

DIAGNOSIS AND EVALUATION OF ACTIVE TUBERCULOSIS (TB) DISEASE

- I. TITLE:** Protocol for the diagnosis and evaluation of persons suspected of having tuberculosis disease.
- II. TYPE OF STANDARD:** Service
- III. OUTCOME:** Successful diagnosis of persons suspected of having active TB disease to provide them with timely, appropriate, and complete treatment to cure.
- IV. PERSONNEL:** Medical Doctor (M.D.), Doctor of Osteopathy (D.O.), Advanced Registered Nurse Practitioner (A.R.N.P.), Physicians Assistant (P.A.), Registered Nurse (R.N.), Licensed Practical Nurse (L.P.N.), within the constraints of their respective practice acts and protocols; H.S.R. within the constraints of their job descriptions and protocols.

Subjective and objective data gathering: M.D., D.O., A.R.N.P., P.A., R.N., Nurse Case Manager (N.C.M.), L.P.N., H.S.R.

Assess and evaluate: M.D., D.O., A.R.N.P., P.A., R.N., N.C.M.

Planning\Education\Counseling: M.D., D.O., A.R.N.P., P.A., R.N., N.C.M., L.P.N., H.S.R.

Intervention: M.D., D.O., A.R.N.P., P.A., R.N., N.C.M.

Emergency: M.D., D.O., A.R.N.P., P.A., R.N., N.C.M.

Documentation: M.D., D.O., A.R.N.P., P.A., R.N., N.C.M., L.P.N., H.S.R.

- V. COMPETENCIES:** Health care providers must demonstrate knowledge of transmission, pathogenesis, clinical symptomatology, and diagnostic tests used in the evaluation of TB. This should include didactic, practicum, and clinical training as appropriate for their individual practice acts and job descriptions.

VI. AREAS OF RESPONSIBILITY:

1. ASSESSMENT:

- A. Subjective: Key to the diagnosis of TB is to "Think TB" which means consider the possibility of this diagnosis in any client who is at high-risk for developing the disease who presents with symptoms which may be compatible with TB.
- 1) Obtain from the client/informant a complete history of possible exposure to people with TB, exposure to Multidrug-Resistant TB (MDR-TB), past history of TB, previous positive tuberculin skin test, and any previous history of treatment either for TB infection or disease.
 - 2) Assess the client's family/significant other/support system.

- 3) Assess home environment and the need for immediate contact investigation.
- 4) Obtain history of medical risk factors for TB such as diabetes mellitus, HIV (including high-risk behaviors, which may place client at risk for HIV), immunosuppression from chemotherapy, end stage renal disease, chronic GI problems or malabsorptive conditions, intestinal bypass or gastrectomy, cancer, silicosis, substance abuse, and prolonged corticosteroid or other immunosuppressive therapy.
- 5) Obtain a socio-economic history including where the client has resided within the past 2 years (including residence in congregate living facilities, e.g. correctional facilities, homeless shelters), occupation as it relates to occupational exposure to TB and significant exposure to silica (e.g. cement cutting, sandblasting), country of origin, and other demographic information relevant to TB.
- 6) Obtain history of clinical signs and symptoms of pulmonary/laryngeal TB which may include prolonged and productive cough of over two weeks duration, hoarseness, chest pain, or hemoptysis. Systemic symptoms of TB may include unexplained weight loss, fever, night sweats, loss of appetite, easy fatigability, or chills.

Approximately 15% of TB cases in HIV negative clients and up to 67% in HIV positive clients are extrapulmonary, symptoms of which will depend on the site affected. Examples are: TB of the spine may cause back pain; TB of the kidney may cause blood in the urine; TB meningitis may present as headache, neck pain and/or rigidity, vomiting, high fever, convulsions, etc.

Extrapulmonary TB should be considered in the differential diagnosis of ill persons who have systemic symptoms, who are at high risk for TB (e.g. HIV positive clients) and come from demographic areas that increase the person's risk for exposure to TB such as immigrants from Africa, Asia, Mexico, Latin America, and Eastern Europe.

B. Objective:

- 1) Perform physical examination. A physical examination is an essential part of the evaluation, though few clients will have physical findings, which are specific for the disease. It cannot be used to confirm or rule out TB, but it can provide valuable information about the client's overall condition and other factors, which may affect how TB is treated.

Assess the following:

- a. Client's clinical status and potential for infectiousness
- b. Client's nutritional status
- c. Client's psychological, behavioral and emotional stability to

determine capability of understanding and following instructions for adherence and need for directly observed therapy. Consider directly observed therapy (DOT) for every client. (See TA-TB 11 - Procedures for Directly Observed Therapy (DOT))

- d. Client's immune status

2. PLANNING/EDUCATION/ COUNSELING

- A. Tailor all counseling and education to be culturally, linguistically, and educationally appropriate for each individual client.
- B. Identify all barriers and address them appropriately by using a team approach (this includes nurse case manager, physician, social worker, psychologist or mental health discipline, nutritionist, etc.).
- C. Include the client in the planning process as an integral part of the team.
- D. Provide basic information regarding tuberculosis including but not limited to transmission, treatment, infection control to client as well as family.
- E. Provide and document health education and counseling (complete the Acknowledgement of Tuberculosis Counseling, DH 1179, form). Stress the importance of keeping appointments, adherence with medications through the course of the prescribed therapy to cure, and infection control measures.

3. INTERVENTION

- A. Devise a treatment plan for every case of TB.
- B. Discuss plan of care with the client.
- C. Perform a physical examination at the time of the initial visit.
- D. For clients who have symptoms compatible with active TB disease, obtain a chest radiograph (at least a posteroanterior (PA) view) and sputum for Acid Fast Bacilli (AFB) smear, nucleic acid amplification test (NAA) (e.g. *Mycobacterium tuberculosis* Direct Test (MTD)), and culture.
- E. Initial chest x-ray:

This can be used to differentiate between TB infection and active pulmonary TB disease in a person with a positive tuberculin skin test (TST) by Mantoux method.

Chest x-rays are indicated for the following persons:

- 1) Tuberculin skin test converters
- 2) Persons with first time positive TST
- 3) Persons in whom follow-up readings of TST are anticipated to be difficult to obtain such as the homeless, migrant workers, refugees, etc.
- 4) Persons with clinical signs and symptoms of TB

- 5) Persons who are HIV positive where TST cannot be relied upon but are highly suspected of having TB

A PA view of the chest is the standard radiograph needed for detection of TB related abnormalities. In some instances, other views such as lateral and/or apical lordotic, may be needed based on the discretion of the attending physician. In active pulmonary TB disease, lung abnormalities are often found in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. However, lesions may appear anywhere in the lungs and may differ in size, density, and cavitation, especially in HIV-infected and other immunosuppressed persons. Abnormalities can vary from enlarged hilar and paratracheal lymph nodes, with or without evidence of pleural effusion, parenchymal infiltrates, atelectasis, millet seed appearance, fibronodular densities, or cavitation.

Cavitation in the upper lobe, when present, is highly suggestive of TB. Abnormalities on the chest x-ray may be suggestive of TB but cannot be used solely to make a final diagnosis. Serial chest x-rays may be used to judge resolution of pulmonary TB.

In HIV-infected persons with pulmonary TB, the chest x-ray may have an unusual appearance. For example, infiltrates may occur in any lung zones, cavitation is not a common finding, or mediastinal or hilar lymphadenopathy may be the only abnormality seen. In fact, the chest x-ray of an HIV-infected person may appear entirely normal.

Chest x-rays should be interpreted by a certified radiologist or a clinician (see section VI. 5. TB Physicians Network) with comparable experience in x-ray interpretation.

- 6) Collect sputum specimens for AFB smear, nucleic acid amplification test (e.g. MTD test), culture, and susceptibility testing and provide specimen containers for subsequent sputum specimens with clear instructions on sputum collection and specimen handling.

F. Sputum Collection

Diagnostic microbiology should be done on every TB case or suspect.

1. Obtain at least three early morning sputum specimens for AFB smear and culture, ideally on consecutive days for each person suspected of having pulmonary or laryngeal TB. A health care worker should coach and directly observe the client while using appropriate protective respiratory precautions based on OSHA standards (See TA-TB 4 - Tuberculosis (TB) Infection Control). The quality and quantity of the specimen submitted is paramount for the accurate diagnosis of active TB disease. Unsupervised clients seldom provide a reliable, adequate specimen.

Clients should be properly instructed on how to produce a good, reliable specimen as follows:

The client should be informed that sputum is the material brought up from the lungs, not mucus from the nose or saliva from the mouth.

The following step-by-step instructions should be given:

- a. Clean and thoroughly rinse the mouth with water upon arising in the morning.
 - b. Take three deep breaths (a tickling feeling at the end of each deep breath is usually experienced).
 - c. After the third breath, cough hard and try to bring up sputum from deep in the lungs.
 - d. Remove the lid and expectorate the sputum into the sterile container, collecting at least one teaspoon (5 ml). Secure the lid on the container when finished.
 - e. Remain in the isolation room until coughing stops. (Refrigerate the specimen immediately after obtaining to reduce overgrowth of other organisms.)
2. For clients unable to cough up sputum, aerosol induction (utilizing hyper or hypo solutions) can be used to stimulate the production of sputum. Clients should be given sufficient time to produce sputum, 15 minutes is usually sufficient. **Aerosol induced specimens should be labeled as such** to ensure that the laboratory does not discard it because induced sputum is watery and resembles saliva.
 3. Bronchoscopy can be done by a pulmonologist if the client cannot produce sputum when pulmonary TB is reasonably suspected. Bronchial washings, brushings, and biopsy may be obtained, depending on diagnostic possibilities and findings.
 4. Gastric aspiration of overnight swallowed sputum is the best way to obtain specimens from infants and young children who cannot produce sputum even with aerosol induction, but this is uncomfortable and invasive.
 5. Health care workers must follow precautionary measures for infection control during sputum induction, bronchoscopy, and other sputum/specimen collection. Refer to TA-TB 4 - Tuberculosis (TB) Infection Control for further information.

Detection of AFB in the stained specimen (smear) examined microscopically may provide the first bacteriologic clue of TB. Fluorescent staining with Aureomine O is the preferred staining method because it is more sensitive than the traditional methods in which Kenyoun or Ziehl-Neelsen is used. Smear results should be available within 48-72 hours after the specimen is sent to the Bureau of Laboratories.

Laboratories should report positive smears and cultures within 24 hours of identification by fax or telephone to the primary health care provider followed by a written report.

Nucleic Acid Amplification Tests (e.g. *Mycobacterium tuberculosis* Direct Test (MTD) or the Amplicor TB Test) are the newest methods for detecting the presence of TB in specimens. The test, based on amplification of nucleic acids present in *M.tb* organisms, is highly sensitive (~80%), highly specific (~98%), and

rapid (results available within 24 hours). The MTD test is FDA approved for smear negative and positive respiratory specimens from untreated (less than 7 days of therapy) clients. The Bureau of Laboratories in Jacksonville provides the MTD testing free of charge on all smear positive specimens and upon request on other specimens. The MTD may be performed on non-respiratory specimens (including those that have been preserved in formalin or paraffin) but it must be remembered that this use of the test is not FDA approved and results may be unreliable. It also must be remembered that a negative MTD result does not necessarily rule out the presence of active TB disease, and clinical acumen must be used in conjunction with laboratory and other diagnostic data in order to make an accurate diagnosis of active TB disease.

Diagnosis of TB can be confirmed by isolation of *M.tb* or *M.tb complex* on culture. Follow-up smears and cultures for initial microbiology positive persons is the most important method to judge infectiousness and response to therapy. At a minimum, specimens should be obtained at monthly intervals until the culture converts to negative.

6. For all persons with positive cultures for *M.tb*, the initial isolate must be tested for drug susceptibilities. It is crucial to identify drug resistance as early as possible to ensure appropriate treatment. It should be emphasized that the presence of resistance to rifampin should be confirmed with the Bureau of Laboratories (904-791-1571) and another culture be tested to confirm the resistance.

Drug susceptibility must be repeated for clients who do not respond adequately or who continue to have positive cultures after two months of therapy.

- G. Perform a tuberculin skin test using the Mantoux method. The TST is used to diagnose Latent TB Infection (LTBI). The TST is the best-studied test available to diagnose TB infection. The TST is not used to diagnose active TB disease, but rather to detect the presence of infection with TB. A positive TST does not necessarily signify active TB; in fact the TST may be falsely negative in up to 20% of clients with active TB disease. Further diagnostic tests (e.g. CXR, sputum for AFB smear, culture, MTD) should be carried out before a definitive diagnosis of active TB disease can be established. False positive reactions to the TST may result from exposure to nontuberculous mycobacteria (NTM).

A negative reaction to the TST does not exclude the diagnosis of active TB disease or LTBI. Some persons may have a false negative reaction to the TST if they are tested too soon after exposure to TB. In general, it takes 2 to 12 weeks after initial infection for the person's immune system to respond to the tuberculin antigen (delayed hypersensitivity reaction). Children younger than six months of age may have a false negative reaction to the tuberculin antigen because their immune systems are not yet fully developed. Persons with overwhelming TB disease and those who are immunocompromised or are HIV infected may also have false negative TSTs.

It is customary to consider TST reactions of less than 10 mm induration as negative and attribute them to cross reactivity with environmental NTM except for

persons who are HIV positive (or those with other known significant immunosuppressive conditions), high-priority contacts of TB cases and those with radiographic findings of healed TB where a reaction of 5 mm or more induration is considered a positive reaction.

1. Client with a significant PPD reaction who has unexplained unilateral pleural effusion should be referred to a pulmonologist for a thoracentesis and/or pleural biopsy. Pleural fluid from TB pleuritis may rarely show positive AFB smear (~30%) and has generally low yield for positive culture (~50%). However, when culture is combined with histologic examination, the diagnosis can be made in approximately 80-90 % of cases. Pleural biopsy should be done prior to aspiration of pleural fluid. Pleural fluid is exudative with protein content >4 g/dl and with predominance of lymphocytes. The pleural fluid may also be sent for other ancillary tests, which may aid in the diagnosis of TB pleuritis such as adenosine deaminase (ADA), MTD, and gamma-interferon.

Clients with undiagnosed exudative pleural effusion with an initially negative TST reaction should have a repeat Mantoux TST in 2 weeks, since it is not uncommon for clients with TB effusion to have a negative skin test.

- h. In some instances where microbiology confirmation cannot be obtained, a client can still be considered a case of TB for reporting purposes in the presence of **all** of the following criteria: a positive TST, clinical and/or radiographic abnormalities consistent with TB, improvement with the use of at least two anti-TB medications, and completed diagnostic evaluation. (This condition is called culture negative or clinical TB and occurs in 10-20% of active TB cases)
- i. Any person who has a single positive culture (rarely two positive cultures) but does not have other findings compatible with active TB disease (e.g. asymptomatic, negative CXR, negative PPD, no risk for TB, etc.) should be considered for the possibility of a laboratory cross contamination or error. While it is possible to have TB with only one culture positive, whenever the clinical scenario does not match the laboratory results the possibility of laboratory error should be considered. In these cases, consultation with the Bureau of Laboratories TB Laboratory 904-791-1571 and the TB Physicians Network 1-800-4TB-INFO (1-800-482-4636) should be sought.

4. EVALUATION

- A. The client should have a monthly clinic evaluation.
- B. For clients who are not on DOT, combination pills should be prescribed (e.g. Rifamate[®] or Rifater[®]) and monthly pill counts and assessment for adherence should be done.
- C. All clients should undergo evaluation of clinical response to therapy by taking monthly weights, assessing status of cough, fever, appetite, night sweats, and other symptoms.
- D. A monthly sputum smear and culture should be obtained to evaluate response to treatment. It is most important to obtain a sputum specimen for AFB smear and

culture for two months after beginning therapy to assure that the client has converted his/her cultures to negative.

- E. Follow-up chest x-rays may be done at least three months after the initial x-ray and at the end of treatment.

5. TB Physicians Network

The purpose of the TB Physicians Network is to provide clinical and programmatic support to TB programs and community physicians. The network is available for clinical services including diagnostic, radiologic interpretation, clinical consultations, and therapeutic recommendations. The physicians are also available for programmatic consultation as well as referrals to the TB Bureau's Legal Counsel for potential legal interventions. The TB Physicians Network can be contacted through 1-800-4TB-INFO.

B Physicians Network can be contacted through 1-800-4TB-INFO (1-800-482-4636).

VII. SUPPORTIVE DATA

1. CDC/ATS. *Diagnostic standards and classification of tuberculosis in adults and children*. Am. J. Respir. Crit. Care Med. 2000;161:1376 - 1395.
2. CDC. *Core Curriculum on Tuberculosis*. U.S. Department of Health and Human Services-Public Health Service, Fourth edition, 2000.
<http://www.cdc.gov/nchstp/tb/pubs/corecurr/default.htm>
3. Rom WN editor. *Tuberculosis*. Little and Brown Publishers 2003
4. Iseman MD. *A Clinicians Guide to Tuberculosis*. Lippincott Williams and Wilkins 2000.