculosis with care for other conditions.

Incentives: *Interventions to motivate the patient, tailored to individual patient wishes and needs and, thus, meaningful to the patient* *

- Food stamps or snacks and meals
- Restaurant coupons
- Assistance in finding or provision of housing †
- Clothing or other personal products
- Books
- Stipends
- Patient contract

* Burman WJ, Cohn DL, Rietmeijer CA, Judson FN, Sbabaro JA, Reves RR. Noncompliance with directly observed therapy for Tuberculosis: Epidemiology and effect on the outcome of treatment. Chest 1997;111:1168-1173

** Bayer R, Stayton C, Devarieux M, Heaton C, Landsman S, Tsai W. Directly observed therapy and treatment completion in the United States; is universal supervised therapy necessary? Am J Public Health 1998;88:1052-1058

† Vomink J, Matchaba P, Gainer P. Directly observed therapy and treatment adherence. Lancet 2000;355:1345-1350

TABLE 2. ANTITUBERCULOSIS DRUGS CURRENTLY IN USE IN THE UNITED STATES

First-line

Isoniazid
Rifampin
Rifapentine
Rifabutin*
Ethambutol
Pyrazinamide

Second-line

Cycloserine
Ethionamide
Levofloxacin*
Moxifloxacin*
Gatifloxacin*
Para-aminosalicylic acid
Streptomycin
Amikacin/Kanamycin *
Capreomycin

* Not approved by United States Food and Drug Administration for use in tuberculosis

TABLE 3. DOSES OF ANTITUBERCULOSIS DRUGS

Drug	Preparation		Daily	Weekly		
				1x	2x	3x
FIRST LINE DRUGS						
Isoniazid	Tablets (50 mg, 100 mg, 300 mg); Elixir (50 mg/5 ml); Aqueous solution (100 mg/ml) for intravenous or intramuscular injection.	Adults (Max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
		Children (Max.)	10-15 mg/kg (300 mg)	--	20-30 mg/kg (900 mg)	--
Rifampin	Capsule (150 mg, 300 mg). Powder may be suspended for oral administration. Aqueous solution for intravenous injection.	Adults (Max.)	10 mg/kg (600 mg)	--	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (Max.)	10-20 mg/kg (600 mg)	--	10-20 mg/kg (600 mg)	--
Rifabutin	Capsule (150 mg)	Adults [†] (Max.)	5 mg/kg (300 mg)	--	5 mg/kg (300 mg)	5 mg/kg (300 mg)
		Children	Appropriate dosing for children is unknown.			
Rifapentine	Tablet (150 mg film coated)	Adults	--	10 mg/kg (continuation phase)	--	--
		Children	The drug is not approved for use in children.			
Pyrazinamide	Tablet (500 mg scored)	Adults	See Table 6	--	See Table 6	See Table 6
		Children (Max.)	15-30 mg/kg (2000 mg)	--	50 mg/kg	50 mg/kg
Ethambutol	Tablet (100 mg; 400 mg)	Adults	See Table 7	--	See Table 7	See Table 7
		Children ^{††} (Max.)	15-20 mg/kg daily (2.5 gm)	--	50 mg/kg	--

Drug	Preparation		Daily	Weekly		
				1x	2x	3x
SECOND-LINE DRUGS						
Cycloserine	Capsule (250 mg)	Adults (Max.)	10-15 mg/kg/day, (1.0 gm in two divided doses) usually 500-750 mg per day in two divided doses *	There are no data to support intermittent administration.		
		Children (Max.)	10-20 mg/kg/day (1.0 gm per day)	--	--	--
Ethionamide	Tablet (250 mg)	Adults* (Max.)	15-20 mg/kg/d (1.0 gm per day), usually, 500-750 mg per day in a single daily dose or two divided doses**	There are no data to support intermittent administration.		
		Children (Max.)	15-20 mg/kg/d (1.0 gm per day)			
Streptomycin	Aqueous solution (1 gm vials) for IM or IV administration.	Adults (Max.)	15 mg/kg/d (1g), and 10 mg/kg in persons > 59 years of age (750 mg). Usual dose 750mg-1000mg IM or IV typically given as a single dose 5-7 days a week and reduced to 2-3 times a week after first 2-4 months or after culture conversion, depending on the efficacy of the other drugs in the regimen.			
		Children (Max.)	20-40 mg/kg/d (1 g)	--	20mg/kg	--

Drug	Preparation		Daily	Weekly		
				1x	2x	3x
Amikacin/ Kanamycin	Aqueous solution (500 mg and 1 gm vials) for IM or IV administration.	Adults (Max.)	15 mg/kg/d (1g), and 10 mg/kg in persons > 59 years of age (750 mg). Usual dose 750mg-1000mg IM or IV typically given as a single dose 5-7 days a week and reduced to 2-3 times a week after first 2-4 months or after culture conversion, depending on the efficacy of the other drugs in the regimen.			
		Children (Max.)	15-30 mg/kg/d (1 g) IM or IV as a single daily dose	--	15-30mg/kg	--
Capreomycin	Aqueous solution (1 gm vials) for IM or IV administration.	Adults (Max.)	15 mg/kg/d (1g), and 10 mg/kg in persons > 59 years of age (750 mg). Usual dose 750mg-1000mg IM or IV typically given as a single dose 5-7 days a week and reduced to 2-3 times a week after first 2-4 months or after culture conversion, depending on the efficacy of the other drugs in the regimen.			
		Children (Max.)	15-30 mg/kg/d (1 g) as a single daily dose	--	15-30mg/kg	--
para-Amino Salicylic Acid (PAS)	Granules (4 gm packets) can be mixed with food. Tablets (500 mg) are still available in some countries, but not in the United States. A solution for IV administration is available in Europe.	Adults	8-12 grams per day in 2 or 3 doses	There are no data to support intermittent administration.		
		Children	200-300 mg/kg/day in 2-4 divided doses (10gm)			
Levofloxacin	Tablets (250 mg, 500 mg, 750 mg); aqueous	Adults	500 - 1000 mg daily	There are no data to support intermittent administration.		

Drug	Preparation		Daily	Weekly		
				1x	2x	3x
	solution (500 mg vials) for IV injection.	Children	The long-term (>several weeks) use of levofloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. However, most experts agree that the drug should be considered for children with tuberculosis caused by organisms resistant to both INH and RIF. The optimal dose is not known.			
Moxifloxacin	Tablets (400 mg); aqueous solution (400 mg/250 mL) for IV injection	Adults	400 mg daily	There are no data to support intermittent administration.		
		Children	The long-term (>several weeks) use of moxifloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. The optimal dose is not known.			
Gatifloxacin	Tablets (400 mg); aqueous solution (200/20 mL; 400 mg/40 mL) for IV injection	Adults	400 mg daily	There are no data to support intermittent administration.		
		Children	The long-term (>several weeks) use of gatifloxacin in children and adolescents has not been approved because of concerns about effects on bone and cartilage growth. The optimal dose is not known.			

†Dose may need to be adjusted when there is concomitant use of protease inhibitors or non-nucleoside reverse transcriptase inhibitors.

††The drug can likely be used safely in older children but should be used with caution in children <5 yrs in whom visual acuity cannot be monitored. In younger children, EMB at the dose of 15 mg/kg/d can be used if there is suspected or proven resistance to INH or RIF.

*It should be noted that, although this is the dose recommended generally, most clinicians with experience using cycloserine indicate that it is unusual for patients to be able to tolerate this amount. Serum concentration measurements are often useful in determining the optimum dose for a given patient.

**The single daily dose can be given at bedtime or with the main meal.

TABLE 4. SUGGESTED PZA DOSAGES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40-90 KG

	<u>Weight (Kg)</u>		
	<u>40-55</u>	<u>56-75</u>	<u>76-90</u>
<u>Daily</u>	1000 mg	1500 mg	2000 mg
(mg/kg)	(18.2-25.0)	(20.0-26.8)	(22.2-26.6)
<u>Thrice weekly</u>	1500 mg	2500 mg	3000
(mg/kg)	(27.3-37.5)	(33.3-44.6)	(33.3-39.5)
<u>Twice weekly</u>	2000 mg	3000 mg	4000
(mg/kg)	(36.4-50.0)	(40.0-53.6)	(44.4-52.6)

TABLE 5. SUGGESTED EMB DOSAGES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40-90 KG

	<u>Weight (Kg)</u>		
	<u>40-55</u>	<u>56-75</u>	<u>76-90</u>
<u>Daily</u>	800 mg	1200 mg	1600
(mg/kg)	(14.5-20.0)	(16.0-21.4)	(17.8-21.1)
<u>Thrice weekly</u>	1200 mg	2000 mg	2400
(mg/kg)	(21.8-30.0)	(26.7-35.7)	(26.7-31.6)
<u>Twice weekly</u>	2000 mg	2800 mg	4000
(mg/kg)	(36.4-50.0)	(37.3-50.0)	(44.4-52.6)

TABLE 6. MEDICATION SIDE EFFECTS AND RECOMMENDATIONS FOR MONITORING

Drug	Adverse Effect	Comments	Recommendations for Monitoring
<p>Isoniazid (INH)</p>	<ol style="list-style-type: none"> 1. Asymptomatic liver enzyme elevation (Aminotransferases (AT) AST, ALT) 2. Clinical hepatitis 3. Peripheral neuropathy 4. CNS effects 5. Lupus-like syndrome 6. Hypersensitivity reactions 7. monoamine (histamine/tyramine) poisoning 8. Diarrhea 9. Drug interactions 	<ol style="list-style-type: none"> 1. AT elevations up to 5X upper limit of normal occur in 10-20% of persons receiving INH alone and usually return to normal even with continued administration of the drug. 2. Risk increased with use of other liver-toxic medications, especially RIF. Risk also increased with age, alcohol use, and in post-partum period, especially in Hispanic women. Death rare but has been associated with continued administration of INH despite onset of hepatitis symptoms. 3. Neuropathy is dose-related and uncommon at conventional doses, risk increased with nutritional deficiency, DM, HIV infection, renal ds, alcoholism, and pregnancy/breast feeding. Pyridoxine (B6) is recommended with these conditions. 4. Dysarthria, irritability, seizures, dysphoria, inability to concentrate reported, but effects not well quantified. 5. 20% of persons develop +ANA; <1% develop clinical lupus requiring drug-discontinuation. 6. Fever, rash, Stevens-Johnson, hemolytic anemia, vasculitis and neutropenia are rare. 7. Rare, if flushing occurs patient should avoid certain food and drinks (cheese and wine). 8. Liquid INH contains sorbitol. 9. Serum concentrations of phenytoin (dilantin) and carbamazepine (tegretol) may be increased with INH alone, but are countered if RIF also used. Isoniazid also increases concentrations of benzodiazepines such as diazepam and triazolam, but not oxazepam. INH may increase concentration of disulfiram (antabuse). <p>*Safe in pregnancy, supplement with B6.</p>	<p><u>LTBI:</u> Baseline and follow-up laboratory monitoring is <i>not</i> routinely indicated, except for the following risk factors:</p> <ul style="list-style-type: none"> • Initial evaluation suggests liver disorder (HBV, HCV, cirrhosis) • HIV infection, pregnancy, <3 mo. post-partum, alcohol abuse • *Not routinely indicated in older persons, but may be considered on individual basis and in those taking other medications for chronic medical conditions. <p><u>TB:</u> Baseline measurement of AT recommended for adults.</p> <p><u>Repeat measurements monthly if:</u></p> <ul style="list-style-type: none"> • baseline results are abnormal • patient is at high risk for adverse reactions or has underlying liver disease • patient has symptoms of adverse reactions <p>If taking phenytoin or carbamazepine, measure serum concentrations of these drugs and adjust dose if necessary.</p>

TABLE 6. MEDICATION SIDE EFFECTS AND RECOMMENDATIONS FOR MONITORING (CONT.)

Rifampin (RIF)	<ol style="list-style-type: none"> 1. Pruritis w / wo rash 2. GI reactions 3. Flu-like syndrome 4. Hepatotoxicity 5. Severe immunologic reactions 6. Orange discoloration of body fluids (urine, tears, etc.) 7. Drug Interactions 	<ol style="list-style-type: none"> 1. Rash occurs in 6% of patients and is generally self-limited. Continued treatment may be possible, but RIF should be stopped for more severe hypersensitivity reactions (rare). 2. GI symptoms rarely severe enough to require discontinuation of drug. 3. Rarely occurs with 2x weekly dosing but not with daily dosing. 4. Transient asymptomatic hyperbilirubinemia or more severe clinical hepatitis with cholestatic pattern. 5. Thrombocytopenia, hemolytic anemia, acute renal failure, TTP (all rare). 6. May stain contact lenses or clothing. 7. See Table 12. <p>*Safe in pregnancy.</p>	<p>LTBI</p> <ul style="list-style-type: none"> • No routine monitoring tests are required. <p>TB</p> <ul style="list-style-type: none"> • Consider baseline lab monitoring RIF given with INH or other liver toxic medications. • Drug interactions may be significant; measure serum concentrations of medications affected by co-administration with RIF or use alternative agents.
Rifabutin (RBT)	<ol style="list-style-type: none"> 1. Neutropenia 2. Uveitis 3. Polyarthralgias 4. Hepatotoxicity 5. Pseudo-jaundice (skin discoloration but normal Bili) 6. Rash 7. Flu-like syndrome 8. Drug interactions 	<ol style="list-style-type: none"> 1. Severe neutropenia in 2% and requires discontinuation. Effect is dose related and occurs more often with daily than intermittent dosing. 2. Rare, occurs more often when other drugs such as protease inhibitors or macrolides reduce RBT clearance. 3. More common at higher doses. 4. Asymptomatic elevation of liver enzymes and rare clinical hepatitis (like RIF). 5. Self-limited, resolves with discontinuation of drug. 6. Rarely associated with RBT. 7. Rare 8. See Table 12. <p>*Insufficient data in pregnancy, use with caution.</p>	<ul style="list-style-type: none"> • Monitoring is similar to RIF. • Drug interactions are less common but still occur.
Rifapentine (RPT)	(similar to RIF)	<p>*Insufficient data in pregnancy, use with caution.</p>	<ul style="list-style-type: none"> • Monitoring is similar to RIF • Drug interactions may be significant

TABLE 6. MEDICATION SIDE EFFECTS AND RECOMMENDATIONS FOR MONITORING (CONT.)

<p>Pyrazinamide (PZA)</p>	<ol style="list-style-type: none"> 1. Hepatotoxicity 2. GI symptoms (n/v) 3. Nongouty polyarthralgia 4. Acute gouty arthritis 5. Rash 6. Photosensitive dermatitis 	<ol style="list-style-type: none"> 1. Hepatotoxicity rare at standard doses. 2. Mild nausea, anorexia common, vomiting rare. 3. Polyarthralgias occur in 40%, rarely require drug discontinuation, responds to aspirin or NSAIDS. 4. Gout rare unless pre-existing. 5. Morbilliform rash usually self-limited and not an indication for discontinuation of drug. <p>*Insufficient data in pregnancy, avoid unless benefits outweigh risks.</p>	<ul style="list-style-type: none"> • Serum uric acid measurements are not recommended as a routine but may be a surrogate marker of adherence. • Monitor liver chemistries if used in persons with underlying liver disease.
<p>Ethambutol (EMB)</p>	<ol style="list-style-type: none"> 1. Retrobulbar neuritis 2. Peripheral neuritis (rare) 3. Cutaneous reactions 	<ol style="list-style-type: none"> 1. Not routinely used in children whose visual acuity cannot be monitored, but should be used if drug resistance suspected or adult-type disease is present <p>*Safe in pregnancy.</p>	<ul style="list-style-type: none"> • Baseline and monthly monitoring of visual acuity (Snellen chart) and red/green color discrimination. Check each eye separately.
<p>Streptomycin (SM)</p>	<ol style="list-style-type: none"> 1. Ototoxicity (vestibular and hearing) 2. Renal dysfunction 3. Pain at injection site 4. Neurotoxicity 5. Nephrotoxicity 	<ol style="list-style-type: none"> 1. Avoid or reduce dose to 10mg/kg/d in adults >59y . 2. In renal insufficiency, reduce frequency to 12-15mg/kg/dose 2-3Xweek. 3. Ultrasound and warm compression may reduce pain at injection site. 4. Commonly causes circumoral paresthesias immediately after injection. 5. Nephrotoxicity less common with SM than amikacin, capreomycin or kanamycin. Risk higher with use of diuretics. 6. May rarely interact with muscle relaxants to cause postoperative respiratory weakness. <p>*Contraindicated in pregnancy.</p>	<ul style="list-style-type: none"> • Baseline audiogram, vestibular testing, Romberg testing and serum creatinine. • Monthly assessment of renal function and questioning regarding auditory or vestibular systems. Repeat audiogram and vestibular testing if evidence of 8th nerve damage.

TABLE 6. MEDICATION SIDE EFFECTS AND RECOMMENDATIONS FOR MONITORING (CONT.)

Amikacin and Kanamycin	<ol style="list-style-type: none"> Ototoxicity (deafness more than vestibular dysfunction) Renal dysfunction Nephrotoxicity 	<ol style="list-style-type: none"> Avoid or reduce dose to 10mg/kg/d in adults >59y . In renal insufficiency, reduce frequency to 12-15mg/kg/dose 2-3Xweek. Nephrotoxicity risk higher with use of diuretics. Nearly always complete cross-resistance with the 2 drugs. Most SM-resistant strains are susceptible to them. <p>*Contraindicated in pregnancy.</p>	<ul style="list-style-type: none"> Baseline audiogram, vestibular testing, Romberg testing and serum creatinine. Monthly assessment of renal function and questioning regarding auditory or vestibular systems. Repeat audiogram and vestibular testing if evidence of 8th nerve damage.
Cycloserine	<ol style="list-style-type: none"> CNS effects Depression Drug interactions (phenytoin) 	<ol style="list-style-type: none"> Mild headache or restlessness to severe psychosis or seizures. Peripheral neuritis rare. <p>**Insufficient data in pregnancy, Use if no other options.</p>	<ul style="list-style-type: none"> B6 may prevent or treat neurotoxic side effects at 100-200mg/day. Neuropsychiatric status should be assessed at least monthly and more often if symptoms develop. Measure serum phenytoin levels if on both drugs.
Ethionamide	<ol style="list-style-type: none"> GI upset Hepatotoxicity Neurotoxicity Endocrine effects Hypersensitivity Metallic taste 	<ol style="list-style-type: none"> GI effects may be profound and improve if taken with food or at bedtime. Similar in structure to INH and may have similar side effects (hepatotoxicity). Neurotoxicity includes peripheral neuritis, optic neuritis, anxiety, depression, psychosis. Endocrine disturbances include gynecomastia, alopecia, hypothyroidism, impotence. DM may also be more difficult to manage. <p>*Contraindicated in pregnancy.</p>	<ul style="list-style-type: none"> Liver function tests should be monitored at baseline. Measure at monthly intervals If underlying liver disease present or if symptoms occur. TSH should be measured at baseline and at monthly intervals.
Capreomycin	<ol style="list-style-type: none"> Nephrotoxicity Ototoxicity 	<ol style="list-style-type: none"> Nephrotoxicity may result in reduced creatinine clearance or potassium and magnesium depletion. Proteinuria is common. Vestibular dysfunction, tinnitus, deafness more often in elderly persons and underlying renal insufficiency. <p>*Contraindicated in pregnancy.</p>	<ul style="list-style-type: none"> Monitoring as per Streptomycin. Measure monthly potassium and magnesium.

TABLE 6. MEDICATION SIDE EFFECTS AND RECOMMENDATIONS FOR MONITORING (CONT.)

<p>Para-Amino Salicylic Acid (PAS)</p>	<ol style="list-style-type: none"> 1. Hypothyroidism 2. Hepatotoxicity 3. GI distress 4. Malabsorption syndrome (steatorrhea and low folate) 	<ol style="list-style-type: none"> 1. Hypothyroidism risk increased with concomitant use of ethionamide. Goiter may occur; thyroid function returns to normal after drug stopped. <p>*No human studies, but has been used safely in pregnancy. Use only if no other options for pregnant woman with MDR TB.</p>	<ul style="list-style-type: none"> • Hepatic enzymes and thyroid function should be measured at baseline. With prolonged therapy (>3 months), thyroid function should be measured every 3 months.
<p>Fluoroquinolones Levofloxacin Moxifloxacin Gatifloxacin</p>	<ol style="list-style-type: none"> 1. Neurologic effects 2. Cutaneous reactions 3. GI disturbance 	<ol style="list-style-type: none"> 1. Dizziness, insomnia, tremulousness and headache. 2. Rash, pruritis, photosensitivity. 3. May cause nausea and bloating. 4. Antacids and other medications containing divalent cations decrease absorption of FQs; separate dosing by 2h. 5. Cross-resistance is a class effect. <p>*Avoid in pregnancy and children.</p>	<ul style="list-style-type: none"> • No specific monitoring required.

TABLE 7. MONITORING SCHEDULE FOR TB PATIENTS THROUGHOUT THERAPY

TEST	INITIATION	1 MONTH	2 MONTH	3 MONTH	6 MONTH	BEYOND 6 MONTHS
HEPATIC ENZYMES, BILIRUBIN, CBC, PLATELET COUNT, SERUM CREATININE, HIV (IF STATUS IS UNKNOWN)	Yes	As ordered by physician				
SPUTUM STUDIES	3 Specimens (1 per day for 3 consecutive days)	Yes	Yes	and every month until sputum is negative for two consecutive months		
CHEST X-RAYS	Yes	As ordered by physician			After treatment complete	
CLINICAL MONITORING	Evaluate monthly and PRN for side effects, adherence and other potential problems.					

TABLE 8. INSTRUCTION FOR GIVING STREPTOMYCIN AND OTHER INJECTABLE TB DRUGS

I. Equipment

- A. 22 gauge 1 - 1/2" needle vanish point syringe
- B. Bottle of Streptomycin or other injectable TB drug
- C. Alcohol swabs
- D. Gloves

II. Protocol

- A. Using a safety syringe with a 22 gauge needle, draw up the required amount of medication.
- B. Have the patient lie in a prone position and as relaxed as possible.
- C. Before injection, the skin of the upper outer quadrant of the gluteal area is cleansed with an alcohol swab. This is the preferred site for intramuscular injection.
- D. Spread skin tightly and insert needle quickly and deeply. Pull back gently on plunger watching to see if any blood appears in the syringe. If blood does appear, pull out needle and discard needle and syringe. Start procedures over using another injection site. If blood does not appear, give medication.
- E. Do not recap, bend or break needles. Dispose of needles and syringes in a puncture-resistant container.

III. Precautions: As with other injectable medication anaphylactic reactions can occur, though rarely, following the injection of Streptomycin. For this reason the following precautions should be observed.

- A. Question the patient about any evidence of drug toxicity or allergic reaction to previous injections.

- B. Observe the patient for 15-30 minutes following each injection.
- C. Follow regional or local health department policies for treatment of anaphylaxis, in the event of an anaphylactic reaction.
- D. Report all anaphylactic reactions to the physician as soon as possible.
- E. Document the problem in the patient's record.

TABLE 9. TESTING OF VISUAL ACUITY (SNELLEN CHART)

I. General Guidelines

- A. The health worker performing the test should have normal vision or vision corrected to normal.
- B. A change in a patient's visual acuity may be unilateral or bilateral. Each eye must be tested separately, followed by both eyes tested together.
- C. If a patient is wearing corrective glasses/lenses when drugs are started, especially Ethambutol, the glasses/lenses must be worn for the initial test and all subsequent visual acuity tests.
- D. If corrective eye glasses/lenses are prescribed for a patient during the course of treatment, the first reading taken with glasses/lenses should be recorded "with glasses or corrective lenses."

II. Physical Setting

- A. Select a quiet area that will accommodate the required distance from a desirable wall surface for visual testing.
- B. Place Snellen Chart on a light colored wall.
- C. Measure a 10 or 20 foot distance from the chart; identify this distance by a mark on the floor. The distance will depend upon the type of chart used.

III. Instructions to Patients and Recording of Results

- A. Explain the procedure to each patient.
- B. The patient may be seated or standing. If seated, the mark on the floor which identifies the 20-foot distance should rest under the center of the chair. If standing, instruct patient to stand with toes on the mark.

- C. Tell the patient to keep both eyes open during the test
- D. Have patient cover the eye not being checked. Avoid pressure on the covered eye.
- E. Check the right eye, then the left eye, and finally both eyes together. Visual acuity tests should be done with glasses/lenses on, if corrective glasses/lenses are worn.
- F. Record three readings, one for the right eye, one for the left eye, and one for both eyes tested together. In each instance, record only the lowest line in which the patient correctly identifies all letters or at least more than one-half the number of letters.
- G. Record results in fractions as shown on the Snellen Chart. If the patient can read most but not all letters of a line, record in parenthesis the number of letters missed. For example: 20/30 (-2) would mean that the patient missed 2 letters on the 20/30 line.

IV. Color Discrimination Test

- A. The patient should be asked to identify the red and green color from a series of five colors. These cards may be made by covering 3 x 5 cards with colored tapes or yarn, i.e., brown, yellow, red, blue, and green, or using colored poster board.
- B. If the patient can identify the red and green color the notation in the patient's record should be: Red-green color discrimination is normal. If unable to identify colors, this should also be noted in the record.
- C. Loss of the ability to discriminate red and green color should be called to the attention of the physician before medication is refilled.

TABLE 10. INFECTIOUS DISEASE SOCIETY OF AMERICA / UNITED STATES PUBLIC HEALTH SERVICE RATING SYSTEM FOR THE STRENGTH OF TREATMENT RECOMMENDATIONS BASED ON QUALITY OF EVIDENCE (1)

Strength of the recommendation

Preferred; should generally be offered

Alternative; acceptable to offer

Offer when preferred or alternative regimens cannot be given

Should generally not be offered

Should never be offered

Quality of evidence supporting the recommendation

- I. At least one properly randomized trial with clinical endpoints
- II. Clinical trials that either are not randomized or were conducted in other populations.
- III. Expert opinion

1 Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE Jr, Sweet RL, Wenzel RP. Purpose of quality standards for infectious diseases. *Clin Infect Dis* 1994; 18:421.

TABLE 11. DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS

Regimen	INITIAL PHASE		CONTINUATION PHASE			TOTAL DOSES	RATING* (Evidence) [†]	
	Drugs	Interval and Doses [‡] (minimum duration)	Regimen	Drugs	Interval and Doses ^{‡ #} (minimum duration)	(Minimum duration)	HIV-	HIV+
1	INH RIF PZA EMB	Seven days per week for 56 doses (8 weeks) <i>or</i> five days per week for 40 doses (8 weeks)◊	1a	INH/RIF	Seven days per week for 126 doses (18 weeks) <i>or</i> five days per week for 90 doses (18 weeks)◊	182 OR 146 (26 weeks)	A (I)	A (II)
			1b	INH/RIF	Twice-weekly for 36 doses (18 weeks) Once weekly for 18 doses (18 weeks)	92 OR 76 (26 weeks) 74 OR 58 (26 weeks)	A (I) B (I)	A (II)§ E (I)
			1c**	INH/RPT				
2	INH RIF PZA EMB	Seven days per week for 14 doses (2 weeks) <i>then</i> twice-weekly for 12 doses (6 weeks) <i>or</i> five days per week for 15 doses (3 weeks) ◊ <i>then</i> twice weekly for 10 doses (5 weeks)	2 a	INH/RIF	Twice-weekly for 36 doses (18 weeks) Once weekly for 18 doses (18 weeks)	62 OR 63 (26 weeks) 44 OR 43 (26 weeks)	A(II) B(I)	B (II)§ E (I)
			2 b**	INH/RPT				
3	INH RIF PZA EMB	Thrice-weekly for 24 doses (8 weeks)	3a	INH/RIF	Thrice-weekly for 54 doses (18 weeks)	78 (26 weeks)	B (I)	B (II)
4	INH RIF EMB	Seven days per week for 56 doses (8 weeks) <i>or</i> five days per week for 40 doses (8 weeks)◊	4 a	INH/RIF	Seven days per week for 196 doses (28 weeks) <i>or</i> five days per weeks for 140 doses (28 weeks)◊	252 or 180 (36 weeks) 112 OR 96 (36 weeks)	C (I)	C (II)
			4 b	INH/RIF	Twice-weekly for 56 doses (28 weeks)		C (I)	C (II)

[†]INH=isoniazid, RIF=rifampin, RPT=rifapentine, PZA=pyrazinamide, EMB=ethambutol

Note: Please see following page

TABLE 11. (NOTES) DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS

‡ When DOT is used drugs may be given 5 days per week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice. TDOH recommends that DOT be given 7/7 days during the initial 14 days of therapy or longer if isolation is prolonged.

** Options 1c and 2b should only be used in HIV-negative patients who have negative sputum smears at the time of completion of 2 months of therapy and who do not have cavitation on initial chest radiograph. For patients started on this regimen and found to have a positive culture at 2 months, treatment should be extended an extra 3 months.

Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (28 week; either 196 doses [daily] or 56 doses [twice-weekly]) continuation phase.

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

◇ Five-day-a-week administration is always given by DOT.

Definitions of evidence ratings

*A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; E = Should never be given.

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

TABLE 12. EPIDEMIOLOGICAL CIRCUMSTANCES IN WHICH AN EXPOSED PERSON IS AT INCREASED RISK OF INFECTION WITH DRUG-RESISTANT *MYCOBACTERIUM TUBERCULOSIS**

- Exposure to a person who has known drug-resistant tuberculosis
- Exposure to a person with active tuberculosis who has had prior treatment for tuberculosis (treatment failure or relapse) and whose susceptibility test results are not known.
- Exposure to persons with active tuberculosis from areas in which there is a high prevalence of drug resistance.
- Exposure to persons who continue to have positive sputum smears after 2 months of combination chemotherapy.
- Travel in an area of high prevalence of drug resistance.

**This information to be used in deciding whether or not to add a fourth drug (usually EMB) for children with active tuberculosis, not to infer the empiric need for a second-line treatment regimen.*

TABLE 13. CLINICALLY-SIGNIFICANT DRUG- DRUG INTERACTIONS INVOLVING THE RIFAMYCINS

Drug class	Drugs whose concentrations are substantially decreased by rifamycins (references)	Comments
Anti-infectives	HIV-1 protease inhibitors (saquinavir, indinavir, nelfinavir, amprenavir, ritonavir, lopinavir/ritonavir)	Can be used with rifabutin. Ritonavir, 400-600 mg twice-daily, probably can be used with rifampin. The combination of saquinavir and ritonavir can also be used with rifampin.
	NNRTIs Delavirdine Nevirapine Efavirenz	Delavirdine should not be used with any rifamycin. Doses of nevirapine and efavirenz need to be increased if given with rifampin, no dose increase needed if given with rifabutin
	Macrolide antibiotics (clarithromycin, erythromycin)	Azithromycin has no significant interaction with rifamycins
	Doxycycline	May require use of an alternate drug or drug combination
	Azole antifungal agents (ketoconazole, itraconazole)	Itraconazole and ketoconazole concentrations may be sub-therapeutic with any of the rifamycins. Fluconazole can be used with rifamycins, but the dose of fluconazole may have to be increased
	Atovaquone	Consider alternate form of <i>Pneumocystis carinii</i> treatment or prophylaxis
	Chloramphenicol	Consider an alternative antibiotic
	Mefloquine	Consider alternate form of malaria prophylaxis
Hormone therapy	Ethinylestradiol, norethindrone	Women of reproductive potential on oral contraceptives should be advised to add a barrier method of contraception when on a rifamycin
	Tamoxifen	May require alternate therapy
	Levothyroxine	Monitoring of serum TSH recommended; may require increased dose of levothyroxine
Narcotics	Methadone	Rifampin and rifapentine use may require methadone dose increase Rifabutin infrequently causes methadone withdrawal
Anticoagulants	Warfarin	Monitor prothrombin time, may require 2-3 fold dose increase

TABLE 13. CLINICALLY-SIGNIFICANT DRUG- DRUG INTERACTIONS INVOLVING THE RIFAMYCINS (CONT.)

Immunosuppressive agents	Cyclosporine, tacrolimus	Rifabutin may allow concomitant use of cyclosporine and a rifamycin
	Corticosteroids	Monitor clinically; may require 2-3 fold dose increase
Anticonvulsants	Phenytoin, lamotrigine	Therapeutic drug monitoring recommended; may require dose increase
Cardiovascular agents	Verapamil, nifedipine, diltiazem (A similar interaction is also predicted for felodipine and nisoldipine)	Clinical monitoring recommended; may require change to an alternate drug
	Propranolol, metoprolol	Clinical monitoring recommended; may require dose increase or change to an alternate drug
	Enalapril, losartan	Monitor clinically; may require a dose increase or use of an alternate drug
	Digoxin (among patients with renal insufficiency), digitoxin	Therapeutic drug monitoring recommended; may require dose increase
	Quinidine	Therapeutic drug monitoring recommended; may require dose increase
	Mexilitine, tocainide, propafenone	Clinical monitoring recommended; may require change to an alternate drug
Theophylline	Theophylline	Therapeutic drug monitoring recommended; may require dose increase
Sulfonylurea hypoglycemics	Tolbutamide, chlorpropamide, glyburide, glimepiride, repaglinide	Monitor blood glucose; may require dose increase or change to an alternate drug
Hypolipidemics	Simvastatin, fluvastatin	Monitor hypolipidemic effect; may require use of an alternate drug
Psychotropic drugs	Nortriptyline	Therapeutic drug monitoring recommended; may require dose increase or change to alternate drug
	Haloperidol, quetiapine	Monitor clinically; may require a dose increase or use of an alternate drug
	Benzodiazepines (e.g., diazepam, triazolam, zolpidem, buspirone)	Monitor clinically; may require a dose increase or use of an alternate drug

TABLE 14. SUMMARY OF EVIDENCE* FOR TREATMENT OF PERSONS WITH LATENT TUBERCULOSIS INFECTION
 (Includes Persons with Radiographic Evidence of Prior TB and Negative Sputum Cultures Not Treated Previously)

Treatment Regimen	Rating/Evidence	
	HIV-negative	HIV-positive
INH for 9 months	AII	AII
RIF with or without INH for 4 months	BII	BIII
RIF and PZA for 2 months	DIII	DIII

*for rating system see [Table 10](#).

TABLE 15. DOSING RECOMMENDATIONS FOR ADULT PATIENTS WITH REDUCED RENAL FUNCTION AND FOR ADULT PATIENTS RECEIVING HEMODIALYSIS

Drug	Change in frequency?	Recommended dose and frequency for patients with creatinine clearance < 30 ml / min. or patients receiving hemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg three times/week
Rifampin	No change	600 mg once daily, or 600 mg three times/week
Pyrazinamide	Yes	25-35 mg/kg/dose three times/week (not daily)
Ethambutol	Yes	15-25 mg/kg/dose three times/week (not daily)
Levofloxacin	Yes	750-1000 mg/dose three times/week (not daily)
Cycloserine	Yes	250 mg once daily, or 500 mg/dose three times/week*
Ethionamide	No change	250-500 mg/dose daily
PAS	No change	4 gm/dose twice daily
Streptomycin	Yes	12-15 mg/kg/dose two-three times/week (not daily)
Capreomycin	Yes	12-15 mg/kg/dose two-three times/week (not daily)
Kanamycin	Yes	12-15 mg/kg/dose two-three times/week (not daily)
Amikacin	Yes	12-15 mg/kg/dose two-three times/week (not daily)

- Standard doses are given unless there is intolerance.
- The medications should be given after hemodialysis on the day of hemodialysis.
- Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.
- *The appropriateness of 250 mg daily doses has not been established.
There should be careful monitoring for evidence of neurotoxicity
- Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing using serum concentration monitoring.

TABLE 16. POTENTIAL REGIMENS FOR THE MANAGEMENT OF PATIENTS WITH DRUG-RESISTANT PULMONARY TUBERCULOSIS

Pattern of Drug Resistance	Suggested Regimen	Duration of Rx	Comments
INH (\pm SM)	RIF, PZA, EMB \pm I.A. or FQN	6 months	In BMRC trials, 6-month intermittent regimens have yielded $\geq 95\%$ success rates despite resistance to INH * \dagger . I.A. such as SM, were slightly more active than EMB in these trials. In cases of SM resistance, amikacin, kanamycin, or capreomycin may be employed. Fluoroquinolones were not employed in BMRC studies, but should strengthen the regimen for patients with more extensive disease. To provide a sufficient margin of safety, the oral agents (in addition to RIF) should be continued beyond the first 2 months with RIF and at least one additional active agent being given throughout the 6 months. INH should be stopped in cases of INH resistance (see text for additional discussion).
INH and RIF (\pm SM)	FQN, PZA, EMB, I.A., \pm alternative agent	18 to 24 months	In such cases, extended treatment is needed to lessen the risk of relapse. In cases with extensive disease, the use of an additional agent (alternative agents) may be prudent to lessen the risk of failure and additional acquired drug resistance. Resectional surgery may be appropriate (see text).
INH, RIF, (\pm SM) and EMB or PZA	FQN (EMB or PZA if active) I.A. and two alternative agents	24 months	Use the first-line agents to which there is susceptibility. Add two or more alternative agents in case of extensive disease. Surgery should be considered (see text).
RIF	INH, PZA, EMB, FQN, \pm I.A.	9 to 12 months	A thrice-weekly regimen of INH, PZA, and SM was effective in a BMRC trial \dagger . However, extended use of an injectable agent may not be feasible. An all-oral regimen for 12 months should be effective. But for more extensive disease and/or to shorten duration, an injectable agent may be added in the initial 2-months of therapy.

FQN = fluoroquinolone; most experience involves ofloxacin, levofloxacin, or ciprofloxacin.

I.A. = Injectable agent; may include aminoglycosides (streptomycin, amikacin, or kanamycin) or the polypeptide, capreomycin.

Alternative agents: Ethionamide, cycloserine, para-aminosalicylic acid, clarithromycin, amoxicillin/clavulanate, linezolid.

* Hong Kong Chest service/British Medical Research Council. Five-year follow-up of a controlled trial of five, 6-month regimens of chemotherapy for tuberculosis. Am Rev Respir Dis 1987; 136: 1339-1342.

\dagger Hong Kong Chest Service/British Medical Research Council. Controlled trial of 2,4, and 6-months of pyrazinamide in 6-month, three-times weekly regimens for smear-positive pulmonary tuberculosis, including an assessment of a combined preparation of isoniazid, rifampin, and pyrazinamide: results at 30 months. Am Rev Respir Dis. 1991; 143: 700-706.

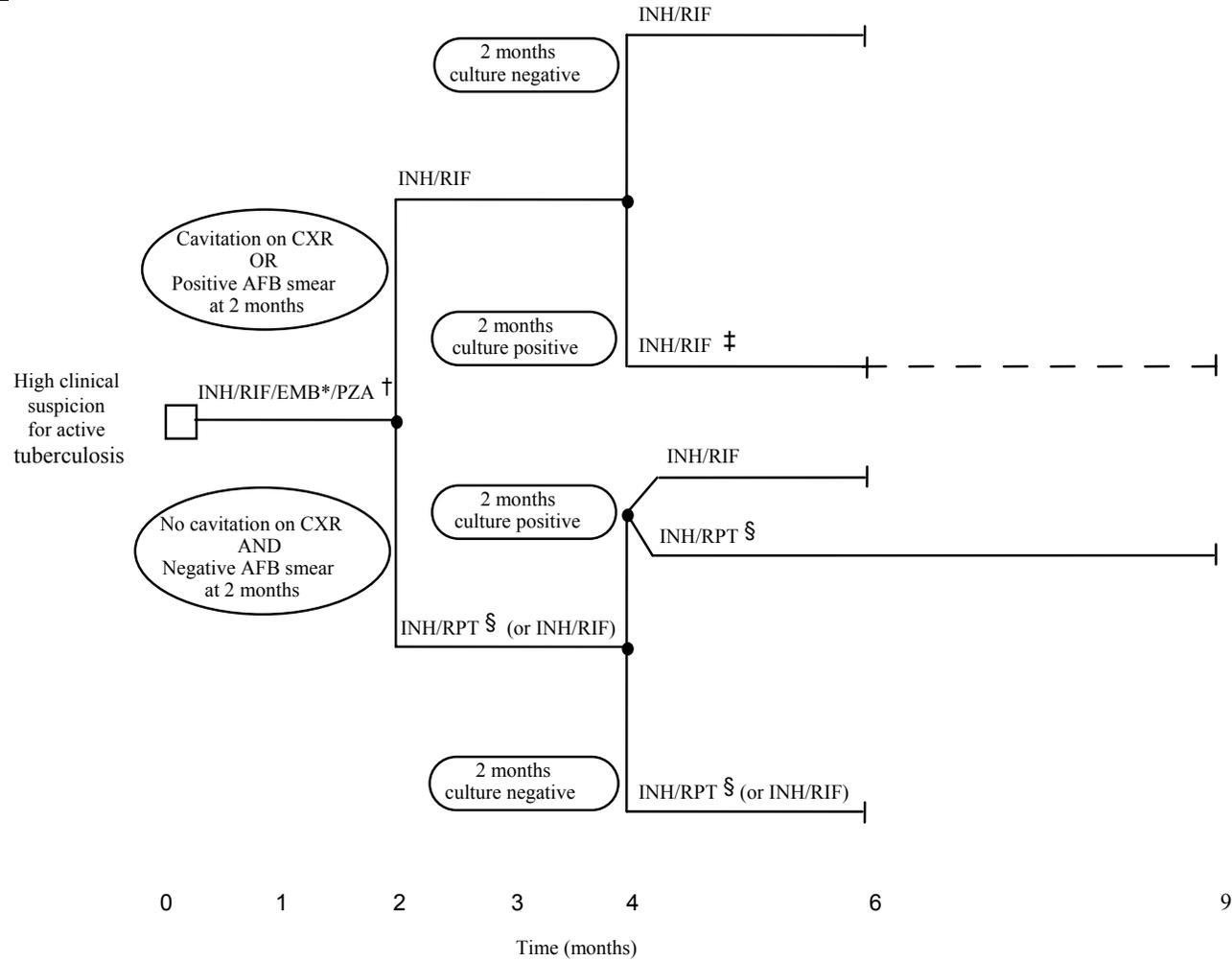
FIGURE 1. (NOTES) TREATMENT ALGORITHM FOR TUBERCULOSIS.

Patients in whom tuberculosis is proven or strongly suspected should have treatment initiated with isoniazid, rifampin, pyrazinamide, and ethambutol for the initial 2 months. A repeat smear and culture should be performed at the time 2 months of treatment is completed. If cavities were seen on the initial chest radiograph, the acid-fast smear is positive at completion of 2 months of treatment or the patient has HIV infection with a CD4 cell count of $>100/\text{ul}$ (upper portion of Figure), the *continuation phase* of treatment should consist of isoniazid and rifampin daily or twice weekly for 4 months to complete a total of 6 months of treatment. If the patient has HIV infection and the CD4 cell count is $<100/\text{ul}$ the *continuation phase* should consist of daily or thrice weekly isoniazid and rifampin. If cavitation was present on the initial chest radiograph and the culture at the time of completion of 2 months of therapy is positive, the continuation phase should be lengthened to 7 months (total of 9 months treatment).

In HIV-uninfected patients having *no* cavitation on chest radiograph *and negative* acid-fast smears at completion of 2 months of treatment, the *continuation phase* may consist of either once-weekly isoniazid and rifapentine, or daily or twice weekly isoniazid and rifampin to complete a total of 6 months (lower portion of Figure). Patients receiving isoniazid/rifapentine whose 2-month cultures are positive should have treatment extended by 3 additional months. (total of 9 months).

Abbreviations: CXR = chest radiograph; EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

FIGURE 1. TREATMENT ALGORITHM FOR TUBERCULOSIS



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

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

‡Therapy should be extended to 9 months for those with both cavitation on CXR and positive culture at 2 months

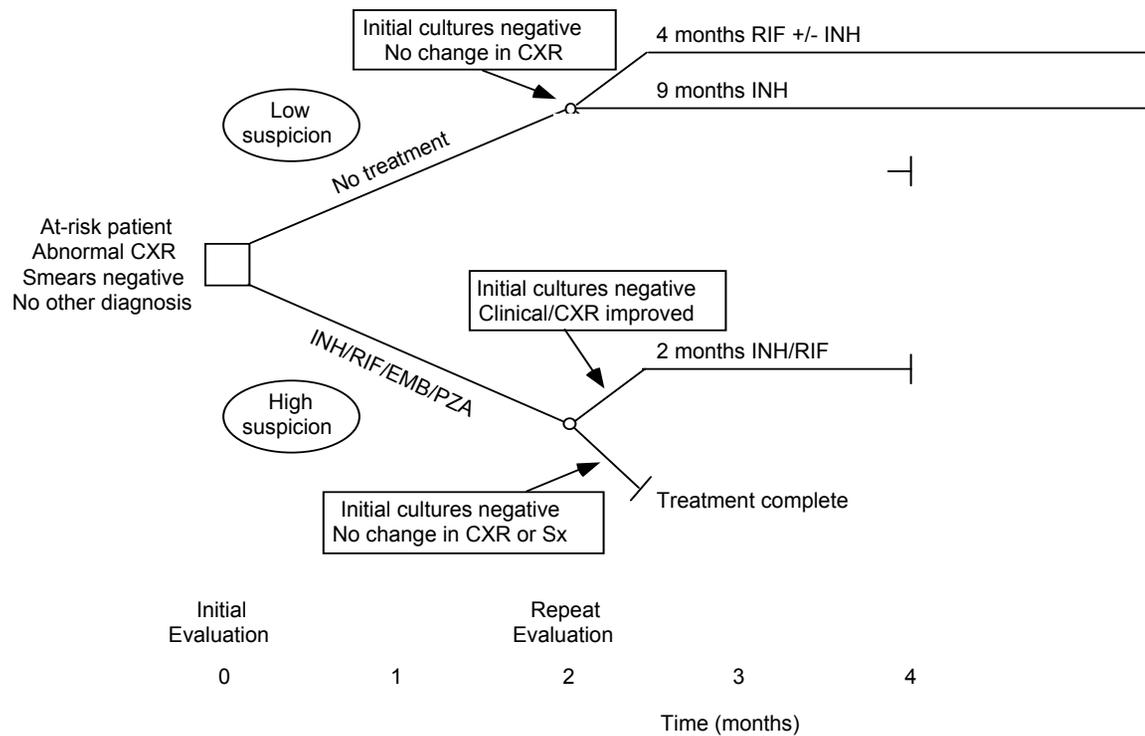
§RPT should not be used in HIV-infected patients with tuberculosis

FIGURE 2: (NOTES) TREATMENT OF ACTIVE CULTURE-NEGATIVE PULMONARY TUBERCULOSIS AND INACTIVE TUBERCULOSIS

The decision to begin treatment for a patient with sputum smears that are negative depends on the degree of suspicion that the patient has tuberculosis. If the clinical suspicion is high (lower portion of figure), then multidrug therapy should be initiated before acid-fast smear/culture results are known. If the diagnosis is confirmed by a positive culture, treatment can be continued to complete a standard course of therapy (see [Figure 1](#)). If initial cultures remain negative and treatment has been with multiple drugs for 2 months, then there are two options depending on repeat evaluation at 2 months (lower portion of figure): 1) if the patient demonstrates symptomatic or radiographic improvement without another apparent diagnosis, then a diagnosis of culture-negative tuberculosis can be inferred. Treatment should be continued with isoniazid and rifampin alone for an additional 2 months; 2) if the patient demonstrates neither symptomatic nor radiographic improvement then prior tuberculosis is unlikely and treatment is complete once treatment including at least 2 months of isoniazid, rifampin and pyrazinamide have been taken. In low-suspicion patients not initially on treatment (upper portion of figure), if cultures remain negative, the patient has no symptoms, and the chest radiograph is unchanged at 2-3 months, there are 2 treatment options. These are 1) isoniazid for 9 months; and 2) rifampin with or without isoniazid for 4 months.

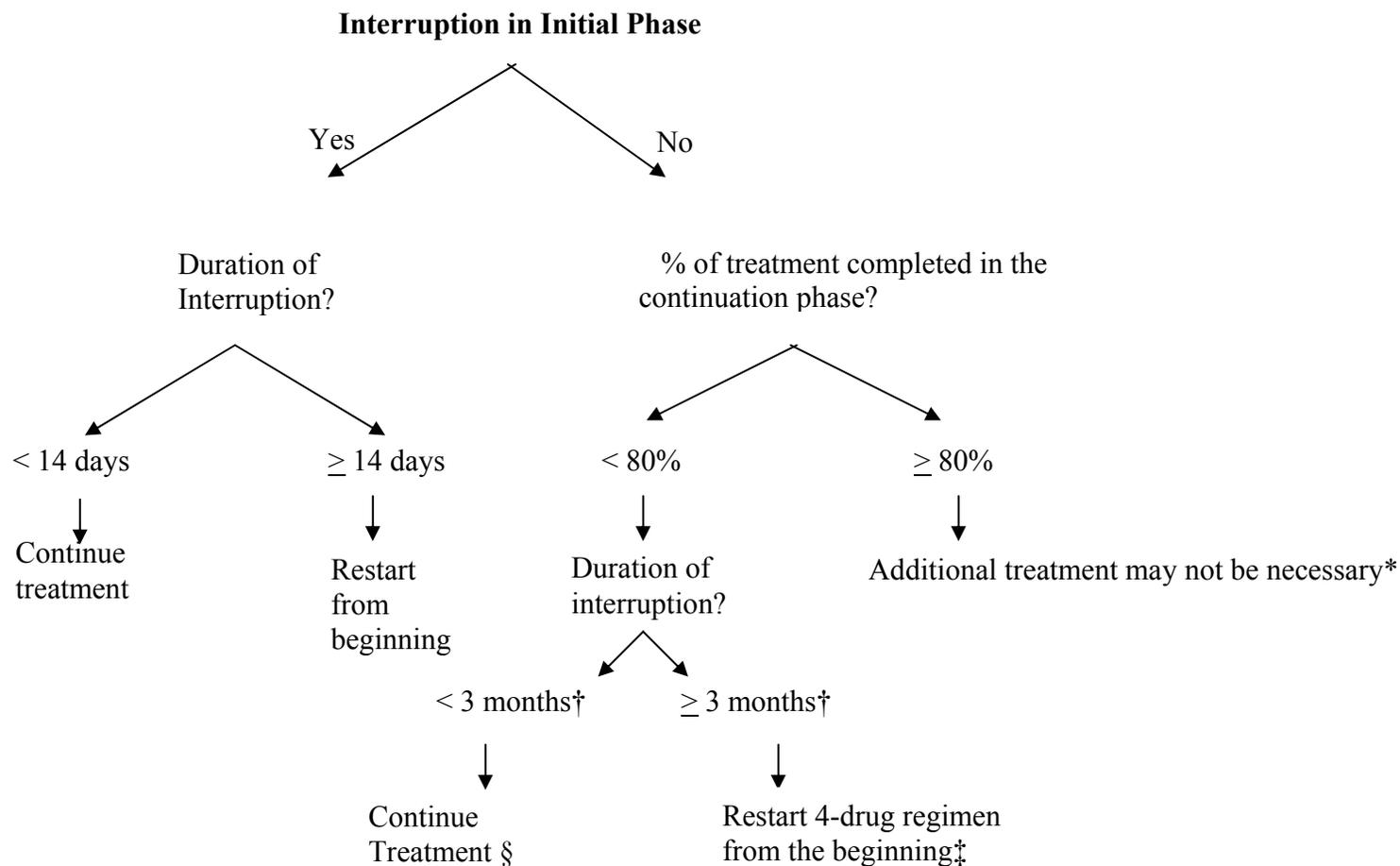
Abbreviations: EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin.

FIGURE 2. TREATMENT OF ACTIVE CULTURE-NEGATIVE PULMONARY TUBERCULOSIS AND INACTIVE TUBERCULOSIS



The decision to begin treatment for a patient with sputum smears that are negative depends on the degree of suspicion that the patient has tuberculosis. The considerations in choosing among the treatment options are discussed in the text.

FIGURE 3. MANAGEMENT OF TREATMENT INTERRUPTIONS



*Patients who were initially AFB smear positive should receive additional therapy.

†Recheck smears and cultures (if positive check drug susceptibility results). Start DOT if not already being used.

§ If repeat culture is positive, restart 4-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, continue therapy to complete regimen within 9 months of original start date.

‡If repeat culture is positive, continue 4-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, consider stopping therapy if patient has received a total of 9 months of therapy.

MYCOBACTERIA OTHER THAN TUBERCULOSIS (MOTT)

The diagnosis, treatment and follow-up of disease in individuals infected with MOTT are not the responsibility of the Tuberculosis Elimination Program. Persons with these mycobacterial diseases should be referred to private providers. State TB Elimination Program funds cannot be utilized for the treatment of medical conditions other than tuberculosis.

X. TB AND HIV CO-INFECTION

TB AND HIV CO-INFECTION

Patients with HIV infection are at much greater risk of developing active TB once infected and the morbidity and mortality associated with co-infection is substantial. Therefore, identification of HIV status is essential to the management of persons with latent TB infection or active TB disease. **All persons with LTBI or TB must be encouraged to have HIV testing regardless of age or sociodemographic factors.** HIV testing is also recommended for all contacts to a TB case or suspect. Informed consent is required prior to HIV testing and should be documented in the patient's medical records.

I. DIAGNOSIS OF TUBERCULOSIS

Patients infected with HIV are evaluated for tuberculosis the same way as uninfected patients, including use of the PPD skin test, radiographic evaluation and laboratory testing. Clinicians must also remember that both the skin test and the chest x-ray can be falsely negative in HIV-infected patients.

- A. Tuberculosis should be considered in all patients with or at risk of HIV infection with pulmonary symptoms. The clinical presentation of TB in HIV-infected persons is often unusual and providers should also maintain a high index of suspicion for TB in HIV+ patients with systemic or other extrapulmonary symptoms.
- B. All HIV-positive patients suspected of having TB should be given a tuberculin skin test (Mantoux). However, a negative TST result does not rule out the presence of TB infection or disease since the immunosuppression associated with HIV infection may cause a false-negative result. **Anergy testing is not recommended** in persons who are infected with HIV or who are otherwise immunocompromised.
- C. **All HIV-infected patients with pulmonary symptoms should be immediately evaluated with a chest radiograph and sputum smear/culture** for AFB. Pulmonary TB in patients with HIV infection cannot be readily distinguished from other pulmonary infections on the basis of clinical and radiographic findings alone; cavitation is less common and infiltrates may be in any lung zone. HIV-infected patients with pulmonary TB may even have a normal chest radiograph. Therefore, sputum examination should be ordered in all HIV-positive patients with pulmonary symptoms.
- D. Extrapulmonary TB, i.e., lymphatic or miliary, is more common in patients with HIV infection and often co-exists with pulmonary disease. **All HIV-infected patients with extrapulmonary TB should therefore be evaluated with chest radiograph and sputum examination.**

- E. Obtain culture *and* susceptibilities in HIV-positive patients to obtain a definitive diagnosis (atypical mycobacteria are also common in HIV+ patients) and to ensure adequate therapy is provided (evaluate for drug resistance).
- F. Other appropriate specimens, including tissue or body fluids, should be cultured for mycobacteria if extrapulmonary TB is suspected. If indicated, bronchoscopy with lavage and transbronchial biopsy, lymph node biopsy, bone marrow biopsy, lumbar puncture or other procedures may be needed to obtain specimens for culture and histologic examination.

II. TREATMENT OF TUBERCULOSIS

- A. In general, HIV-infected patients with TB can be effectively treated utilizing the same treatment regimens and dosages as HIV-negative TB cases (Section IX). However, the management of TB patients with HIV infection can be complicated by factors such as increased risk of medication intolerance/toxicity, drug-interactions, immune restoration syndrome, etc. Thus, treatment of patients with both HIV infection and TB disease should only be provided by or in conjunction with a physician experienced in treating co-infected patients. **All patients with TB and HIV should have DOT for every dose throughout treatment.**
- B. The presence of hepatic abnormalities is not an absolute contraindication to antimycobacterial drugs, but frequent clinical or laboratory monitoring may reduce the risk of toxicity. If hepatic dysfunction occurs or appears to worsen on therapy, TB (and/or HIV) treatment may need to be interrupted and a thorough consideration of other precipitating factors (other hepatotoxic meds, substance abuse etc.) should be made (see Section IX). TB treatment should be restarted cautiously but as soon as possible, with either the same or an adjusted regimen. Consultation regarding this issue may be obtained from the Central Office TB Control Officer.
- C. Several antimycobacterial and HIV drugs may cause hematologic side effects, such as anemia and a low platelet or white blood cell count. Although this is not an absolute contraindication to TB treatment, complete blood counts should be measured before and during therapy.
- D. Refer to this website for recommendations regarding the concurrent use of anti-retroviral and TB medications:
http://www.cdc.gov/nchstp/tb/tb_hiv_drugs/toc.htm.

III. INFECTION CONTROL

- A. See recommendations published by the Centers for Disease Control and Prevention regarding the prevention of transmission of HIV to health care workers (“Guidelines for Prevention of Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Health-Care and Public-Safety Workers, “MMWR 23 June 1989, 38 (S-6). Providers should adhere to the Occupational Safety and Health Administration’s (OSHA) rules governing occupational exposure to bloodborne pathogens.
- B. Apply appropriate infection control procedures when HIV-infected persons are undergoing diagnostic procedures such as sputum induction, bronchoscopy or drawing blood.

IV. EVALUATING HIV-INFECTED PATIENTS FOR LATENT TB INFECTION

- A. All persons with known HIV infection should be given a TB skin test at HIV diagnosis; TST should be repeated annually if the patient has ongoing or new risk factors for TB exposure.
- B. All HIV-positive patients who have LTBI or are identified as a contact to a TB case or suspect should be carefully evaluated for active tuberculosis disease prior to the initiation of LTBI therapy (including chest radiograph), regardless of TST results. Persons with HIV risk factors and unknown HIV status should be encouraged to have HIV testing and should also receive careful evaluation for the presence of TB disease.
- C. HIV-infected contacts should be treated for LTBI once TB disease has been ruled out by exam and chest radiograph, regardless of TST results. Re-evaluation and treatment should be provided with each new exposure to a TB case.

V. TREATMENT OF LTBI

- A. Persons with a positive TST and HIV infection have a 7-10% annual risk of developing TB disease. Therefore these patients should be a high priority for the administration of LTBI.
- B. Isoniazid daily or twice weekly under DOPT for 9 months is the preferred treatment regimen for HIV-positive persons with LTBI. For patients who are non-adherent to self-administered treatment, DOPT

should be implemented. Section IV provides detailed guidelines for the treatment and monitoring of LTBI in HIV-infected persons.

VI. EVALUATING TB PATIENTS FOR HIV INFECTION

- A. All patients with active tuberculosis or LTBI should receive an HIV test, particularly those with increased risk for HIV infection (see below). Contacts to a TB case or suspect should be assessed for HIV risk factors and encouraged to have HIV testing if they are suspected of being at high risk.
- B. Persons who should be considered at high risk for HIV infection include:
1. Men who have sex with other men (e.g., homosexual, bisexual). *Patients who engage in homosexual activity may not identify themselves as bisexual or homosexual.*
 2. Present or past drug users (intravenous or non-intravenous).
 3. Persons with clinical or epidemiological evidence of HIV infection, such as those with signs or symptoms of HIV/AIDS and persons who may have a HIV+ close contact.
 4. Persons who are sexually active with more than one partner.
 5. Male or female prostitutes and their sex partners.
 6. Persons who exchange sex for drugs.
 7. Sex partners of high-risk or HIV-infected persons.
 8. All persons with hemophilia who received clotting-factor products before 1985.
 9. Persons who received a transfusion between 1977 and 1985.
 10. Newborn infants of high-risk or HIV-infected mothers.
- C. If possible, HIV and tuberculosis counseling and testing should be done at the same location, either HIV testing/counseling sites or in TB clinics.
- D. HIV/AIDS is reportable, and persons found to have a positive HIV test should be immediately reported to the appropriate Regional HIV Surveillance Representative.

- E. Infection with atypical mycobacterium is also common in persons with HIV/AIDS. However, the TB Elimination Program does not provide services for treating mycobacteria other than tuberculosis (MOTT). Patients with these infections should be referred to private providers.

- F. HIV testing should be performed in accordance with current Tennessee Department of Health guidelines, including counseling and obtaining informed consent. HIV infection is by Departmental Rule a sexually transmitted disease and falls under the strict rules and statutes regarding confidentiality of STD information.

VIII. DOCUMENTATION

HIV information should be documented in the patient's medical record in accordance with the Tennessee Department of Health's current policy.

XI. DIRECTLY OBSERVED THERAPY

DIRECTLY OBSERVED THERAPY (DOT)

- I. **DOT** is the direct visual observation by a responsible individual of a patient's ingestion of TB medicines.

DOT is the *National* standard of care for all TB suspects and cases.

A. **Priorities for DOT Service**

1. All children and adolescents
2. Adults with certain conditions/ circumstances (see below)
3. All other TB cases and suspects

Note: If staff is unable to provide DOT for all TB cases and suspects, the Central Office TB Elimination Program should be notified by the Health Officer.

B. **Priority Conditions/Circumstances for DOT in Adults:**

1. Pulmonary TB
2. Drug resistance
3. Treatment failure or relapse
4. HIV infection (or other immunosuppression)
5. Previous treatment for TB or LTBI
6. Current or prior substance abuse
7. Psychiatric illness or memory impairment
8. Previous non-adherence to therapy

II. DIRECTLY OBSERVED PREVENTIVE THERAPY (DOPT)

- A. DOPT should be provided for all children <18 years with latent TB infection (LTBI), including children on "window period therapy" as contacts to suspect/cases.

- B. DOPT should be provided to certain adults with LTBI if feasible:
 - 1. HIV+ or other immunosuppression
 - 2. Persons unable to self-administer
 - 3. Mental or psychiatric conditions
 - 4. Substance abuse
 - 5. Contacts to MDR-TB
- C. DOPT should be considered for contacts with recent TST conversions

III. INTERMITTENT DRUG REGIMENS

- A. All first line TB meds can be given daily, 2x per week or 3x per week for suspects and cases.
- B. Isoniazid for LTBI can be given as DOPT 2x week
- C. Rifampin for LTBI can only be given as daily therapy

IV. LOGISTICAL CONSIDERATIONS

A. Who is Responsible for DOT?

- 1. *The public health department bears ultimate responsibility for the provision of DOT/DOPT.*
 - a. DOT must be provided for all Health Department TB cases and suspects.
 - b. If a non-Health Department provider does not order DOT for a TB case or suspect, the TB Clinic Physician should make phone contact with the provider to encourage DOT.

B. Who Can Deliver DOT?

- 1. Although the Health Department bears ultimate responsibility for the provision of DOT, other persons can be trained to share this responsibility.

- a. For patients residing in institutional settings that are conducive to observation of therapy, staff employed by that facility can be trained to provide DOT according to health department standards.
 - 1) Hospital
 - 2) Nursing homes
 - 3) Correctional facilities
 - 4) Methadone or other alcohol and drug treatment sites
 - b. Other responsible DOT providers can/may be health care workers, school or employee nurses, or clergy.
 - c. Medical persons are preferred (can provide clinical monitoring as well), but non-medical persons can be trained to provide DOT.
2. Family members and friends should not be allowed to provide DOT.
 3. Any persons providing DOT must be trained to follow Health Department standards
 4. Patient must provide informed written consent to break confidentiality if non-Health Department staff will provide DOT.

C. Where Can DOT Be Provided?

1. DOT can be provided at any site that is mutually agreeable and allows for staff safety and patient comfort and confidentiality (e.g. office, clinic, patient's home, place of employment, school, street corner, restaurant)

D. Frequency of DOT

1. DOT should be given every day (7 out of 7 days) during the initial 2 weeks of therapy, including over weekends and holidays.
 - a. DOT should be given daily as long as patient is on isolation, even if this extends beyond 2 weeks.
 - b. Provider may order DOT to be continued over additional weekends and holidays.

2. After the initial 2 weeks (or more if isolation prolonged), DOT can be administered 5 out of 7 days a week, 2 days per week, or 3 days per week as ordered.

a. Daily therapy:

- 1) If the patient continues taking daily DOT after isolation discontinued, therapy can be given 5 out of 7 days. The patient can either skip the weekend doses or self-administer for 2 days (unless the provider orders DOT to be continued over additional weekends and holidays). This schedule will still be consistent with CDC TIMS “reporting criteria for DOT.”
- 2) The 5 doses must be given in a Sunday to Saturday period to be counted as a full week of DOT.
- 3) If a daily dose is missed Mon-Fri, it must be given on Saturday by DOT, otherwise it must be added to the end of treatment.
- 4) Patients should not be allowed to self-administer more than 2 out of 7 daily doses. Special permission must be obtained and documented from the TB physician to allow patients to self-administer medications for more than 2 days (i.e. during travel).

b. Intermittent therapy:

- 1) Twice weekly: If ordered 2 x per week, both doses must be given DOT with at least 72 hours between each dose.
- 2) Thrice weekly: If ordered 3 x per week, all 3 doses must be given DOT with at least 48 hours between each dose.
- 3) Once-weekly: If ordered 1 x per week, each dose must be given as DOT with at least 5 days between each dose.
- 4) **Patients should not be allowed to self-administer intermittent doses.** If the patient plans to miss any intermittent doses (i.e. during travel), special permission must be obtained and documented from the TB physician to allow patients to self-administer medications and the patient must take daily therapy during this period.

E. Practical Considerations

1. DOT worker should leave only enough medications for the weekend on the preceding Friday.
2. Medications should never be left with the patient, a family member or other person to be taken later, except in the circumstances outlined above.
3. Medications should not be left at the home or other meeting place, if the patient is not there when the DOT visit is attempted.
4. Face the patient and observe him/her swallow each dose. Ask patient to open his/her mouth and show that the pill has been swallowed. This should preferably be done one pill at a time. Patients can take several pills at once if they prefer, but be sure that all pills are swallowed.
5. Obtain a drink to wash down the pills *prior* to giving the pills to the patient.
6. In settings where more than one person is on DOT/DOPT (i.e. families where more than one member is being treated), administer therapy to one patient at a time.
7. Spend time and talk with the patient after DOT is given to allow time for digestion to begin.
8. Ideally, the same person should administer DOT to a patient throughout therapy. If this is not feasible, have a “case management” session on each patient so that all staff responsible for DOT can agree upon a standard method of DOT to ensure consistency for that patient, (i.e. if the patient prefers to take one pill at a time, all staff should offer the pills one at a time).
9. Try to tailor the DOT to each patient’s needs by arranging DOT around the patient’s work schedule.
10. Be aware of the patient’s concerns and fears about TB/LTBI. Educate all patients and their families frequently during therapy. Take time to answer questions or address patients’ concerns.
11. Interpreters and translated materials should be utilized, if the patient has limited English proficiency.

V. TRICKS PATIENTS MAY USE TO AVOID TAKING MEDICATION

- A. Self-induce vomiting
 - 1. Spend time with patient after the DOT is given to allow digestion to begin (up to 1/2 hour if non-compliance suspected).
 - 2. Do not leave the patient alone during the remainder of your visit.
- B. Hide pills under the tongue or in cheek and spitting them out later:
 - 1. Speak with the patient for a few minutes after giving the medicine.
 - 2. If necessary use a tongue blade to inspect the mouth.
- C. Spit the pills into an opaque cup
 - 1. Use a clear cup
- D. Fake a cough and put pills into their palm
 - 1. Check their hands after they cough

VI. DOT DEFINITIONS

- A. **Totally self-administered**: patient self-administered all doses without supervision
- B. **Totally DOT**: all doses were given under supervision—patient did not self-administer any doses
- C. **Both self-administered and DOT**: one or more doses of medication were self administered, while others were given under observation

VII. HOW TO DETERMINE TREATMENT COMPLETION

- A. **Completion of therapy**
 - 1. Completion of therapy is determined by both the **duration of therapy** and by the **number of doses taken**.
 - 2. Missed DOT doses should be added to the end of therapy to ensure the total number of required doses is provided.

3. If patient is allowed to self-administer any *required* (DOT) doses, consideration should be given to adding those doses to the end of treatment to ensure that a full number of doses were taken.

B. Counting of Weeks of DOT

1. Count the total number of calendar weeks (Sun- Sat.) that the patient received the following minimum amounts of DOT:
 - a. Daily: count week only if 5 or more doses were given by DOT (Sun.-Sat.)
 - b. Twice-weekly: count week only if both doses were given by DOT (Sun.-Sat.)
 - c. Thrice-weekly: count week only if all 3 were given by DOT (Sun.-Sat.)
 - d. Once-weekly: count week only if dose given by DOT (Sun.-Sat.)
2. If patient does not receive the above number of DOT doses, do not count the week

VIII. TRAINING FOR NON-MEDICAL PROVIDERS OF DOT

- A. Educate all DOT providers about the medications and adverse effects that may develop (i.e. nausea, inability to eat, vomiting, abdominal pain, rash, tea-colored urine, yellowing of skin or of the white part of the eyes, or joint pain).
 1. DOT providers should be instructed to visually/verbally identify medications
 2. DOT providers should be able to explain medication dosage and side effects to patient.
- B. Train all DOT providers to follow the health department procedures and guidelines for delivering DOT.
- C. All DOT providers must be instructed to hold medication if side effects present, to notify the Regional TB Nurse or physician immediately, and to relay the patient's complaints to the clinician.

XII. PREVENTING TRANSMISSION OF TUBERCULOSIS

PREVENTING TRANSMISSION OF TUBERCULOSIS

Tuberculosis is transmitted from one person to another by aerosol droplet nuclei containing viable tubercle bacilli. Although the communicability of tuberculosis is reduced soon after institution of effective chemotherapy, infectiousness of the individual patient must be evaluated when care is initiated and appropriate measures must be immediately instituted to reduce the chance of disease transmission.

I. INFECTIOUSNESS OF TUBERCULOSIS

The following quote provides a good summary of the infectiousness of a person with pulmonary tuberculosis:

“There is no way to determine an absolute moment at which a patient on therapy becomes non-infectious. Infectiousness is a relative thing, and depends not only on the ability to find or not to find tubercle bacilli, but also on the patient’s symptoms (particularly cough), environmental situation, and the amount of exposure and susceptibility of exposed people. Infectiousness appears to decline very rapidly after therapy is instituted, but it is not logical to say that all patients are no longer contagious at an arbitrary point in time. Some patients may not be infectious on the day they begin treatment. Others may remain infectious for weeks, or even months. As a general rule, after two to three weeks of therapy, isolation is not indicated. The best way to judge this is by following serial sputum smears. When a response to therapy is indicated by declining numbers of bacilli in the sputum, and especially if this is accompanied by reduction in cough and general improvement in signs and symptoms, the patient can be returned to the community as long as he/she continues to take medication to which his/her organisms are susceptible. Although it is not possible to prove that the patient becomes noninfectious at the point he begins to show bacteriological response to treatment, it is also not possible to prove that he/she remains infectious beyond that point; however, there is no good evidence that the patient remains a hazard if he/she is on treatment and responding, and circumstantial evidence points the other way. . . . Decisions regarding the infectiousness of an individual must be individualized for that patient.”

Farer, L.S.: Infectiousness of Tuberculosis Patients. American Review of Respiratory Disease, 108:152, 1973.

II. RESTRICTIONS OF PATIENT WITH TRANSMISSIBLE TUBERCULOSIS

Infectious patients can be isolated in either an inpatient or outpatient setting. The following reasonable precautions should be observed to protect the patient’s contacts and the public:

- A. The patient should be instructed about the danger of aerosolized secretions. He/she should be instructed to cover his/her mouth and nose when coughing or sneezing. Patients on isolation should wear a mask when in contact with other persons or when leaving/being transported out of their room.

- B. Visitors to the patient should be limited while the patient is considered infectious. Children, individuals with HIV, and other persons with immunosuppression are at high risk of TB infection and of developing TB disease once exposed and should not have any contact with an infectious patient.
- C. Infectious TB patients should not be isolated in a residential setting where other high risk contacts are present (children, HIV+, immunosuppressed by medications or cancer, etc.). However, an exception may be made if these high risk individuals have already been infected and are on LTBI therapy.
- D. A patient's home situation (or other outpatient setting to be used for isolation) should be evaluated by a local or regional TB Program staff member to determine if the setting is suitable for outpatient isolation, preferably prior to discharge to that location (i.e. no high risk contacts present, patient can stay in a separate room from other persons etc.).
- E. Homeless persons with infectious TB must be placed in a setting where isolation can be safely instituted, such as in a hospital or other facility with a negative pressure room or in a residence with friends or family members. A motel where the ventilation is not shared with other rooms or common areas may also be an acceptable setting. Homeless TB patients cannot be allowed to remain on the street or in a shelter until they have become non-infectious.
- F. An infectious patient should not leave his/her residence except for visits to the physician or the clinic. The patient should be instructed to wear a surgical mask prior to entering the physician's office or clinic. If institutionalized, an infectious patient should be restricted to his/her room except when necessary to go for x-rays and other studies, in which case the patient should wear a surgical mask.
- G. Separate bedrooms and/or a separate bed are highly desirable to minimize the prolonged breathing of contaminated air by contacts. However, special precautions are not required regarding preparation of food. Concern over the use by contacts of articles used by the patient, such as dishes, utensils, books, etc., is not warranted. In almost all instances, tuberculosis is transmitted by aerosolized secretions and not spread by fomites.
- H. While the patient is still restricted, someone should be available, in the home, willing and able to provide necessary care, marketing or grocery shopping, etc.

- I. Patients with MDR-TB should preferably remain in an isolation room in the hospital until culture conversion or until discharge to home. The Tuberculosis Control Officer should be consulted prior to discharging an MDR-TB patient or discontinuing isolation while remaining in the hospital.

III. REMOVAL OF RESTRICTIONS

Tuberculosis patients, under certain conditions, even though still harboring a limited number of tubercle bacilli, present a minimal hazard of disease transmission to others. If the following criteria are met, the risk to the community is so minimal that restriction of patients and their activities usually is not justifiable.

- A. Isolation of the patient may usually be discontinued if **all of these criteria** are met:
 1. Patient has had at least 2-4 weeks of continuous adequate TB chemotherapy with standard first-line TB drugs
AND
 2. Patient has responded to treatment, both clinically and bacteriologically and is asymptomatic.
AND
 3. Patient has 3 consecutive negative AFB sputum smears obtained on different days. For patients with advanced pulmonary TB and prolonged positive sputum smears, release from isolation precautions can be made when patient has 3 consecutive negative *cultures* on different days.

Note: Patients with MDR-TB should meet all 3 criteria above prior to transfer from a facility AIIR to a non-isolation room or an outpatient site. In addition, home (or facility) isolation should not be discontinued until these patients have 3 negative cultures.

- B. Additionally, the patient must remain under close medical supervision (DOT), understands the nature of the disease, is cooperative and can be expected to continue on drugs until discontinued by physician or treatment is completed.
- C. Persons with pulmonary TB **MUST be non-infectious (see III.A, above) before they can be released to certain high risk areas**, (long term care facilities, correctional institutions, childcare facilities, group homes, homeless shelters, boarding schools or dormitories, etc.).

IV. RETURN TO WORK OR SCHOOL

The decision to allow a patient to return to school or work will be made by the patient's physician (private or public health) and will depend on the following conditions:

- A. The characteristics of the individual TB patient such as their response to treatment and their willingness and ability to adhere to treatment.
- B. The characteristics of TB disease itself, such as MDR or susceptible TB, AFB smear-positive or negative, and cavitory or non-cavitory disease.
- C. The characteristics of the environment to which the person will be returning, such as the ventilation and level of crowding present (working in a congregate setting or a close enclosed space with others versus working alone or outside) and the susceptibility of other persons in close proximity to the patient (i.e. young children or immunosuppressed persons).

Guidelines for Work for Patients with Tuberculosis (official Statement of American Thoracic Society), American Review of Respiratory Disease, Vol. 108, 1973.

New York City Bureau of Tuberculosis Control, Clinical Policies and Protocols, Third Edition, 1999.

V. ISOLATION AND QUARANTINE

On rare occasions it may be necessary to require isolation and quarantine procedures for patients who will not or can not observe the previously mentioned reasonable precautions. When necessary, the Commissioner of Health, all state, regional, county or metropolitan health officers or their deputies (including TB Clinic Physicians) are empowered to establish isolation and/or quarantine and to designate and define the limits of the area in which the person is to be isolated or quarantined for the purpose of protecting the public health, when such person has or is suspected of having infectious tuberculosis. This authority is described in considerable detail in the "Tuberculosis Control Act of 1971," and as amended by the Legislature in 1977 and in the "*Health Threat Procedures 1994*" (TCA 68-9-202, TCA 68-9-203).

A patient who violates an appropriately placed quarantine order recklessly endangers public health and breaks public health law. It is important that such violations be *dealt with consistently and swiftly*. **Enforcement of quarantine and incarceration is not to be considered "optional," but a legally**

required activity of the TB Elimination Program and the Tuberculosis Control Officer.

It will be the policy of the Central Office to fully support Regional and County efforts to enforce public health law as it pertains to tuberculosis. Contact the Rural Regional or Metropolitan Regional Tuberculosis Elimination Physician and the Central Office for assistance in this matter.

A patient who violates isolation and quarantine may be considered for institutionalization in a detention facility as described below. Contact the Rural Regional or Metropolitan Regional Tuberculosis Elimination Physician and the Central Office for assistance in this matter.

VI. DETENTION FACILITIES

The Tuberculosis Control Act states: “The Department may establish and maintain one or more detention facilities as the Commissioner deems appropriate to sufficiently confine all persons who refuse to be examined, treated, isolated and/or quarantined as provided for in this act.” Detention is available by special arrangements to be made by the Rural Regional or Metropolitan Regional Tuberculosis Elimination Physician with prior approval by the Medical Director of the Tuberculosis Elimination Program, Tennessee Department of Health.

Note: All other measures such as isolation, quarantine and directly observed therapy out-patient treatment program must be given a trial before forced detention is attempted.

XIII. CONTACT INVESTIGATION

CONTACT INVESTIGATION

Overview

Every case of tuberculosis (TB) begins as a contact to a person with active pulmonary or laryngeal TB disease. For this reason, the Centers for Disease Control and Prevention (CDC) and the Tennessee TB Elimination Program have identified contact investigation as a fundamental strategy for the prevention and control of TB. A contact investigation is the process of identifying, examining, evaluating, and treating all persons as indicated who are at risk of infection with *Mycobacterium tuberculosis* (*Mtb*) due to recent exposure to a newly diagnosed or suspected case of pulmonary or laryngeal TB.

Public health goals of a contact investigation are to:

- Terminate transmission
- Identify additional cases and ensure proper treatment
- Prevent the development of disease among contacts

These guidelines were developed as a tool for persons in any setting with a role in TB contact investigations, including public health nurses, outreach workers, disease control investigators, translators, social workers, health educators, clinic nurses, physicians, infection control practitioners, etc. The guidelines focus on what to do and how to do it, and provide process standards to establish a minimum standard of care for conducting contact investigations. Effective contact investigation activities require administrative direction, commitment, and support. This support includes staff education and training, quality assurance, and allocation of adequate resources.

A contact investigation should be conducted for all suspected or confirmed cases of pulmonary and/or laryngeal TB. Since TB transmission does not occur (except under highly unusual circumstances) from patients with extrapulmonary TB, a contact investigation is neither necessary nor appropriate for cases which are only extrapulmonary. Pediatric TB cases and certain children with positive tuberculin skin test (TST) results may require an investigation to determine the source of their infection. Source case investigation is defined in this section on page XIII-18.

County health departments should prioritize contact investigations depending on local resources and should ensure that the most infectious cases and suspects have a prompt and thorough contact investigation.

A systematic approach to contact investigations is essential to focus investigative efforts and ensure that resources are spent providing services to persons who are most at risk for

TB infection or disease. County health departments should assess their ability to meet objectives for contact investigations contained in Appendix 7 (CDC National Objectives for Contact Investigations).

Definitions

For the purpose of these guidelines, the following definitions apply:

- **Contact** – A person who shares air with a person who has infectious TB.
- **Close Contact** – An individual who has shared air with a person with infectious TB and is at high risk of developing infection with *M. tuberculosis* because of the length of time, frequency or environment/setting of their exposure; i.e., close, prolonged contact.
- **High-Risk Contact** – A contact in any environment who is at increased risk of progression from TB infection to TB disease and/or is likely to suffer increased morbidity or mortality from TB disease because of his/her vulnerability, even if the length of time or circumstances of the exposure are not judged to meet the criteria of “close”.
- **“Other Than Close” Contact** – An individual with less intense or less frequent contact to the index patient than the close contacts, causing them to be at less risk of developing infection with *M. tuberculosis* because of less time and intensity of exposure. All contacts have risk; the greater risk is for Close Contacts and High-Risk Contacts.
- **Non-contact** – A person who has probably not shared air with the index case but is evaluated during the contact investigation, usually due to request, i.e., a worried person who was probably not exposed.
- **Young Child** – For TB testing purposes, the definition of a young child is someone less than 5 years of age.
 - **Clinically Evaluated** – Medical exam that may include a skin test, review of TB signs and symptoms, physical exam, a chest radiograph, and collection of clinical specimens when appropriate.
- **Concentric Circle** – A standard method of investigation used in TB control which permits the investigator to examine contacts in sequence beginning with those contacts at highest risk for infection the Concentric Circle (Appendix 6).
- **Contact Investigation** – The process of identifying, examining, evaluating and establishing treatment for all persons who are at risk of TB infection or TB disease due to recent exposure to infectious or suspected tuberculosis. This process includes interviewing people who have spent time with a person with

infectious tuberculosis disease, and skin testing them to see if they have become infected.

- **Conversion** – An increase in skin test reaction size of 10 mm or more within a period of two years; indicative of a recent infection with *M. tuberculosis*.
- **Culture-Confirmed Tuberculosis** – Tuberculosis disease that has been confirmed by culture-positive identification on a clinical specimen.
- **Exposure** – The condition of being subjected to something (e.g., infectious agents) that could have a harmful effect. A person exposed to *M. tuberculosis* does not necessarily become infected.
- **Extrapulmonary Tuberculosis** – Tuberculosis in any part of the body other than the lungs.
- **Field Investigation** – Visiting a TB patient's home, workplace or other locations where the person spent time while infectious; considered a mandatory component of a contact investigation.
- **High-risk Tuberculosis Contact** – A person with TB infection that may progress to active disease and may easily become infectious, if it remains untreated.
- **Immunosuppression** – The suppression of natural human responses to infection as caused by disease, malnutrition, or medical treatment involving drugs or irradiation.
- **Index Case** – A suspected or confirmed case of pulmonary or laryngeal TB; a person with TB disease who is initially reported to the health department; the first person brought to your attention, usually the focus for a contact investigation.
- **Infection** – The condition in which organisms capable of causing disease enter the body and elicit a response from the host's immune system.
- **Infectious Tuberculosis** – Tuberculosis disease of the respiratory tract, capable of producing infection or disease in others as demonstrated by clinical evidence such as the presence of acid-fast bacilli in the sputum or bronchial secretions, chest radiograph abnormalities or clinical symptoms.
- **Laryngeal Tuberculosis** – Tuberculosis of the larynx; often considered more infectious than pulmonary TB; organisms are generally exhaled by the person with the disease.

- **Latent TB Infection** – Infection with *M. tuberculosis*, usually detected by a positive PPD skin test result, in a person who has no symptoms of active TB and is not infectious. Tubercle bacilli are present in the body but the disease is not clinically active. TB infection may or may not lead to active TB disease; however, persons with infection remain at life-long risk of developing active disease if their infection goes untreated.
- **Level of Infection** – The percentage of contacts with a similar amount of exposure that have a newly identified positive skin reaction.
- **Period of Infectiousness** – The time period in which a person with TB disease is capable of transmitting tuberculosis.
- **Determining Infectious Period** – Very important in considering how to focus a contact investigation to those individuals exposed to TB disease when the patient was considered most “infectious”.
- **Start Date** – 3 months PRIOR to the onset of symptoms OR 3 months prior to the collection of specimens and/or date of initial abnormal chest x- ray, whichever is earliest.
- **End Date** – The date patient is considered “noninfectious” is when all of the following criteria is met:
 - Symptoms have improved.
 - The patient has been receiving adequate treatment for at least two to three weeks.
 - The patient has had three consecutive negative sputum smears from sputum collected on different days.
- **Positive Skin Test for a Contact to Active Tuberculosis** – A change in the individual’s tuberculin skin test from negative to positive (5mm or greater).
- **Second Round Testing**– Contact investigation testing done on identified contacts whose initial skin tests were negative. This testing is done 10 to 12 weeks after their last exposure to infectious tuberculosis.
- **Source Case Investigation** – Conducted to find the source of TB transmission to an index pediatric case/suspect or to a child less than 18 years of age who is found to have a positive TB skin test. It is also conducted to find the source of transmission for a cluster of persons who have had skin test conversions. Source case investigation required for any child < 5 years of age.
- **Suspected Tuberculosis** – An illness marked by symptoms consistent with TB disease such as prolonged cough, prolonged fever, anorexia, weight loss,

fatigue, hemoptysis, chest pain; compatible radiographic or medical imaging findings; or laboratory tests that may be indicative of tuberculosis.

- **Transmission** – The spread of an infectious agent from one person to another. The likelihood of transmission is directly related to the duration and intensity of the exposure to *M. tuberculosis* and the vulnerability of the person who has been exposed.
- **Window Period** – The 10 to 12 week time span in a contact investigation between final exposure to the infectious tuberculosis case and the repeat skin test for those individuals whose initial skin test was negative.
- **Window Prophylaxis** –Treatment for LTBI given during the “window period” to contacts less than 5 years of age whose initial skin tests were negative.

CONFIDENTIALITY STATEMENT

The Tennessee Department of Health’s (TDOH) workforce is required by a new federal law entitled Health Insurance Portability and Accountability Act (HIPAA) to safeguard patients’ Protected Health Information (PHI). PHI is individually identifiable information about a person’s past, present, or future health or condition, the provision of health care to a person, or payment for health care. TDOH staff is required to give all patients a notice of TDOH privacy practices for the information collected and retained about individual persons.

PROCESS OF THE CONTACT INVESTIGATION

- Collection of pertinent medical information
- Prioritizing contact investigations
- Further review of the medical record
- Interviewing the patient
- Investigating in the field
- Assessing the likelihood of TB transmission
- Prioritizing testing of contacts
- Evaluation of highest priority contacts
- Treating and following-up contacts
- Deciding whether to expand screening
- Evaluation of contact investigations

Collection of Pertinent Medical Information

Prior to an interview and subsequent contact investigation, the following information should be collected to assign priority to the contact investigation according to the characteristics of the known or suspected TB index patient.

1. Site of disease
2. Type and date of onset of symptoms
3. Chest x-ray result(s)
4. Specific TB medications and their start dates (including use of quinolones as out-patient)
5. Pertinent laboratory results
6. Obtain all records from hospital, clinic and other provider sites

Prioritizing Contact Investigations

Contacts of individuals who have smear positive and culture positive pulmonary or laryngeal TB are much more likely to become infected with *M. tuberculosis* than are contacts of individuals who have smear-negative or culture-negative pulmonary TB. The policy of the Centers for Disease Control and Prevention (CDC) is to assign priority to contact investigation according to the characteristics of the index case and to the characteristics of the contact. Refer to Appendix 5 (CDC Prioritization of Initiation of Contact Investigations).

In order of priority, a contact investigation should be initiated if the known or suspected TB index patient has the following characteristics:

1. Sputum smears that are positive for acid-fast bacilli (AFB).
2. Sputum smears that are negative or not done, and the chest w-ray shows cavitary disease.
3. Sputum smears that are negative or not done, and the chest x-ray is abnormal but non-cavitary.
4. Negative AFB smears but positive *M. tuberculosis* cultures from sputum or laryngeal specimens.
5. A positive rapid mycobacteria identification test (i.e. MTD)
Note: MTD can be falsely negative and should not be relied on to rule out *Mtb*.
6. Negative cultures for *M. tuberculosis* but a cavitary chest x-ray (in this situation, the decision to pursue contact investigation will be at the discretion of the examining physician, depending on the degree of clinical suspicion for active TB).
7. Definite clinical evidence of active pulmonary TB, but AFB smears and/or cultures were not obtained prior to the initiation of anti-TB treatment.
8. Definite clinical evidence of active pulmonary TB with negative AFB smears and/or cultures (i.e., smears could be negative for other reasons than TB treatment, such as use of quinolone prior to diagnosis, poor

- specimen collection, etc.).
9. Symptoms compatible with pulmonary TB disease (e.g., weight loss, a cough of at least 3 weeks duration, fever, night sweats, etc.).

In addition, a Source Case Investigation is required, if an individual less than 5 years of age has a positive skin test (without known risk factors) or TB disease. The purpose of the Source Case Investigation is to seek the infectious source patient who infected this individual. If resources permit, a source case investigation should be performed for children 5 years of age to 18 years of age with a positive skin test and no known risk factors.

Setting priorities between two or more contact investigations is a decision that should be made by regional and local TB staff based on the likelihood of infectiousness of index case patients.

If program resources are limited, priority for resources and staff time should be placed on identifying contacts and conducting follow-up with contacts who:

- were exposed to the TB patients that are most likely to be infectious
- are at highest risk for TB infection or TB disease.

Factors Affecting the Risk of TB Transmission

Factor	Contacts at Higher Risk
Infectiousness of the TB patient	Contacts exposed to patients with a high degree of infectiousness based on the following factors <ul style="list-style-type: none"> • Laryngeal or pulmonary TB • AFB sputum smear-positive • Cavitory disease on chest x-ray • Cough • Positive culture for <i>Mycobacterium tuberculosis</i>
Environmental characteristics	Contacts exposed to the patient in <ul style="list-style-type: none"> • Small or crowded rooms • Areas that are poorly ventilated • Areas without air-cleaning systems
Characteristics of the contact's exposure	Contacts who <ul style="list-style-type: none"> • Frequently spend a lot of time with the patient • Have been physically close to the patient

**For further information on prioritization please see Appendix 5 to review CDC's organizational flow chart: "Prioritization of Initiation of Contact Investigation".

Interviewing the Index Case

The designated nurse case manager should conduct the contact interview within three (3) working days of the notification of a TB suspect or case. The interview can be conducted in the patient's home environment, in a hospital or in a clinic setting. If the initial visit was not in the home, **a home visit should be made within 5 working days of notification for all infectious or potentially infectious TB cases** to assist in validating the interviewer's assessment of the patient's home environment and to assist in the safe and expedient discharge of a hospitalized patient. Preferably, a home visit should be made prior to the patient's discharge from the hospital but no later than 24 hours after discharge from the hospital.

If the patient is receiving treatment from a non-health department health care provider, **the health care provider should be informed that a contact interview will be conducted**. The health care provider should also be informed of the purpose of the contact interview and that the information obtained from the contact interview will be kept strictly confidential. In addition, the nurse case manager will review all documentation pertinent to the patient's TB disease to ensure the appropriate time frame is determined for the period of infectiousness.

Interview Steps:

1. The interviewer should stress to the patient that all information obtained will be kept completely confidential, in most cases. (In certain situations an employer or teacher must be notified and their assistance required during the performance of a contact investigation. It will be necessary to obtain the patient's written permission to disclose information, and a signed agreement from the employer or teacher should be obtained stating that the employer or teacher will not disclose any personal or medical information related to the employee/student.)
2. The interviewer should review all previously documented information with the patient to ensure that this information is correct and ensure that the necessary information has been obtained to complete the required Report of Verified Case of Tuberculosis (RVCT) form.
3. The interviewer should repeatedly assess the patient's ability to comprehend the information being presented. If there are any concerns regarding the patient's ability to understand because of mental or physical incapacities, cultural, language, or other barriers, the interviewer should immediately obtain assistance from other members of the case management team or from an interpreter; whichever is appropriate.
4. The interviewer should educate and repeatedly assess the patient's understanding of TB and how it is transmitted.

5. The interviewer should determine the patient's infectious period as follows:
 - The infectious period begins 3 month's prior to the date of the onset of TB symptoms, or date of first abnormal chest x-ray, or date first sputum obtained
 - It ends when all of the following have occurred:
 - 1) the patient has shown clinical improvement, and
 - 2) has been on adequate TB treatment for at least 14 days, and
 - 3) has had 3 consecutive smears negative for AFB.
6. Obtain information concerning the patient's contacts.
 - Collect information concerning contacts in the patient's home environment, school and/or work settings, and in leisure and/or social settings during the estimated infectious period. In order to ensure that all appropriate contacts from the different settings are named, open-ended questions should be used (e.g., How do you spend your time during a typical day? What do you do and where do you go on the weekends?). Note: Mentioning holidays gives a time frame for the patient identifying contacts, such as, "What did you do at Christmas?"
 - Use the social networking approach. This may be particularly useful when interviewing a patient who is homeless or claiming not to have any contacts. Ask the patient where and how he spends his time. Find out where he has been staying or hanging out; and for high-priority, highly infectious patients, consider conducting targeted testing in these areas.
7. Always re-interview the patient several times to ensure identification of all contacts.
 - Contact investigations are a dynamic process. TB patients will be receiving care for a minimum of six months and the nurse case manager should continue efforts to identify additional contacts throughout the treatment period.
8. Determine the risk status for all contacts identified.
 - Review the infectiousness potential of the index case.
 - Review the environmental conditions of the exposure to the index case.
9. Examples of Higher Risk Exposures:
 - Significant exposure to the index patient, repeated exposures, short or long term (examples of significant exposure would be household contacts with daily extended exposure, school or work contacts in close daily or frequent contact with the index patient, leisure exposures of frequent and extended social activities, very close friends, steady partners, etc.).
 - Less frequent exposure but of longer duration. (examples: regular hairdresser appointments, weekly card games).

- Exposure in areas of poor ventilation and congregate living situations, i.e., jails, prisons, nursing homes.
 - Contact with a coughing patient (known or suspected to have TB) or unprotected exposure during cough inducing procedures.
10. Examples of Lower Risk Exposures:
- Exposure is short/occasional/casual.
 - Exposure is out-of-doors or under well-ventilated conditions.
11. Always review the host susceptibility of identified contacts.
- Some individuals have been found to be more susceptible to TB infection and certain others are at higher risk to progress from infection to disease if they become infected. These individuals include children less than 5 years of age, individuals with HIV infection or at risk for HIV infection, and individuals who are otherwise immunocompromised.

Quality Assurance and Interviewing

The quality of interviewing skills will have a direct impact on the outcome of the contact investigation. Therefore, it is essential that all designated TB staff members are trained in the skills of interviewing.

All TB Interviewers should be observed at regular intervals as part of quality assurance and staff development. This regular observation is important in the skills development phase of an interviewer as well as with the identification of areas needing improvement for an experienced interviewer.

Conducting a Field Investigation

The next step is to conduct a **field investigation**. This means visiting the patient's home or all other places where the patient said he or she spent time while infectious. The field investigation is mandatory and should be done even if the patient interview has already been conducted.

The purpose of the field investigation is to identify contacts and evaluate the environmental characteristics of the place in which exposure occurred. The field investigation may provide additional information for the risk assessment and identify additional contacts.

During field visits, the health care worker/investigator should:

- **Observe environmental characteristics** such as room size, crowding, and ventilation, to estimate the risk of TB transmission
- **Identify additional contacts** (especially children) and their locating information, such as phone numbers and addresses
- **Look for evidence of other contacts** who may not be present at the time of the visit (for example, pictures of others who may live in or visit the house,

- shoes of others who may live in the house, or toys left by children)
- **Interview and skin test close contacts** that are present and arrange for reading of the results.
 - **Educate the contacts** about the purpose of a contact investigation, the basics of transmission, the risk of transmitting *M. tuberculosis* to others, and the importance of testing, treatment, and follow-up for TB infection and disease
 - **Immediately refer contacts who have TB symptoms** to the health department for a medical evaluation including sputum collection

Field Safety

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

General safety precautions that are recommended for the health care worker include

- Wearing identification with a current photo
- Working in pairs when visiting a potentially dangerous area or visiting at night
- Informing someone of your itinerary and expected time of return, especially if you anticipate problems
- Making initial visit during daytime hours, if possible

Initiate Contact Follow-up Activities

1. Examination of high risk contacts for TB infection and disease should be performed by a Nurse Case Manager or by a trained designee under the supervision of a Nurse Case Manager **within 7 working days (includes TB skin test)**, and the completion of initial medical assessments of high risk contacts should be completed **within 10 working days** after contact identification.

Initial Medical Assessment:

- a. Contacts should be questioned concerning:
 - Previous exposure to TB.
 - Previous documented tuberculin skin tests.
 - Previous treatment for Latent TB Infection
 - Symptoms of TB.
 - Risk factors for developing TB disease.
- b. A Mantoux tuberculin skin test (TST) should be provided unless:
 - There is a documented history of TB disease.

- There is a documented history of a previous positive Mantoux TST with a reading in millimeters.
 - There is a documented history of an adverse reaction to a Purified Protein Derivative (PPD) in the past, or contact describes a history of vesiculation or anaphylaxis.
- c. HIV testing should be offered for all close contacts to active, infectious/potentially infectious TB cases.

Note: For close contacts to active TB patients who are co-infected with HIV, or are at high risk for HIV, HIV tests should always be provided.

All close contacts to TB cases who have documented HIV infection, are at high risk for HIV infection, or are otherwise immunocompromised (including those with organ transplants), should be evaluated for active TB disease immediately (regardless of TST results):

- Provide a chest x-ray and medical evaluation as soon as possible
 - Evaluate for symptoms suggestive of TB (i.e., chronic productive cough/hoarseness of 3 or more weeks, weight loss, etc). Three sputum smears should be collected immediately on 3 consecutive days for symptomatic contacts.
 - Provide appropriate education and recommend for treatment of LTBI until completion.
 - If there is a possibility that the HIV infected (or other significantly immunocompromised) patient has active TB disease, begin therapy with four drugs until active disease is ruled out.
- d. A chest x-ray and medical evaluation should be provided immediately (*prior to TST results*) for the following contacts to infectious/potentially infectious TB:
- Children less than 5 years of age.
 - Those with symptoms suggestive of TB (i.e., chronic productive cough, weight loss, etc.). Three sputum specimens should be collected immediately on 3 consecutive days for symptomatic contacts.
- e. For all other (non-immunocompromised) close contacts to an infectious/potentially infectious pulmonary or laryngeal TB case who have a Mantoux TST reading of 5 mm or more:
- Arrange for a chest x-ray and medical evaluation.
If the chest x-ray and medical evaluation are normal and the contact is asymptomatic, place the contact on treatment for latent TB infection, unless medically contraindicated, and ensure completion of treatment.
 - If the chest x-ray is abnormal and/or the contact is symptomatic, evaluate as a TB suspect. Please refer to Section IV, Treatment for Latent Tuberculosis Infection.

f. For all other (non-immunocompromised) close contacts to infectious/potentially infectious pulmonary or laryngeal TB case with a Mantoux TST of 0-4 mms:

(1) For those contacts less than 5 years of age:

- Arrange for a chest x-ray and medical evaluation.
- If the chest x-ray and medical evaluation are normal, recommend “window period” treatment for LTBI and continue until the follow-up Mantoux TST is placed and read. Repeat the Mantoux TST 10-12 weeks after the date of last exposure.
- If the repeat Mantoux TST remains less than 5mm, discontinue treatment for LTBI and discharge from supervision, if the index case is non-infectious and/or contact has been broken with the index case.
- If the Mantoux TST has converted to 5 mm or larger, complete treatment for LTBI.

(2) For those contacts 5 years of age or older:

- If the initial Mantoux TST is 0-4 mms, repeat the TST 10-12 weeks from the date of last exposure. If repeat TST remains 0-4 mms, discharge from follow-up.
- If the Mantoux TST converts to 5 mm or larger, provide a chest x-ray and medical evaluation.
- If the chest x-ray and medical evaluation are normal, and if the contact is asymptomatic, place the contact on treatment for LTBI, unless medically contraindicated, and ensure completion.
- If the chest x-ray or medical evaluation is abnormal, or if the contact is symptomatic, evaluate as a TB suspect.

g. For management of all contacts with a previously documented positive Mantoux TST:

- Screen carefully for TB symptoms.
- If symptomatic, obtain a chest x-ray and medical evaluation.
- If asymptomatic with no other medical or other risk factors, and no previous LTBI treatment completion, evaluate medically and epidemiologically the need for x-ray and treatment for LTBI.
- If not immunocompromised, asymptomatic, and the contact has completed an adequate course of treatment for LTBI, no further follow-up is recommended
- If immunocompromised, asymptomatic, and no previous history of LTBI treatment completion, obtain a chest x-ray and medical evaluation and if these are normal, recommend treatment for LTBI and ensure completion. If the chest x-ray or medical evaluation is abnormal, manage as a TB suspect.
- If immunocompromised, asymptomatic, and the contact has

completed an adequate course of LTBI treatment, arrange for a chest x-ray and refer for medical evaluation to review the possible need for a repeat course of treatment for LTBI. If the chest ray is abnormal manage as a TB suspect.

- Educate the contact regarding signs and symptoms of TB disease and advise to see their health care provider immediately if signs and symptoms occur.

Note: A chest x-ray should also be considered for the following individuals who have a history of a previous positive skin test but have subsequently been in close contact with a person who has AFB smear-positive pulmonary or laryngeal TB:

- Persons with medical risk factors for TB, other than HIV infection
- Children younger than 18 years of age
- Asymptomatic, HIV-seronegative persons who have had heavy exposure to a person with highly infectious pulmonary or laryngeal TB (i.e., the presence of secondary cases or documented conversions in other contacts).

Note: In some instances, a TB patient's cultures may convert to negative and then become positive again. This may happen if a patient is lost to follow-up and discontinues his or her medication before completing treatment, or if treatment was not adequate because of multi-drug resistance.

- If the patient is found after a treatment lapse of 3 months or longer and his or her cultures have become positive again, or if the patient relapses while on treatment after becoming culture negative, a second window period should be defined and the patient should be re-interviewed.
 - Contacts identified during the initial investigation should be re-evaluated, if they were exposed again.
 - If new contacts are identified, they should be tested and evaluated.
- h. For management of contacts to INH resistant TB: Rifampin daily for 4 months (MMWR.Vol.49/No.RR-6/June 9, 2000).
- i. For management of contacts to INH and rifampin resistant TB (MDR-TB):
- Evaluate contacts based on risk.
 - Always obtain expert consultation with the TB Program Medical Director prior to initiating a treatment regimen of latent TB infection for contacts to clients with multi-drug resistant disease

- j. Management of contacts by health care providers other than the Health Department:
- For contacts located in municipal or county jails refer to CDC Guidelines -“Prevention and Control of Tuberculosis (TB) in Short-Term Correctional Facilities (Municipal and County Jails)”
 - Contacts followed by non-health department care providers are subject to the same follow-up guidelines as contacts followed by the health department.
 - The nurse case manager must obtain from the health care provider documentation of the Mantoux TST results in millimeters, chest x-ray report, and a documented medical evaluation with the treatment plan.
 - The pharmacy should be called monthly to confirm that the medication is being picked up. The physician should be notified, if the contact fails to pick up medication for 2 weeks.
 - If the contact was seen by a private provider and is receiving medication for latent TB infection from the health department, the private health care provider must provide documentation of the TB skin test in millimeters, the chest x-ray report and a prescription that follows health department protocol.

Special Considerations for Infant and Child Contacts

Children less than 5 years of age who live in the same household as an infectious TB patient should be kept out of the home setting until one of the following conditions is met:

- The infectious patient is taking anti-TB treatment and has demonstrated an adequate response to treatment (i.e., negative AFB smears and a decrease in symptoms).
- The child has started preventive treatment (including window prophylaxis).

Evaluation of Contact Investigation Outcomes

Concentric Circles of Investigation

The extent of contact investigations will be determined utilizing the concentric circle approach. Contact investigations are initiated by examining the inner circle of contacts, those who have had the greatest risk of exposure to the index case in the home, work/school, or leisure/social settings.

Concentric Circle Analysis

** Refer to Appendix 6 - Diagram of Concentric Circle/Analysis of Results

Evaluate the results of the contact investigation involving the close contacts. If there is evidence of transmission to close contacts with 15% or more having positive Mantoux TST's, or converting to positive, or any secondary active TB cases, expanding the contact investigation to the next circle of contacts that are more casual in their exposure to the index client should be considered. This should include contacts in the following settings: at home, at work/school or those considered social/leisure settings.

The expected percentage of positive Mantoux TSTs among close contacts to infectious TB clients has been documented to be approximately 15-20%. For the majority of TB patients in Tennessee, it would be appropriate, e.g., if more than 15% of close contacts are infected, expanding the concentric circle.

On-going Evaluation

The progress of the contact investigation and follow-up should be reviewed by the health care worker/nurse case manager at several intervals. These include:

- (1) After assessment of risk is determined
- (2) After or near completion of the initial contact investigation (initial skin test)
- (3) After completion of **all** contact follow-up activities, (initial ST, 2nd ST, cxr's, and tx implementation and completion), and
- (4) At any time when problems delaying appropriate investigation occur.

Closing the Contact Investigation-Evaluation Activities

The Contact Investigation Form should be sent to the Regional TB Nurse within 14 days working days of completion.

To complete the investigation, an evaluation of the contact investigation activities should be conducted with or by a regional TB coordinator within 14 working days after receiving the Contact Investigation Form to determine the following:

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

The answers to these questions will help determine the success of the contact

investigation and identify areas of needed improvement.

LTBI TREATMENT

Completion of treatment for latent TB infection for identified high-risk contacts is the only way to prevent future TB cases in the community. If this treatment is not completed, previously related contact follow-up efforts to identify, test and implement therapy are essentially in vain as there is little or no resulting public health benefit to the community. Strategies including client-centered case management, use of interpreters, use of incentives and enablers, education and re-education of the client, and directly observed treatment regimens should be utilized to improve completion of treatment outcomes.

Treatment of LTBI for HIV Infected and Other Severely Immunocompromised Individuals (see Section IV “Treatment of Latent Tuberculosis Infection”)

- All HIV infected and other severely immunocompromised individuals deemed to require treatment for LTBI should be **strongly** considered for Isoniazid (INH) Directly Observed Preventive Treatment (DOPT) for 9 months. This can be given either daily or biweekly, but biweekly administration **must** be given by DOPT.

Based on the CDC and the American Thoracic Society reports of increased toxicity with the use of 2 months of Rifampin and Pyrazinamide (2RZ), Tennessee Department of Health (TDOH) no longer recommends its use. Isoniazid (INH) for 9 months will remain the preferred regimen for all patients. INH for 6 months or Rifampin for 4 months is also acceptable, when shorter regimens are indicated.

SOURCE CASE INVESTIGATION

Purpose:

A source case investigation is an investigation to determine the source of TB infection in a child under 18 years of age or documented converter. Although source cases would be infectious or there would be no pediatric converters, additional new cases and a high yield of infected individuals may be found originating from a common source of infection. Examination of the closest **associates** is usually all that is necessary, but the investigation may be expanded if more persons with LTBI are found and the source case is not immediately identified.

Note: In a source case investigation, “associate” refers to those individuals who have had the closest association or contact with the infected child or converter, similar to a contact in a TB case investigation.

Priority of Source Case Investigations:

Source case investigations are of lower priority than the critical TB core activities such as, treatment to completion of active TB cases, contact follow-up and treatment of contacts with LTBI, and targeted testing and related LTBI treatment. If resources are available and these core activities are being effectively managed, the first priorities for source case investigation are children less than 5 years of age diagnosed with any form of verified TB disease, abnormal chest x-ray or positive PPD. Utilizing the concentric circle of epidemiological investigation, begin the investigation by examining the closest associates to the child, expanding the circle only if it clearly appears a source of infection must be close by and yet unidentified. Source case investigations should be performed on children 5 yrs. of age up to 18 yrs. of age, as resources permit.

Medical Management of Associates to a Source Case

1. Clinical evaluation of associates
2. Place Mantoux TST
 - If the associate is symptomatic, obtain a chest x-ray and medical evaluation.
3. Read Mantoux TST
 - If the Mantoux TST is negative and the associate is asymptomatic, discharge associate from follow-up.
 - If the Mantoux TST is 10 mm or more, obtain a chest x-ray and medical evaluation.
 - ⇒ If the x-ray and medical evaluation are normal consider treatment for latent TB infection; if the chest x-ray or medical evaluation is abnormal, follow as a TB suspect.

CONGREGATE-SETTING INVESTIGATIONS AND INTERVIEWS

Tuberculosis investigations are conducted in the following congregate settings if the tuberculosis patients are found to be infectious, or potentially infectious.

- Employment sites
- Schools
- Correctional Facilities
- Homeless Shelters
- Nursing Homes
- Alcohol and Drug Treatment Facilities

These commonly identified places should be prioritized and investigated further through a congregate setting investigation. The key to these on-site investigations is the identification of additional close contacts. The basics for congregate setting

investigations should always include the fundamentals of sound TB control practices as written in these guidelines.

The ultimate goal of the congregate setting investigation is to stop transmission of TB in that setting and in the community and to educate both the identified contacts and the concerned public in a planned, well-organized manner.

The elements of a congregate setting investigation are:

1. Review medical information to determine whether the patient is infectious or potentially infectious. Analyze patient's test and examination results with emphasis upon the review of
 - Smear results of all respiratory specimens (negative or quantified positive)
 - Radiographic findings (presence or absence of cavity)
 - Symptoms (presence or absence of cough or hoarseness)

Note: If there is sufficient evidence of potential TB transmission within the congregate setting based on the factors above, then initiate an interview/tuberculosis contact investigation.

2. Explain to the index patient of the need to conduct public health investigations at the congregate setting
3. Discuss with patient confidentiality issues and the need to notify the congregate setting management staff of the contact investigation. Obtain signature on the patient consent form.
4. Set up a management meeting with the following agenda items:
 - Explain purpose of meeting
 - Review of local health department guidelines for patient confidentiality
 - Discuss potential media interest
 - Provide TB education for management
 - Review patient history (basis of diagnosis)
 - Discuss Directly Observed Therapy (DOT)
 - Request site tour
 - Explain and discuss infectious period
 - Identify high priority contacts
 - Discuss notification process of contacts
 - Discuss provision of education session for all associated with congregate setting
 - Review legal ramifications (if applicable) of contact non-adherence
 - Discuss and establish initial/post exposure medical evaluations for identified contacts

- Discuss potential of expansion of contact identification
5. Tour the facility and observe physical structure of the building to help determine the risk of transmission. Inquire about and visit specific areas the index case frequented within the facility. Pay particular attention to total square feet and the airflow/ventilation within the areas the infectious patient spent time. This will indicate possible exposure areas and the identification of close contacts who will require initial/repeat testing for TB.
 6. Determine the Risk of Transmission – Environmental Characteristics

The risk of transmission depends on the concentration of infectious droplet nuclei in the air – that is, the number of droplet nuclei in a certain amount of air. The greater the concentration of droplet nuclei, the more likely that TB organisms have been transmitted. The patient's infectiousness affects the number of droplet nuclei generated. In addition, the amount of droplet nuclei in a room depends on three environmental characteristics:

- Size of the room
- Amount of ventilation
- Presence of air cleaning systems

Size of the room. The risk of transmission is high when an infectious patient spends time in a small, enclosed space. It is also high when many people are crowded together in close physical proximity to each other. The risk of transmission may be lower when an infectious patient is in a very large room that is not very crowded.

Amount of ventilation. In a room that is well ventilated (for example, a room with an open window or an air ventilation system), fresh air comes into the room, diluting the concentration of droplet nuclei. Also, some of the droplet nuclei may be carried outside. Therefore, in rooms with good ventilation the concentration of droplet nuclei, and therefore the risk of transmission, may be lower. In rooms that receive no ventilation, the risk of transmission is increased.

Air cleaning systems. Infectious droplet nuclei can be removed from the air if the air is filtered through high-efficiency particulate air (HEPA) filters. Alternatively, the tubercle bacilli contained in the droplet nuclei can be killed by ultraviolet lights. These features, which are used in many hospitals and in some shelters, clinics, correctional facilities, and drug treatment center, may lower the risk of *M. tuberculosis* transmission.

7. Determine the individuals to be tested and determine the plan to notify the closest contacts of required testing, exams and possible treatment.

Note: It is important to test only those individuals with the closest contact to the infectious case as determined by length of contact and type of environment where the contact took place. Mass testing of all persons within a facility is not an appropriate use of limited public health resources and may detract from priority activities or result in a high number of false-positive TST results.

8. Plan, implement and evaluate testing results:
 - Establish place, date and time of PPD testing and schedule medical personnel who will administer and read the test
 - Identify place and time of the medical evaluations for infected contacts (chest x-ray, treatment for LTBI)
 - Establish date of second PPD (10-12 weeks after initial testing or last exposure)

9. Expanding the Testing:

The decision to expand a contact investigation and begin testing casual contacts will depend on the percentage of close contacts infected in each environment (home, leisure, work/school). See Appendix 6, the Concentric Circle Diagram/Analysis sheet.

The Tennessee Department of Health TB Elimination Program recommends that testing be expanded if 15% or more of close contacts are infected. **Example:** If 2 out of 10 closest contacts are infected, which would be 20%, then a second round of testing should occur among those contacts with less exposure (casual contacts).

Extrapulmonary TB Cases

Contact investigations should not be performed for persons with extrapulmonary TB if co-existing pulmonary TB is ruled out. However, in certain situations an extrapulmonary case may provide an opportunity to identify other high risk persons who may benefit from TB testing and treatment; for example, a foreign born person with extrapulmonary TB may have foreign born family members or friends who could be provided education and evaluation for LTBI.

Note: These persons should not be considered contacts but should be counted under targeted testing totals. Targeted testing of such persons is a lower priority and should be performed only if higher priority contact investigation activities have been computed.

Special Consideration in Correctional Facilities

1. A representative from the Tennessee Department of Health TB Elimination Program, shall determine the extent of the contact testing, diagnostic and radiologic surveillance required relative to the exact circumstances of each case. The epidemiologic investigation(s) will be tailored to the individual circumstances.
2. The purpose of an investigation is to determine the following:
 - a. The likelihood that transmission of infection with *M. tuberculosis* has occurred in the facility
 - b. The extent to which *M. tuberculosis* has been transmitted
 - c. To identify exposed and infected persons so they can receive appropriate clinical management.
 - d. To identify factors that could have contributed to the transmission/infection
 - e. To implement appropriate interventions
 - f. To evaluate the effectiveness of the interventions implemented to ensure exposure and transmission of *M. tuberculosis* have been terminated.

These Contact Investigation Guidelines are adapted from the following references:

Tuberculosis (TB) Contact Investigation and Contact Evaluation, State of Florida, Department of Health, Tuberculosis Technical Assistance: TB 2, Revised July 1, 2001

Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, Official Statement of the American Thoracic Society (ATS), Adopted by the ATS Board of Directors, July 1999.

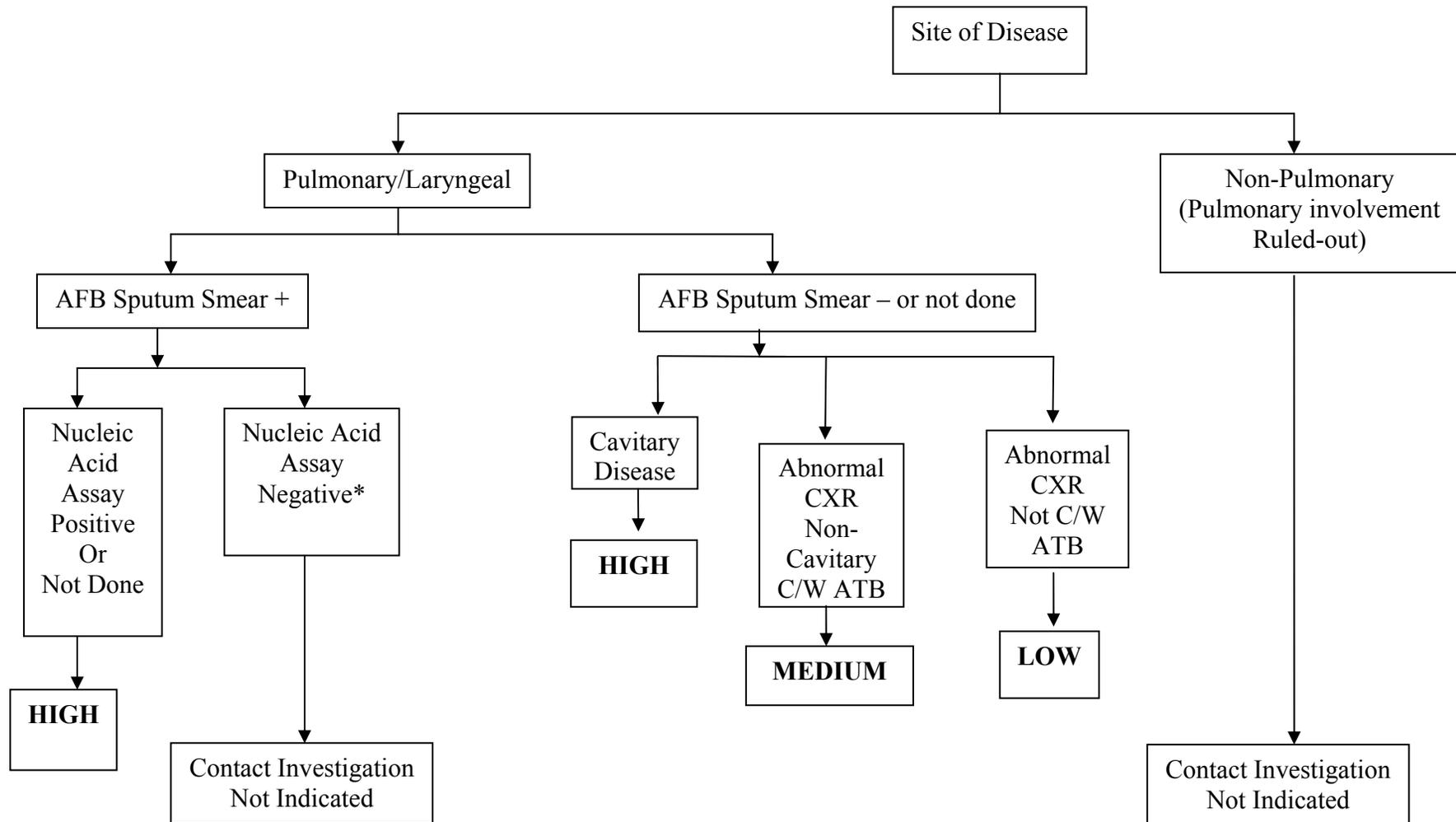
Contact Investigations for Tuberculosis, Self-Study Modules on Tuberculosis, Centers for Disease Control and Prevention, October 1999.

Performance Guidelines for Contact Investigation: The TB Interview, New Jersey Medical School, National TB Center, 2002

Tuberculosis Nursing: A Comprehensive Guide to Client Care, National Tuberculosis Controllers Association, 1997

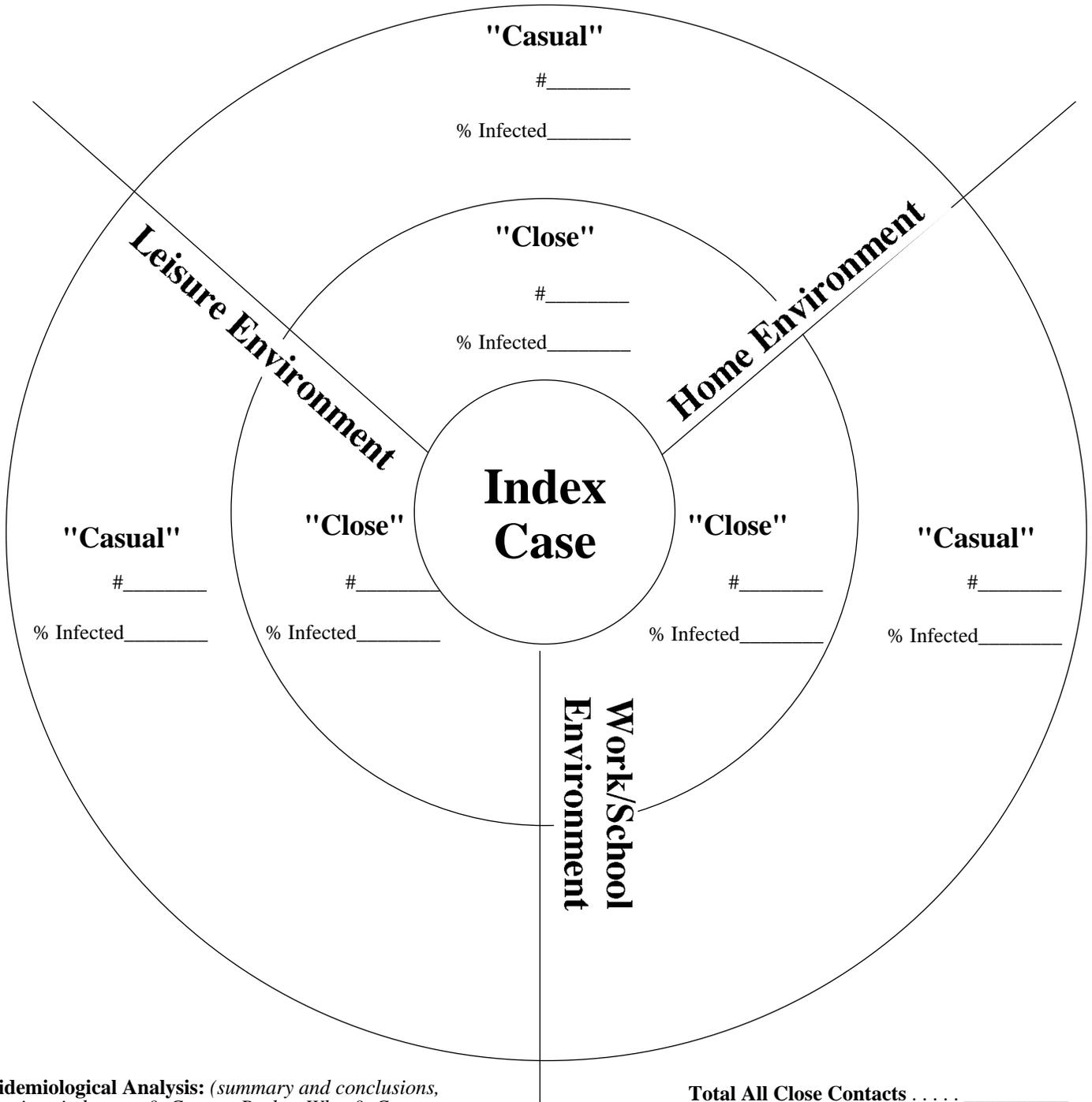
Standards of Practice for Conducting TB Case/Suspect Interviews and Contact Investigations, New Jersey Department of Health and Senior Services, April 2000

Prioritization of Initiation of Contact Investigations



*If done according to CDC Protocol

Concentric Circle Analysis



Epidemiological Analysis: (summary and conclusions, infectious index case? Contact Broken When? Contact Management Recommendations)

Total All Close Contacts _____
 Number Infected _____
 Number Not Infected _____
 Percent Infected _____%
Number Convertors (last 2 years) _____
Total All Casual Contacts _____
 Number Infected _____
 Number Not Infected _____
 Percent Infected _____%
Number Convertors (last 2 years) _____
Total All Others Evaluated _____
 Percent Infected _____%

**Centers for Disease Control (CDC)
National TB Program Objectives for Contact Investigation**

1. Contacts will be identified for at least 90 percent of newly reported sputum AFB smear-positive TB cases.
2. At least 95 percent of contacts to sputum AFB smear-positive TB cases will be evaluated for latent TB infection (LTBI) and active TB disease.
3. At least 85 percent of infected contacts that are started on treatment for LTBI will complete therapy.

Source: "The Performance Guidelines for Contact Investigations: The TB Interview",
New Jersey Medical School, National Tuberculosis Center

**Tennessee Department of Health
TB Elimination Program**

**TUBERCULOSIS CONTACT RECORD (PH 1631)
INSTRUCTIONS**

According to the Centers for Disease Control and Prevention (CDC) guidelines, a contact investigation should begin as soon as TB is diagnosed or strongly suspected.

Time Requirements for Conducting Contact Investigations:

- **Within 3 working days** after the case is reported to the local health department – initiate contact investigation interview.
- **Within 7 working days** after the case is reported to the local health department – assess high-risk contacts for TB infection and disease and skin test.
- **Within 10 working days** after contact identification – complete medical assessments of high-risk contacts.

Completion of Contact Record:

The Tuberculosis Contact Record should be completed by the interviewer, marked “initial” and submitted to the Regional TB Nurse to review no later than 30 days after the interview and initial examination results are obtained. If the last exposure occurred within 10-12 weeks of diagnosing the patient, a second test is required. Results of second tests should be documented; the “Final” box checked and the form submitted to the Metropolitan or Rural Regional TB nurse.

2. **Initial** – Check when submitting initial examination results and further testing or additional information is needed.
3. **Final** – Check when submitting results of examination(s) and no further testing or information is required
4. **Patient Name:** Last Name, First Name, Middle Initial of the index case or suspect.
5. **Address:** Current address of the index case or suspect. If there is more than one address during the infectious period, include them in Comments section or on a separate page.
6. **DOB:** Date of Birth for the index case or suspect.
7. **Phone #:** Phone number for the index case or suspect. (Obtain alternate emergency phone number from the patient if possible).
8. **Employer:** The current or most recent employer name, address and phone number. If there are several places of employment during the infectious period, include information in Comments section or on separate page. If person attends school, list name/address/phone of school.

9. **Metro/Regional Case #:** Case # assigned by a Metro or Rural Region to the Registered Verified Case of Tuberculosis (RVCT), if tuberculosis case reported in TIMS.
10. **Date Case Reported:** Date case reported to the health department.
11. **Date Interviewed:** Date of the Initial Interview of the index case or suspect.
12. **Date CI completed:** Date the investigation is completed and closed.
13. **Infectious Period:** Time period during which the index case or suspect is capable of transmitting TB.
- From:** Estimated 3 months prior to the onset of symptoms or in the absence of symptoms, 3 months prior to the collection of specimens or abnormal chest x-ray.
- To:** The period of infectiousness ends when all three criteria are met:
- Symptoms have improved
 - Patient has received adequate treatment for at least 2 to 3 weeks
 - Patient has had three consecutive negative sputum smears from sputum collected on three different days.
14. **Reason for Interview:** Check appropriate reason for interview: Case, Suspect (with symptoms), Source. Note: source case investigation required for child up to 5 years old with positive skin test; recommended for child up to age 18 years of age).
15. **Check if applicable:** Check appropriate category:
- Sputum Smear positive or neg. for AFB or Sputum Culture pos. or neg. for *Mtb*.
 - Other Source - List any other specimen sources as Smear pos. or neg. for AFB or Culture pos. or neg. for *Mtb*.
16. **Name/Address/Phone:** Contact's name, current address and telephone number.
- Relationship to Case:** Examples: sister, brother, mother, father, spouse, girlfriend, co-worker, neighbor, church member, etc.
17. **D.O.B.:** Date of Birth. Mark UNK for unknown.
18. **Age:** Age of contact.
19. **Sex:** Male or female.
20. **Exposure Dates (First-Last):** Dates of first and last exposure during infectious period of index case.

21. **Hours Per Week:** Approximate number of hours per week exposed to the index case. (List number of hours and not “household” or “24 x 7”.)
22. **1st PPD Date:** Date of initial PPD.
23. **Results:** Results of initial PPD in mm.
24. **CXR Date:** Date of chest x-ray
25. **CXR Results:** Results of chest x-ray.
26. **Tx Y/N:** Was treatment indicated based on examination? Yes or No
27. **Tx Start Date:** Date treatment was initiated.
28. **Tx Stop Date:** Date treatment stopped or completed
29. **Tx Stop Code:** Reason therapy was stopped. Use Disposition Codes at bottom of form.
30. **2nd PPD Date:** Date of second PPD.
31. **2nd PPD results:** Results in mm of second PPD.
32. **Remarks:** History of TB infection or disease, high-risk category and any other pertinent patient information. Comments may be included in this section.
33. **Interviewer Name/Signature/Phone #:** Interviewers complete information.
34. **Date Initial Submitted:** Date initial contact record submitted to Metro/Regional TB nurse for review. Note - The initial may be the final contact record if no second PPDs are indicated based on exposure/infectious periods.
Final Review Date: Date of Final Review by Interviewer
35. **Reviewed by Metro/Regional TB Nurse:** Name of regional/metro TB nurse reviewing record.
36. **Initial Review Date:** Date of first review.
37. **Final Review Date:** Date of final review by Metro/Regional Nurse.
38. **Additional Comments:** Document special notes and comments.

Note: The Contact Investigation Record may be kept in the patient’s record, but should be removed before making copies of the record for anyone other than the Department of Health.

APPENDIX 9

Affix Patient Label Here 1

TENNESSEE DEPARTMENT OF HEALTH
TB Elimination Program
TUBERCULOSIS CONTACT RECORD

Initial 2

Final 3

Patient Name: 4 Last MI First Address: 5 Street City State Zip

DOB: 6 Phone#: 7 Employer: 8 Metro/Regional Case # 9

Name/Address/Phone of Employer

Date Case Reported: 10 Date Interviewed: 11 Date CI Completed: 12 Infectious Period: From: 13 To: 13

Reason For Interview: Case 14 Suspect 14 *Source case 14 Check if Applicable: Sput Sme + 15 Sput Sme neg. 15 Sput M.tb Cul+ 15 Cul neg. 15

(*Required for child less than 5 yrs./ Recommended for child up to 18 yrs.) Other Source 15 Sm + 15 Sm neg 15 Cul + 15 Cul neg 15

HIGH RISK AND CLOSE CONTACT INFORMATION

NAME/ADDRESS/PHONE	DOB <u>17</u>	S E X	Exposure Dates (First-Last) <u>20</u>	1 st PPD Date <u>22</u>	CXR Date <u>24</u>	Tx Y/N <u>26</u>	Tx Start Date <u>27</u>	Tx Stop Date <u>28</u>	2 nd PPD Date <u>30</u>	Remarks <u>32</u>
RELATIONSHIP TO CASE <u>16</u>	AGE <u>18</u>	<u>19</u>	Hours Per Week <u>21</u>	Result <u>23</u> (mm)	Results <u>25</u>			Code <u>29</u>	Result <u>31</u> (mm)	

Disposition Codes: AC – Active TB developed; AE – Adverse effect of medicines; DE – Death; NT – No TB found; PL –Lost to follow-up, PM –Moved, follow-up unknown; PT – Chose to stop; TC – Treatment completed; RM – Refuses medication/treatment; RT – High risk person refuses skin test, PD-Provider decision; AT-already treated; RE-refused evaluation

- **High Risk Contact Categories:** HIV infected; child under 5 years old; IV drug user; diabetic; other medical condition
- **Interviewer Name/Signature/Phone #:** 33 **Dates Submitted to Metro/Regional Nurse for Initial Review :** 34 **Final Review:** 34

Reviewed by Metro/Regional Nurse: 35 Initial Review Date: 36 Final Review Date: 37

TENNESSEE DEPARTMENT OF HEALTH
TB Elimination Program
TUBERCULOSIS CONTACT RECORD

Patient Name: _____ Metro/Regional Case #: _____

HIGH RISK AND CLOSE CONTACT INFORMATION

NAME/ADDRESS/PHONE <i>RELATIONSHIP TO CASE</i>	DOB	SEX	Exposure Dates (First-Last)	1 st PPD Date	CXR Date	Tx Y/N	Tx Start Date	Tx Stop Date	2 nd PPD Date	Remarks
	AGE		Hours Per Week	Result (mm)	Results			Code	Result (mm)	

SAMPLE

Additional Comments: _____ 38 _____

Disposition Codes: AC – Active TB developed; AE – Adverse effect of medicines; DE – Death; NT – No TB found; PL –Lost to follow-up; PM –Moved, follow-up unknown; PT – Chose to stop; TC – Treatment completed; RM – Refuses medication/treatment; RT – High risk person refuses skin test; PD-Provider decision; AT-already treated; RE-refused evaluation

APPENDIX 10

Affix Patient Label Here

TENNESSEE DEPARTMENT OF HEALTH
TB Elimination Program
TUBERCULOSIS CONTACT RECORD

Initial
 Final

Patient Name: _____ Address: _____
Last MI First Street City State Zip

DOB: _____ Phone#: _____ Employer: _____ Metro/Regional Case # _____

Name/Address/Phone of Employer

Date Case Reported: _____ Date Interviewed: _____ Date CI Completed: _____ Infectious Period: From: _____ To: _____

Reason For Interview: Case _____ Suspect _____ *Source case _____ Check if Applicable: Sput Sme + ___ Sput Sme neg. ___ Sput M.tb Cul+ ___ Cul neg. ___

(*Required for child less than 5 yrs./ Recommended for child up to 18 yrs.) Other Source _____ Sm + ___ Sm neg ___ Cul + ___ Cul neg ___

HIGH RISK AND CLOSE CONTACT INFORMATION

NAME/ADDRESS/PHONE <i>RELATIONSHIP TO CASE</i>	DOB	SEX	Exposure Dates (First-Last)	1 st PPD Date	CXR Date	Tx Y/N	Tx Start Date	Tx Stop Date	2 nd PPD Date	Remarks
	AGE		Hours Per Week	Result (mm)	Results			Code	Result (mm)	

Disposition Codes: AC – Active TB developed; AE – Adverse effect of medicines; DE – Death; NT – No TB found; PL –Lost to follow-up, PM –Moved, follow-up unknown; PT – Chose to stop; TC – Treatment completed; RM – Refuses medication/treatment; RT – High risk person refuses skin test, PD-Provider decision; AT-already treated; RE-refused evaluation

- **High Risk Contact Categories:** HIV infected; child under 5 years old; IV drug user; diabetic; other medical condition
- **Interviewer Name/Signature/Phone #:** _____ **Dates Submitted to Metro/Regional Nurse for Initial Review :** _____ **Final Review:** _____

Reviewed by Metro/Regional Nurse: _____ Initial Review Date: _____ Final Review Date: _____

TENNESSEE DEPARTMENT OF HEALTH
TB Elimination Program
TUBERCULOSIS CONTACT RECORD

Patient Name: _____ Metro/Regional Case #: _____

HIGH RISK AND CLOSE CONTACT INFORMATION

NAME/ADDRESS/PHONE <i>RELATIONSHIP TO CASE</i>	DOB	SEX	Exposure Dates (First-Last)	1 st PPD Date	CXR Date	Tx Y/N	Tx Start Date	Tx Stop Date	2 nd PPD Date	Remarks
	AGE		Hours Per Week	Result (mm)	Results			Code	Result (mm)	

SAMPLE

Additional Comments: _____

Disposition Codes: AC – Active TB developed; AE – Adverse effect of medicines; DE – Death; NT – No TB found; PL –Lost to follow-up; PM –Moved, follow-up unknown; PT – Chose to stop; TC – Treatment completed; RM – Refuses medication/treatment; RT – High risk person refuses skin test; PD-Provider decision; AT-already treated; RE-refused evaluation

TB SUSPECT/CASE INTERVIEW CHECKLIST

Pre-Interview Activities

- Review index patient's medical record
- Establish preliminary infectious period
- Develop an interview strategy
- Arrange interview time and place

Introduction

- Introduce self
 - ⇒ Provide identification
 - ⇒ Explain role in TB control
 - ⇒ Build trust and rapport
- Explain purpose of interview
- Ensure confidentiality

Information and Education Exchange

- Observe patient's physical and mental state and evaluate communication skills
- Use interpreter for patients with limited English proficiency
- Obtain parental consent, if patient is a minor
- Assess disease comprehension/provide TB education
- Obtain/confirm TB symptom history
- Discuss disease intervention behaviors (treatment/infection control/medical appointments)
- Determine infectious period/review significance with patient
- Collect and confirm the following information:

⇒ Name	⇒ Recent hospitalizations or out patient treatment for TB
⇒ Alias(es)/nicknames	⇒ Medical provider for TB
⇒ Date of Birth	⇒ Medical provider for future care
⇒ Address	⇒ Transportation availability
⇒ Telephone number	⇒ Other medical conditions
⇒ Alternate contact number	⇒ Outpatient/DOT plan
⇒ Next of kin	⇒ Barriers to adherence
⇒ Other locating information	
⇒ Physical description of patient	
⇒ Known exposure to TB	

Contact Identification

- Focus on infectious period
- Explain close and casual exposure
- Stress importance of identification of all close contacts
- Collect information on patient's contacts in the household/residence, workplace, school, other congregate settings, social/recreational environments during the infectious period including:

- | | |
|----------------------------------|---|
| ⇒ Name | ⇒ Dates of first and last exposure |
| ⇒ Alias(es)/nicknames | ⇒ Hours of exposure per week |
| ⇒ Age/race/sex | ⇒ Place of exposure |
| ⇒ Address/telephone number | ⇒ Physical characteristics of place of exposure |
| ⇒ Other locating information | |
| ⇒ Contact's physical description | |

Conclusion

- Request/answer patient's questions
- Review/reinforce adherence plan
- Restate next appointment (if known)
- Arrange re-interview and home visit (if not already completed)
- Leave name and telephone number
- Thank patient and close interview

XIV. PUBLIC HEALTH NURSING SERVICES

PUBLIC HEALTH NURSING SERVICES

The Public Health Nurse (PHN) plays a crucial role in the elimination of tuberculosis in Tennessee. The PHN is responsible for ensuring the highest standards in maintaining the three priorities of the TB Elimination Program:

1. Identification, evaluation and management of TB cases and suspects;
2. Performance of contact investigations and appropriate evaluation and management of TB contacts; and
3. Identification, evaluation and management of persons at high-risk for Latent TB Infection (LTBI) through targeted tuberculin testing programs.

The duties of the PHN may include TB control activities at the county, regional or metropolitan health department, as well as activities at other community sites such as local hospitals, medical clinics, prisons, jails, homeless shelters, long-term care facilities, alcohol and drug facilities, etc. The PHN will perform these duties in conjunction with a physician or nurse practitioner and other TB control personnel.

I. Identification, Evaluation and Management of Patients with Active TB

A. Initial Contact

A report of a newly diagnosed TB case or suspect may come from the Regional Office, private provider, hospital or laboratory. The diagnosis may be based on bacteriologic studies positive for AFB, radiographic findings compatible with TB or the report of an active case by a physician. The Regional TB Nurse, and the Regional TB Physician or Health Officer should be notified immediately of any new TB suspect or case. Medical records should be obtained within 24 hours.

An initial contact by the public health nurse should be made within 24 hours after receiving the report of a newly diagnosed TB case or suspect. This may be a home, office, or hospital visit, or a phone call.

An initial visit by the public health nurse should be made within 3 working after receiving the report of a newly diagnosed TB case or suspect.

If the initial visit is not a home visit, a home visit shall be made by a PHN to do a complete assessment of the patient's home environment no later than 5 working days after receiving report of a newly diagnosed TB case or suspect. A home visit should be made preferably prior to the patient's discharge but no later than 24 hours of discharge from the hospital. These visits are often the key to successful completion of adequate treatment for the patient and ensure cooperation and follow-up of contacts. Subsequent visits may be made by a Public Health Representative or other TB worker.

Individuals with positive sputum smears are usually highly infectious, and it is appropriate to start the patient on TB chemotherapy and initiate the contact investigation. The PHN managing the care of the patient is responsible for confirming that appropriate medications, dosages and length of treatment have been ordered for the TB case or suspect and that the contact investigation is current. The PHN is responsible for notifying the Regional TB Nurse, TB Physician, or Health Officer of any problems related to these activities.

B. Patient Records

1. Within 24 hours of notification of a patient's discharge from a hospital, the hospital's Infection Control Nurse should be contacted by the county health department and a summary of hospital treatment should be requested and placed in the patient's health department medical records when received. If not received within 3 working days, another request should be made. If not received within 24 hours of the second request, the Regional TB Nurse should be notified.
2. Prior to the patient being seen in TB clinic, all appropriate medical records should be obtained from private or other providers, faxed immediately to the Regional TB Nurse. The PHN should ensure that all appropriate medical records have been obtained, faxed to the Regional Nurse, and placed in the patient's county health department records. This procedure should be followed prior to each TB Clinic visit to ensure updated records are available for the TB Clinic Physician to review.

C. Initial Assessment Visit

1. Documented assessment of patients with TB/LTBI:
 - a. Identify communication barriers (need for interpreter, literacy, level of comprehension).
 - b. Administer TB/LTBI Risk Assessment Tool (PH 3714) and obtain appropriate details about positive responses.
 - 1) If there is a history of contact with tuberculosis, determine when, where, to whom, and under what conditions contact occurred.
 - 2) Identify other risk factors for TB/LTBI or conditions that promote progression from LTBI to active disease.

- 3) If there is a previous history of treatment for TB or LTBI, determine which drugs were administered, length of treatment, and if there were any adverse reactions to the drugs. Obtain provider's name and location and a written release of protected health information from patient (form PH-1778, rev. 05-03) to obtain all relevant medical records.
 - 4) Determine if TB treatment other than drug treatment has previously been administered, i.e., prolonged hospitalization, thoracoplasty, lobectomy, collapse procedures, etc.
 - 5) Assess patient for HIV risk factors and determine if HIV status is known. **If HIV status is unknown, counsel the patient appropriately and encourage HIV testing for ALL TB cases and suspects, regardless of apparent risk** (written consent must be obtained prior to testing).
 - 6) Observe and question the patient regarding clinical manifestations of pulmonary or extrapulmonary TB, such as fever, cough, sputum production, hemoptysis, night sweats, malaise and loss of weight.
- c. Determine if the patient has other health problems, such as liver or kidney disease, epilepsy, diabetes, cancer, etc., that might affect the management and treatment plan for TB.
 - d. Determine if the patient is currently taking any medications (prescribed, over-the-counter, herbal or home remedies) or has medication allergies that might affect the TB treatment plan.
 - e. Determine if patient is a current or past alcohol user, IV drug user, and/or non-IV drug user.
 - f. Determine level of education, socioeconomic background, present or last occupation, last date at work, work schedule, and recreational interests and hobbies.
 - g. Consider barriers to adherence and how to overcome them: (examples- substance abuse, language, cultural issues, education level, mental or physical disabilities, transportation, work schedule, etc).

2. Physical observations

- a. Determine if there is evidence of anemia, jaundice, chronic illness, etc.

- b. Measure temperature, pulse, blood pressure, weight, and respirations.
 - c. Assess for risk of pregnancy, if within child bearing years.
3. Diagnostic tests
- a. Obtain or review chest x-ray film/report for ALL pulmonary and extrapulmonary cases or suspects and persons with positive TST.
 - b. Obtain or review other radiographic studies or reports as appropriate.
 - c. Obtain sputum smear, cultures and sensitivities on ALL pulmonary or extrapulmonary cases or suspects.
 - 1) Natural collection if possible at clinic or at home (see Section VIII.)
 - 2) Give patient additional labeled sputum containers and instructions on mailing sample to lab.
 - 3) Induce if necessary (see Section VIII.)
 - d. Obtain or review bacteriologic specimens from other body tissues or fluids as appropriate.
4. Plan of care: treatment, monitoring, and follow-up
- a. Obtain medical orders for treatment from health department physician or private physician.
 - 1) Prior to dispensing the drug regimen prescribed by the physician, screen patient for contraindications to the drugs. If contraindications to the drugs are found, contact the physician for recommendations.
 - 2) If treatment has already been initiated:
 - a) Assess appropriateness of prescribed therapy (drugs used, dosage amount and schedule, contraindications to drugs etc.). Contact TB physician or Regional TB Nurse if problems identified.

- b) Monitor for patient adherence and signs and symptoms suggestive of possible drug toxicity.
- 3) If the patient is to be hospitalized, ensure appropriate information is sent to the attending physician at the hospital facility.
- a) If the Tuberculosis Program is to be payor, obtain prior approval from Central Office per protocol.
- 4) Administer medications:
- a) Directly observed therapy (DOT) is the standard of care for ALL TB cases and suspects for the duration of therapy, regardless of provider. The PHN should obtain DOT orders from the private provider and coordinate an acceptable schedule with the patient to administer DOT. **The Regional Health Officer or TB Clinic Physician should be notified if no DOT order can be obtained. The Health Department Physician should telephone the private provider to advise that DOT is the standard of care. Self-administration of TB medications is strongly discouraged.**
 - b) Directly observed preventive therapy (DOPT) should be provided for all children with LTBI less than 18 years of age. This also includes pediatric TB contacts that have negative TB skin tests and are placed on LTBI (window) therapy until a second skin test is done. If the second skin test is negative, the medication may be discontinued. For adults with LTBI, self-administration is acceptable and only one month's supply of medications should be provided. DOPT should be considered for high risk adults with LTBI (i.e., contacts, HIV) to increase adherence and minimize toxicity.
 - c) Ensure that all medications are labeled by Regional Pharmacist or packaged by a PHN under the supervision of a physician. Label should be written in the patient's language if possible and should include:
 - i. Name of Patient.
 - ii. Date issued.
 - iii. Generic name or standard abbreviation of the drug and capsule or tablet strength.

- iv. Amount dispensed.
 - v. Directions for taking (Examples: “2 capsules one hour before breakfast” or “3 tablets at bedtime”.)
 - vi. Name of prescribing physician.
 - vii. Patient’s resident county.
 - d) Drug Screening and Monitoring Record (PH-2040) should be completed for all patients receiving any anti-tuberculosis medication at the time anti-tuberculosis drug therapy is started.
- 5) Perform baseline laboratory tests and vision or hearing testing as appropriate for patient’s regimen, and obtain other labs as ordered.
- 6) Formulate follow-up care plan:
 - a) Propose schedule for sputum collection and other tests as indicated.
 - b) Arrange home visit if not already made.
 - c) Arrange schedule for DOT/DOPT or for medication refills.
 - d) Arrange periodic monitoring for possible side effects and adherence for all patients on tuberculosis medications, including those seen by private or other providers.
- 7) Schedule regional TB clinic and/or private physician visits as indicated.
 - a) Obtain progress notes from private physician after every visit and have TB physician review.
- 5. Emotional reaction of the patient and family. (Consider psychosocial and cultural background).
 - a. Evaluate and record:
 - 1) Patient’s feelings regarding diagnosis and recommended treatment.
 - 2) Family’s feelings regarding patient’s diagnosis and treatment.

- 3) Patient and family resources to cope.
6. Educate patient and family and ensure that patient has full understanding of the following:
 - a. The active disease process, mode of transmission, differences between TB and LTBI, clinical outcomes of TB/LTBI if left untreated, and risks/benefits of treatment.
 - b. The importance of covering nose and mouth with tissue when coughing or sneezing and proper disposal of tissue. A mask should be worn around other persons until patient is no longer infectious (for cases and suspects)
 - c. Household precautions such as (for cases and suspects):
 - 1) Instruct in provision of adequate ventilation.
 - 2) Indicate that dishes, linens and other fomites require no special precautions.
 - 3) Sleep apart from the rest of the family during infectious period.
 - 4) Children < 5 years old should be moved out of the house until the suspect/case is deemed non-infectious, or the child has started “window therapy” (LTBI treatment given to a child < 5 years of age between the time of the first PPD, which is negative and the 2nd PPD given 10-12 weeks later. If the second PPD is negative, the treatment may be discontinued.)
 - d. Reason for contact investigations, identification, and evaluation of contacts (cases, suspects and contacts).
 - e. Reasons for treatment of cases and contacts (cases, suspects, and contacts).
 - f. The importance of continuous, uninterrupted treatment.
 - g. The importance of maintaining regular medical supervision.
 - h. The signs and symptoms of possible toxic effects of prescribed medications and what course of action to follow should these occur. Stress importance of contacting local health department immediately and stopping medication if signs/symptoms of

toxicity occur. Provide emergency numbers for weekends/holidays.

D. Follow-up visits with patients on TB drugs

Follow-up visits with patients on TB drugs may be office or home visit by local PHN, public health representative (PHR), or other individual who has been trained by the health department to administer DOT. These visits will be made under the direction of a PHN.

1. Obtain interval history to review and update data obtained in initial visit.
2. Perform Drug Monitoring:
 - a) Monitor for signs and symptoms of possible adverse effects to medications and document abnormal findings in nurses notes. Perform appropriate laboratory monitoring.
 - 1) General non-directive questions and observations should be used to elicit information regarding possible drug toxicity.
 - 2) Avoid relating to the patient a specific symptom from a particular drug.
 - b) If any signs of drug toxicity exist discontinue medication. The PHN or PHR that receives this information or who advises a patient to discontinue anti- tuberculosis medication is responsible for contacting the patient's physician (personal or public health) for an alternate plan of treatment. This must be done on the day medication is discontinued, or if other than regular working hours, very early on the next regular working day. The Regional or Metropolitan TB physician must also be notified in the same time frame.
 - c) Discuss/revise DOT or DOPT schedule with patient and/or provide re-supply of self-administered medication.

Note: IF A PATIENT IS ALLOWED TO SELF-ADMINISTER, ONLY ONE MONTH'S SUPPLY OF MEDICATIONS SHOULD BE DISPENSED. **SELF-ADMINISTRATION IS STRONGLY DISCOURAGED FOR ALL SUSPECTS AND CASES.**

IF TB CASE OR SUSPECT IS ALLOWED TO SELF-ADMINISTER, WRITTEN JUSTIFICATION SHOULD BE DOCUMENTED IN PATIENT'S RECORD.

3. Obtain additional sputum or other bacteriologic samples as indicated or ordered.
4. Repeat radiologic studies as indicated.
5. Continue patient and family education.
6. Schedule visits for continued medical or nursing follow-up.
7. Document the following in patient's record:
 - a) Interval history.
 - b) Drug monitoring.
 - c) Re-supply of medication.
 - d) Patient education.
 - e) Continued care plan.

E. Special considerations:

1. To recognize patients who are delinquent for services, PHN should establish a system for tracking patient compliance with recommended follow-up visits for medication refill and medical evaluation.
2. Recommendations for any TB/LTBI medication made by the Metropolitan or Regional TB Physician shall be considered doctor's orders, and medication should be supplied as prescribed. If the patient has a private physician who accepts treatment responsibilities and states specifically he/she does not want the patient on this medication, this should be documented in the patient's record, and the Regional or Metropolitan TB physician should be notified immediately.
3. Regional TB nurse and Regional TB Physician should be notified immediately of any orders which cannot be or are not implemented (i.e. patient refuses, medication not available, etc.)
4. If any prescription written by a private physician recommends a dose of medication or method of administration different from the recommendations of the Division of Tuberculosis Elimination, the Regional or Metropolitan TB Physician must be notified before the drug is dispensed and his/her instructions followed.

5. Anti-tuberculosis drugs must be issued by a pharmacist in the manufacturer's sealed package or in labeled pre-packaged containers. The drugs may then be counted, packaged and labeled by a registered nurse under the supervision of a Tennessee Department of Health Physician prior to being dispensed to the TB patient.
6. Expiration dates on drugs and antigens should be verified. Out-dated drugs and antigens should be returned to the appropriate Regional Public Health Pharmacy.
7. LTBI patients are to be monitored for medication side effects and adherence at least monthly. Cases and suspects should be monitored for side effects each time medications are administered.

II. Performance of Contact Investigations and Appropriate Evaluation and Management of TB Contacts

- A. For all TB cases or suspects, initiate contact investigation utilizing concentric circle approach within 3 working days of receiving report of newly diagnosed case or suspect.
 1. Interview index TB case/suspect to identify possible contacts at home, work or other locations.
 2. Determine high (close) versus low risk (casual) contacts (see Section XIII.)
 3. Interview and evaluate (high-risk) close contacts within 7 working days of the patient interview
 - a. Patient's household members
 - b. Children
 - c. Immunosuppressed persons
 - d. Other close contacts (non-household family, co-workers, friends etc.).
 4. Schedule contacts for skin test, clinical evaluation and x-ray examinations to rule out TB/LTBI as indicated, (see Section XIII).
Note: Young children and immunosuppressed adults (cancer, HIV+, etc.) are a priority and should be carefully evaluated for active TB as soon as possible. CXR should be performed regardless of TST.

5. Contacts with history or symptoms suggestive of TB disease should be referred for medical evaluation immediately.
6. All contacts with TB disease should be evaluated, treated and monitored (see Section IX.)
7. All contacts with LTBI should be evaluated, treated and monitored (see Section IV.)
8. Once TB disease is ruled out, young children should immediately be given “window period treatment” for LTBI regardless of initial TST result, and this should be continued until follow-up TST is proven negative 10-12 weeks after the 1st skin test. (See Section IV.)
9. Immunosuppressed adult contacts (i.e. HIV+, etc.) should receive a complete course of LTBI therapy regardless of TST results once TB is ruled out.
10. Consider expanding contact investigation to include additional casual contacts based on percentage of positive skin tests found in initial contact testing (see Section XIII)

B. Contact Follow-up Visits

1. Interviewing of index TB case/suspect should be on-going to assure that all known contacts have been named.
2. Re-interviewing of the index case yields additional valuable disclosure of other potential contacts, as the patient becomes more comfortable with public health staff.
3. Examination of high-risk contacts to infectious cases of pulmonary tuberculosis represents the most productive method of case finding.
4. High risk contacts with initial negative skin tests should receive a second skin test in 10-12 weeks according to the recommended schedule (see Section XIII).
5. High risk contacts with positive skin tests and on treatment for LTBI should be followed and monitored as follows:
 - a. Monitor monthly.
 - b. Fill out form PH-2040 - Drug Screening and Monitoring Record. Include in patient’s chart.

- c. Toxic effects should be managed the same as for tuberculosis patients on treatment for disease (see Section IX)
- d. Issue 1 month's supply of properly labeled medication to patients self-administering for LTBI.
- e. Schedule Medical, Nursing or Public Health Representative follow-up.

III. Responsible for Targeted Testing (see Guidelines Section III)

IV. Documentation and maintenance of appropriate records

PHN is responsible for ensuring complete and accurate documentation of all related significant data in patient's chart, on appropriate forms, or in computerized database (TIMS, PTBMIS, etc.).

A. Ensure that all components of the visit are documented in patient's record:

1. Assessment of patient.
2. Evaluation of emotional reaction.
3. Collected data.
4. Obtained contact information.
5. Education of patient and family.
6. Instituted treatment of disease.
7. Instituted treatment of LTBI.
8. Scheduled appointments.
9. Plan for continued care.
10. Sputum containers with written instructions given.

B. The following forms are available and should be completed for all patients with active TB or LTBI, as appropriate:

1. Risk Assessment Tool (PH 3714).
2. Clinical Pathway for TB Suspects and Cases (PH 3742)
3. CDC Report of Verified Case of Tuberculosis (RVCT)
4. CDC Follow-up I and II (FU 1 & FU 2)
5. Tuberculosis Contact Record (PH 1631)
6. Drug Screening and Monitoring Record (PH 2040)
7. Aggregate Report for Tuberculosis Program Evaluation (ARPE) (TIMS Form to track contacts)
8. Summary of Laboratory Reports (PH 2036)
9. Medication Record (PH 2041)
10. Patient Education (PH 2037)

C. Transfer of Records

1. On all transfers the new address and directions for locating the patient should be obtained and documented in the record before transferring the record to assure continued follow-up.
2. To transfer a patient from **county to county**: The transferring county should send a copy of all records to the new county of residency and notify the regional office of the transfer.
3. To transfer a patient from **region to region**: Notify the regional office and send a copy of all records. The regional office referring the patient should then send the records to the regional office receiving the patient.
4. To transfer a patient from **state to state**: The regional office referring the patient should fill out the Interstate Reciprocal Notification of Disease Form, keep a copy and send one to the Central Office TB Elimination Program. The Central Office should contact the State TB Elimination Program in the new state of residency. The Central Office TB Elimination Program should then provide the regional office with the name and address of the contact person in the new state of residency. The regional office should then send the information as requested to the

contact person. The patient's record may be closed when documentation of treatment completion is received.

- D. Release of medical information** from tuberculosis control records should follow the policy established by the Tennessee Department of Health, Bureau of Health Services, Policies and Procedures Manual.
- E. To ensure that no one other than a physician or health care agency of the patient's choice receives a report of chest x-ray findings**, the person preparing the x-ray request form shall ask the patient "To what physician or health care facility do you want this report sent?" If patient has no preference, enter the resident county health department.
- F. Closing Records**

Tuberculosis records may be closed for the following reasons:

1. A change in diagnosis from tuberculosis to non-tuberculosis. (Patients diagnosed with Mycobacterium other than tuberculosis (MOTT) should be referred to a private physician.)
2. Patient expired.
3. Treatment is completed.
4. Patient is lost to follow up.

REGIONAL/METROPOLITAN TUBERCULOSIS NURSES' RESPONSIBILITIES

I. General Responsibilities

- A. Under direction of physician, provides and coordinates patient care.
- B. Supervises other tuberculosis program personnel as appropriate.
- C. Coordinates all TB related services such as surveillance and reporting, patient care, clinics, contact investigations, targeted testing, and documentation.

II. Specific responsibilities include but are not limited to the following:

- A. Screens for contraindications before medication is supplied. Ensures that patient is monitored before re-supply of medication.
- B. Discontinues medication and contacts physician if any signs of medication toxicity exist.
- C. Teaches patient/family regarding disease process, mode of transmission, etc.
- D. Ensures that an initial interview, a re-interview and contact workup are completed.
- E. Performs specific clinic functions, i.e., patient assessment, sputum collection, drawing blood, making x-rays (if properly trained and licensed), etc.
- F. Ensures maintenance of tuberculosis case register.
- G. Maintains mechanism for follow-up of patients who miss appointments.
- H. Maintains appropriate patient records.
- I. Makes hospital and home visits when needed.
- J. Provides in-service training to health department personnel, and personnel from hospitals, nursing homes, corrections, local jails, A & D facilities, homeless shelters, etc., as requested
- K. Makes supervisory visits with TB staff at appropriate intervals to ensure program requirements related to contact investigation and patient care are being followed.

- L. Provides appropriate oversight of local staff that perform TB services such as DOT, contact investigations, etc.
- M. Assures that appropriate program reports are submitted in an accurate, complete, and timely manner.
- N. Maintains collaborative relationships with appropriate local and state program personnel and the private medical sector.
- O. Provides outreach and education to high-risk settings, i.e., jails, prisons, alcohol and drug treatment centers, homeless shelters, etc.
- P. Performs evaluation of local health department TB program and projects such as Targeted Testing.

**XV. HOW TO ORDER TB MEDICATIONS, ANTIGENS,
AND SUPPLIES**

HOW TO ORDER TB MEDICATIONS, ANTIGENS AND SUPPLIES

The ordering of TB drugs and antigens is the responsibility of each Rural Regional Pharmacist or designee. TB drugs and antigens are ordered directly from the vendor. Supplies, (including syringes, x-ray film, etc.) should be ordered through the Rural Regional designated person. The Rural Regional office should order supplies by completing a Purchase Request Form (PH-0009) and submitting it to Central Procurements and Payments. (Bureau Policies and Procedures, Section 4.1.b.).

TB drugs are:

Myambutol (Ethambutol), 400 mg., 100 tablets/btl.

Isoniazid (INH) 100 mg., 100 tablets/btl.

Isoniazid (INH) 300 mg., 30 tablets/btl.

Isoniazid Liquid (INH liquid) , 50 mg./5 ml pint btl.

Vitamin B-6 (Pyridoxine) 50 mg. 100 tablets/btl.

Pyrazinamide (PZA), 500 mg. 500/btl., 500 mg. 60/btl, 500 mg. unit of use 100/bx

PPD Mantoux, 5 TU 1 ml/vial 10 tests/vial

PPD Mantoux, 5 TU 5 ml/vial 50 tests/vial

Rifamate (300 mg. RIF 150 mg. INH) 60 caps/btl.

Rifampin 300 mg. 60 caps/btl., 150 mg. 30 caps/btl.

Streptomycin 1.0 gm vial, 1.0 gm (10 per package)

The following drugs and antigens should not be routinely stocked and should only be ordered on an as-needed basis, (after consultation with the TB Control Officer in Central Office).

capreomycin, (Capastate Sulfate) 1 gm. vial

ethionamide, (Trecator-SC) 250 mg. 100 tablets/btl.

levofloxacin, (Levaquin) 500 mg. or 750 mg. 100 tablets/btl.

cycloserine, (Seromycin Pulvules) 250 mg. 40 tabs/btl.

Any other drug(s) not specifically listed requires authorization from the TB Control Officer in Central Office.

The Rural Regional Pharmacist or designated person will be responsible for disposition of outdated drugs, including returning them to manufacturer for credit or replacement. **Please do not return any outdated drugs to central office.**

Regional, Metropolitan and County Health Departments should order quarterly and maintain no more than a two month's supply of drugs and other tuberculosis supplies. The inventory should be maintained in such a manner as to assure that these do not become outdated.

XVI. INFECTION CONTROL PLAN

(TO BE ISSUED)

XVII. OTHER GUIDELINES

(TO BE ISSUED)

XVIII. OUTBREAK RESPONSE PLAN

(TO BE ISSUED)

XIX. EDUCATION AND TRAINING MATERIAL

(TO BE ISSUED)

XX. PROGRAM EVALUATION AND STANDARDS

(TO BE ISSUED)

XXI. LAWS AND REGULATIONS

(TO BE ISSUED)

XXII. GLOSSARY

GLOSSARY

ACID-FAST BACILLI (AFB) - Bacteria that retain certain dyes even when washed with an acid solution. Only rarely are acid-fast bacteria seen on a smear not mycobacteria. A presumptive diagnosis of tuberculosis is often made on the basis of a positive “AFB smear”; however, the diagnosis is not confirmed until a culture is grown and identified as *M. tuberculosis*.

ACQUIRED DRUG RESISTANCE (ADR) - A resistance to one or more anti-TB drugs that develops while a patient is receiving therapy and which usually results from the patient’s nonadherence to therapy or the prescription of an inadequate regimen by a health care provider.

ADVERSE REACTIONS - Any undesirable effect of a medication. Any drug may cause such reactions, although rare. Periodic monitoring of tuberculous patients while in treatment may help detect adverse reactions that occur.

ALVEOLI - The small air sacs in the lungs at the end of the bronchial tree; the site of gas exchange in the lungs and the site where tuberculous infection usually begins.

ANEMIA - A condition in which there is a decreased volume of red cells in the blood. There are many causes for anemia, including chronic infections such as untreated tuberculosis.

ANERGY - The inability of a person to react to skin test antigens (even if the person is infected with the organism tested) because of immunosuppression.

ANOREXIA - Loss of appetite. Symptoms frequently seen in many illnesses, including tuberculosis.

ASYMPTOMATIC - Without symptoms.

ATTENUATED - Refers to the weakened ability of bacteria to cause disease. For example, BCG is a vaccine derived from an attenuated strain of *Mycobacterium bovis*.

BACTERICIDAL - Capable of killing bacteria. Isoniazid (INH) and Rifampin (RIF) are the two most potent bactericidal antituberculous drugs. (See BACTERIOSTATIC.)

BACTERIOLOGICAL SPECIMEN - Refers to any body fluid, secretion or tissue sent to the laboratory where smears and cultures for tubercle bacilli are performed. The specimen may consist of sputum, urine, spinal fluid, material obtained at biopsy or through bronchial washing, etc.

BACTEC[®] - One of the most often used radiometric methods for detecting the early growth of mycobacteria in culture. It provides rapid growth (in 7-14 days) and rapid

drug-susceptibility testing (in 5-6 days). When BACTEC[®] is used with rapid species identification methods, *M. tuberculosis* can be identified within 10-14 days of specimen collection.

BACTERIOSTATIC - Any agent which arrests or hinders the growth of bacteria.

BCG (Bacillus of Calmette and Guerin) - A vaccine for TB named after the French scientists Calmette and Guerin. BCG is not widely used in the United States, but it is often given to infants and small children in other countries where TB is common.

BOOSTER PHENOMENON - A phenomenon in which some persons (especially older adults) who are skin tested many years after infection with *M. tuberculosis* have a negative reaction to an initial skin test, followed by a positive reaction to a subsequent skin test. The second (i.e., positive) reaction is caused by a boosted immune response. Two-step testing is used to distinguish new infections from boosted reactions (see Two-step testing).

CAVITY - A hole in the lung resulting from the destruction of pulmonary tissue by TB or other pulmonary infections or conditions. TB patients who have cavities in their lungs are referred to as having cavitory disease, and they are often more infectious than TB patients without cavitory disease.

CHEST X-RAY - A picture of the inside of your chest. A chest x-ray is made by exposing a film to x-rays that pass through your chest. A doctor can look at this film to see whether TB bacteria have damaged your lungs.

CHEST X-RAY: LATERAL VIEW - An X-ray film taken from the side of the chest.

CHEST X-RAY: POSTERIOR ANTERIOR (PA) FILM - The most common x-ray view with the patient standing facing the film and with the x-ray source coming from the back.

CHEST X-RAY: TOMOGRAMS - X-ray films taken using a special technique, which can focus on lesions in a particular plane (e.g., 5 centimeters from the back) in the chest.

COLONIZATION - Residence of bacteria in or on part of the body, which causes neither disease nor a response by the individual's immune defense system. Patients colonized with nontuberculous mycobacteria may not require treatment.

COLONY COUNT - Laboratory term used to quantify the numbers of tubercle bacilli in a cultured specimen. Each microscopic bacterium, when grown in the laboratory, gives rise to one visible colony.

COMPLIANCE - Refers to the willingness and/or ability of patients to maintain their share of the responsibility for their treatment by taking medications as prescribed and by keeping necessary clinic appointments.

CONSUMPTION - A term meaning to “waste away” and used for tuberculosis prior to the 20th century.

CONTACT - A person who has shared the same air with a person who has infectious TB for a sufficient amount of time and/or in a poorly ventilated or confined space to allow possible transmission of *M. tuberculosis*.

CONTAMINATION - In tuberculosis, objects contaminated with tubercle bacilli (see “FOMITES”) are very rarely associated with transmission. Air contaminated with infectious droplet nuclei is almost always the vehicle implicated in the spread of infection. May also refer to sputum specimens from which no bacteria can be cultured because of overgrowth (contamination) by other more rapidly growing bacteria.

CONVERTER - A person who has had an initial tuberculin skin test without a “significant” reaction and within two years has another skin test with an increase of 10 or more millimeters. This conversion may represent new infection, which is associated with a high risk for developing disease, or may occur as a result of the “booster phenomenon.”

CULTURE - The process of growing bacteria in the laboratory so that organisms can be identified. It generally takes 6 weeks for *M. tuberculosis* to grow.

CYCLOSERINE (CS) - A seldom-used oral antituberculous drug.

DIRECTLY OBSERVED THERAPY (DOT) - a way of helping patients take medicine for TB. The patient meets with a health care worker every day or several times a week at a mutually agreeable site (such as the TB clinic, patient’s home or work, other convenient location). The health care worker observes the patient swallow the medication.

DISEASE - A condition marked by subjective complaints, a specific history, and clinical signs, symptoms and laboratory or radiographic findings.

DNA probe - A technique that allows rapid and precise identification of mycobacteria (e.g., *M. tuberculosis* and *M. bovis*) that are grown in culture. The identification can often be completed in 2 hours.

DRUG RESISTANCE, PRIMARY - A resistance to one or more anti-TB drugs that exists before a patient is treated with the drug(s). Primary resistance occurs in persons exposed to and infected with a drug-resistant strain of *M. tuberculosis*.

EXTRAPULMONARY TB - TB disease in any part of the body other than the lungs (for example, the kidney or lymph nodes).

FOMITES - Linens, books, dishes, or other objects used or touched by a patient. These objects are *not* involved in the transmission of *M. tuberculosis*.

GASTRIC ASPIRATE - A procedure sometimes used to obtain a specimen for culture when a patient cannot cough up adequate sputum. A tube is inserted through the mouth or nose and into the stomach to recover sputum that was coughed into the throat and then swallowed. This procedure is particularly useful for diagnosis in children, who are often unable to cough up sputum.

GENOTYPING - A laboratory method to determine the similarities or differences of *M. TB* strains. It is a useful tool in contact investigations to determine the source and spread of a specific *M. TB* strain.

HIGH-EFFICIENCY PARTICULATE AIR (HEPA) FILTER - A specialized filter that is capable of removing 99.97% of particles $\geq 0.3 \mu\text{m}$ in diameter and that may assist in controlling the transmission of *M. tuberculosis*. Filters may be used in ventilation systems to remove particles from the air or in personal respirators to filter air before it is inhaled by the person wearing the respirator. The use of HEPA filters in ventilation systems requires expertise in installation and maintenance.

HIV INFECTION - Infection with the human immunodeficiency virus, the virus that causes AIDS (acquired immunodeficiency syndrome). A person with both TB infection and HIV infection is at very high risk for developing TB disease.

INDURATION - An area of swelling produced by an immune response to an antigen. In tuberculin skin testing, the diameter of the indurated area is measured 48-72 hours after the injection, and the result is recorded in millimeters.

INFECTIOUS TB - TB disease of the lungs or throat, which can be spread to other people through coughing, talking, laughing, singing or yelling.

INFECTIOUS PERSON - A person with TB disease who is capable of transmitting TB to others.

INTERMITTENT THERAPY - Therapy administered either two or three times per week, rather than daily. Intermittent therapy should be administered only under the direct supervision of a Health Care Worker or other designated person (see Directly Observed Therapy [DOT]).

INTRADERMAL - Within the layers of the skin. (The tuberculin skin test is administered intradermally.)

ISONIAZID (INH) - An oral bactericidal drug used alone for preventive treatment of tuberculous infection (also known as latent TB infection or LTBI), and in combination with one or more other drugs in the treatment of active tuberculosis disease.

JAUNDICE - Condition in which the skin and eyes appear yellow. This is often the result of hepatitis (or other liver diseases), which may rarely be caused by some antituberculous drugs, such as Isoniazid (INH) or Rifampin (RIF).

KANAMYCIN (KM) - Injectable antituberculous drug related to Streptomycin (SM).

KOCH, ROBERT - German scientist and physician who discovered the tubercle bacillus in 1881.

LATENT TB INFECTION - Infection with *M. tuberculosis*, detected by a positive tuberculin skin test. This is a dormant form of TB and is not infectious.

LOWENSTEIN-JENSEN (LJ) MEDIUM - A nutrient substance used in the laboratory on which tubercle bacilli and other mycobacteria are grown.

LYMPH NODES - Small nodules of specialized immune cells located throughout the body. Those in the chest may be involved early in tuberculosis when bacilli are carried there by the lymphatics. Nodes elsewhere in the body may also be affected later.

LYMPHATICS - Small channels which carry fluid (lymph), white blood cells and invading bacteria to the lymph nodes.

LYMPHO-HEMATOGENOUS - Refers to the spread of tubercle bacilli from the initial site of infection in the lungs by way of the lymphatics and bloodstream to other parts of the body.

MALaise - A general feeling of discomfort associated with illness.

MANTOUX TEST - A method of skin testing that is performed by injecting 0.1 ml of PPD-tuberculin containing 5 tuberculin units into the dermis (i.e., the second layer of skin) of the forearm with a needle and syringe. This test is the most reliable and standardized technique for tuberculin testing.

MICRON - A metric unit of length. A micron = 1/1000 millimeter (approximately 25,000 microns to the inch).

MIDDLEBROOK 7H-11 MEDIUM - A type of medium used to culture tubercle bacilli and other mycobacteria.

MILIARY - Those cases of tuberculosis in which large numbers of tubercle bacilli have been disseminated through the bloodstream to many parts of the body. Also refers to the appearance of the chest film in disseminated tuberculosis (looks like scattered millet seeds).

MULTIDRUG-RESISTANT TB (MDR TB) - Active TB caused by *M. tuberculosis* organisms that are resistant to more than one anti-TB drug; in practice, refers to organisms that are resistant to both INH and rifampin with or without resistance to other drugs.

M. TUBERCULOSIS - bacteria that cause TB infection and TB disease.

NEGATIVE - Usually refers to a test result. A negative TB skin test reaction indicates the person probably does not have TB infection, however HIV + patients should be x-rayed regardless of skin test results.

POSITIVE PPD REACTION - A reaction to the purified protein derivative (PPD)-tuberculin skin test that suggests the person tested is infected with *M. tuberculosis*. The person interpreting the skin-test reaction determines whether it is positive on the basis of the size of the induration and the medical history and risk factors of the person being tested.

PRIMARY DRUGS - Term sometimes used to refer to the most commonly used antituberculous drugs: Isoniazid (INH), Rifampin (RIF), Ethambutol (EMB) and Pyrazinamide (PZA).

PRIMARY DRUG RESISTANCE - Drug resistance that is present when the patient is first diagnosed and before TB drugs are started.

PULMONARY - Referring to the lungs.

PULMONARY TB - TB disease that occurs in the lungs, usually producing a cough that lasts longer than 2 weeks. Most of the TB cases in the United States are pulmonary (85%).

PURIFIED PROTEIN DERIVATIVE (PPD) - Type of purified tuberculin preparation derived from old tuberculin (OT) and developed in the 1930's. It is a cell-free purified protein fraction obtained from a human strain of *Mtb* grown on a protein-free synthetic medium, and inactivated. The standard Mantoux test uses 5 TU (tuberculin units) of PPD.

PYRAZINAMIDE (PZA) - One of the first-line oral antituberculous drugs.

RAPID GROWERS - Certain species of nontuberculous mycobacteria (e.g., *m. fortuitum*) which can produce visible colonies, when cultured in the laboratory, in as little as one week. (*M. tuberculosis* usually takes three-six weeks to produce equal size colonies.)

REACTIVATION - Refers to patients who have achieved clinical well-being, negative bacteriology and radiologic stability as a result of chemotherapy, but who later become ill (and possibly infectious) after having had discontinued or completed therapy.

REGIMEN - Any particular treatment plan for tuberculosis specifying which drugs are used, in what doses, according to what schedule, and for how long treatment will be continued.

RELAPSE - Similar to reactivation, but more precisely refers to patients who have improved clinically and bacteriologically but who then become ill and/or have positive smears and cultures again while still on therapy. May be due to inadequate regimen, poor compliance, or drug resistance.

RESISTANCE - Refers to the ability of some strains of bacteria (including *M. tuberculosis*) to grow and multiply even in the presence of certain drugs that normally kill them. (Such strains are referred to as “drug resistant strains.”)

RIFAMPIN (RIF) - An oral bactericidal antituberculous drug which, when used along with Isoniazid (INH) for the treatment of TB disease, provides the basis for short-course therapy.

ROENTGEN, WILHELM - German physician and scientist who discovered X-rays in 1895. Often, the term “roentgen” used as a measure of radiation.

ROENTGENOGRAM - An X-ray film.

SARCOIDOSIS - A chronic disease whose cause is not known and which may affect the lungs as well as other parts of the body. The appearance on X-ray films of sarcoidosis may occasionally mimic that seen in tuberculosis.

SMEAR (AFB SMEAR) - A laboratory technique for visualizing mycobacteria. The specimen is smeared onto a slide and stained, then examined using a microscope. Smear results should be available within 24 hours. In TB, a large number of mycobacteria seen on an AFB smear usually indicates infectiousness. However, a positive result is not diagnostic of TB because organisms other than *M. tuberculosis* may be seen on an AFB smear (e.g., nontuberculous mycobacteria).

SOURCE CASE – A TB case that is discovered while investigating a positive skin test in a child < 18 years of age or a cluster of positive skin tests. This is known as a Source Case Investigation.

SPUTUM - Phlegm coughed up from deep within the lungs. If a patient has pulmonary disease, an examination of the sputum by smear and culture can be helpful in evaluating the organism responsible for the infection. Sputum should not be confused with saliva or nasal secretions.

TB SKIN TEST - A test that is used to detect TB infection. A liquid called tuberculin is injected under the skin on the lower part of your arm. If you have a positive reaction to this test, you probably have TB infection.

TRANSMISSION - The spread of an infectious agent from one person to another. The likelihood of transmission is directly related to the duration and intensity of contact to *M. tuberculosis* as well as the virulence of the specific organism.

TRUDEAU, EDWARD - American physician who, after having recovered from tuberculosis himself, helped launch the sanitarium movement in this country before the turn of the century.

TUBERCLE BACILLUS - Term often used to refer to *Mycobacterium tuberculosis* and to *Mycobacterium bovis*).

TUBERCULIN - A liquid that is injected under the skin on the lower part of your arm during a TB skin test. If you have TB infection, you will probably have a positive reaction to the tuberculin.

TUBERCULIN SKIN TEST - A method used to evaluate the likelihood that a person is infected with *M. tuberculosis*. A small dose of PPD-tuberculin is injected just beneath the surface of the skin, and the area is examined 48-72 hours after the injection. A reaction is measured according to the size of the induration. The classification of a reaction as positive or negative depends on the patient's medical history and various risk factors (see Mantoux test, PPD test).

TUBERCULOSIS - The disease caused by *M. tuberculosis* (or *M. bovis*). Condition in which tuberculous infection has progressed so that the individual typically has signs and symptoms of illness, an abnormal X-ray film, a "positive" bacteriological examination (smear and/or culture), as well as a "significant" tuberculin reaction. Individuals with disease may be infectious.

TUBERCULOUS INFECTION - Condition in which living tubercle bacilli are present in an individual, without producing clinical disease. The infected individual, although having a "significant" tuberculin reaction, usually feels well, has a normal chest X-ray film, does not have a "positive" bacteriological examination (smear and culture), is not infectious, and is not considered a "case" of tuberculosis. However, the infected individual remains at lifelong risk of developing disease.

TWO-STEP TESTING - A procedure used for the baseline testing of persons who will periodically receive tuberculin skin tests (e.g., HCWs) to reduce the likelihood of mistaking a boosted reaction for a new infection. If the initial tuberculin-test result is classified as negative, a second test is repeated 1-3 weeks later. If the reaction to the second test is positive, it probably represents a boosted reaction. If the second test result is also negative, the person is classified as not infected. A positive reaction to a subsequent test would indicate new infection (i.e., a skin-test conversion) in such a person.

TB DISEASE - An illness in which TB bacteria are multiplying and attacking different parts of the body. The symptoms of TB disease include weakness, weight loss, fever, no appetite, chills, and sweating at night. Other symptoms of TB disease depend on where in the body the bacteria are growing. If TB disease is in the lungs (pulmonary TB), the symptoms may include a bad cough, pain in the chest, and coughing up blood.

ULTRAVIOLET (UV) LIGHT - A form of radiation intermediate between visible light and X-rays. UV radiation is effective in killing many bacteria including tubercle bacilli. May be artificial (from a special light fixture) or natural (from sunlight).

VENTILATION - Refers to the flow of air into and out of the area surrounding an infectious tuberculosis patient. If the flow is sufficient, tubercle bacilli become dispersed, and there is a diminished risk of transmission of infection.

VIRULENCE - Refers to the ability of a microorganism, such as *M. tuberculosis*, to produce serious disease. *M. tuberculosis* is a virulent organism. Some nontuberculous mycobacteria are virulent (e.g., *M. kansasii*), while others (e.g., *M. goodii*) are not. (PATHOGENICITY is a related--though not identical--concept).

ZIEHL-NEESEN - The acid-fast method for staining mycobacteria in preparation for examination of a sputum smear. The stain results in a red appearance of mycobacteria under the microscope.

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- _____ (00-3327) **Prevention and Control of Tuberculosis in Facilities Providing Long-Term Care for the Elderly.** MMWR, 7/13/90.
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