Tuberculosis

Guidelines for Screening for Tuberculosis Infection and Disease during the Domestic Medical Examination for Newly Arrived Refugees

Background

Tuberculosis (TB) rates in the United States have continued to decline, reaching their lowest point on record in 2007 (1). Although TB is decreasing overall in the United States, there is a disproportional increase in TB in foreign-born individuals. For example, in 2007, the TB rate among foreign-born persons in the United States was 9.7 times that of U.S.-born persons (1). In cities that are home to many newly arriving immigrants and refugees, rates of TB can be well above the national average. Additionally, the prevalence of drug-resistant TB and extrapulmonary disease is higher among foreign-born persons, making the diagnosis and management of these cases both challenging and essential for effective prevention and control of TB among newly arriving refugees (2). The rate of TB disease appears to remain high for many years after immigration, making it essential that clinicians identify and treat latent tuberculosis infection (LTBI) prior to the development of TB disease. In addition, because of the high rate of reactivation, health-care providers who serve immigrants and refugees should maintain a high index of suspicion, regardless of the results of medical examinations performed overseas (3).

This document provides an overview of the overseas medical screening process for refugees relocating to the United States, and outlines guidelines for clinicians evaluating refugees for TB during the medical examination for new arrivals. This document does not replace existing guidelines but is meant to highlight specific needs in refugees and should augment and be used in conjunction with existing guidelines from national authorities (ATS/CDC/IDSA) and state TB control programs.

Overview of overseas pre-departure tuberculosis screening for refugees

Prior to departure for the United States, all refugees receive an overseas medical examination. This examination is to identify individuals with conditions that, by law, necessitate exclusion from, or treatment before departure for, the United States. CDC stipulates the content of this examination through Technical Instructions (TIs) issued to panel physicians and organizations that perform the medical screening examinations. The TB TIs issued in 1991 were revised in 2007 (4). The TB TIs are being implemented in priority countries on a rolling basis, as determined by factors such as refugee volume and burden of tuberculosis disease. Current requirements for specific countries, date of implementation for each country, and a comparison of the 1991 and 2007 TIs are listed in table 1, and updates can be found at:
http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html.

Panel physicians provide information on screening and treatment results. This information accompanies the refugee and should be available to the evaluating provider in the United States. In addition, the information is provided through the Electronic Disease Notification (EDN) system to individual State health departments. If the evaluating provider in the United States is not receiving this information, the state

refugee health program should be contacted for guidance. This information should always include screening information, as well as any diagnostic procedures and treatment rendered, including such data as:

- Pre-resettlement medical screening evaluations.
- Pre-departure screening evaluations (screening performed within 3 weeks of departure, which includes a medical examination, chest radiograph, and three sputum smears for culture and AFB). These requirements are applied when CDC determines the risk of importation of tuberculosis is great enough to warrant these efforts for specific populations. As such, they are not applied to all refugees.
    - Pre-departure tuberculosis classifications (Table 1)
    - Testing for TB infection documentation
        - Tuberculin skin test documentation (including name of product, expiration date, amount administered, and type of product used, such as 5TU PPD-S or 2TU of RT 23)
            OR
        - IGRA test documentation, if used.
    - Chest radiograph findings, when performed for screening
- Pre-departure treatment information
    - Directly observed therapy (DOT) regimen received, including doses of all medications, start and completion dates, and periods of interruption.
- Chest radiograph findings before, during, and after treatment.
- Laboratory results
    - Sputum smear AFB microscopy results obtained before, during, and after treatment.
    - Cultures for mycobacteria obtained before, during, and after treatment, including any that were contaminated.
    - Drug susceptibility test results performed on any positive culture.
- Clinical course, including such information as clinical improvement or lack of improvement during and after treatment.

Domestic Refugee Screening for Tuberculosis

The primary goal of the domestic refugee medical screening evaluation for TB is to identify individuals with latent TB infection (LTBI) or TB disease, to facilitate timely treatment and control. Individuals with LTBI or disease, and contacts of known cases of disease should be treated according to U.S. standards of care (www.cdc.gov/nchstp/tb/pubs/mmwrhtml/Maj_guide/Treatment.htm). Cases of confirmed or suspected TB disease must be reported to appropriate authorities (i.e., state or local health department) for monitoring and further public health intervention, such as contact investigation. Some areas may also require reporting of individuals with latent TB infection.

Medical history and physical examination of refugees for tuberculosis during the domestic medical screening evaluation

Tuberculosis disease should infrequently be encountered during the domestic refugee medical screening evaluation but, when identified, it may represent primary pulmonary or extrapulmonary disease (Appendix A). Patients with TB disease may be minimally symptomatic, particularly those with extrapulmonary disease. In fact, some individuals with tuberculosis disease, particularly children, may be asymptomatic. Others may deny symptoms due to cultural issues, fears or other concerns.

Symptoms of pulmonary tuberculosis are often indolent and include malaise, weight loss, night sweats, cough, pleuritic chest pain, fever, and hemoptysis. Symptoms of extrapulmonary disease generally reflect the organ involved (e.g., abdominal pain with gastrointestinal TB). Although extrapulmonary TB can be found in virtually any organ of the body, statistically, lymphadenopathy is the most commonly identified extrapulmonary manifestation. Symptoms may also be nonspecific, such as failure to thrive in children.

All predeparture medical records for the refugee should be closely reviewed. A thorough medical history must be obtained. In addition to current signs or symptoms of disease (e.g., weight loss, night sweats, fever, cough), specific information may be helpful in identifying a person at higher risk of tuberculosis disease or latent tuberculosis infection:

- Previous history of TB
- Illness suggestive of TB (i.e., cough > 3 weeks, dyspnea, weight loss, fever, night sweats or hemoptysis)
- Prior treatment suggestive of TB treatment
- Prior diagnostic evaluation suggestive of TB
- Family or household contact with a person who currently has or had TB disease, treatment, or diagnostic evaluation suggestive of TB

In addition, in children, a history of recurrent pneumonias, failure to thrive, or recurrent or persistent fevers should increase the provider's index of suspicion. Providers should keep in mind that children experience higher rates of extrapulmonary TB disease, including meningitis, and disease of the middle ear and mastoid, lymph nodes, bones, joints, and skin.

The physical examination should include height, weight, temperature, respiratory rate, blood pressure, thorough pulmonary examination, and inspection and palpation of all major palpable lymph node beds (see history and physical examination guidance document: www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/guidelines-history-physical.html). In addition, a careful skin examination is important, as it may reveal cutaneous disease, scars from scrofula or bacille Calmette-Guérin (BCG) vaccination, or hints of prior chest surgery that may alert the clinician.

Testing Newly Arrived Refugees for Tuberculosis Infection and Disease

Screening tests

Screening can be performed by using one of two modalities: the Mantoux tuberculin skin test (TST) or an interferon-gamma release assay (IGRA) for *Mycobacterium tuberculosis* (Figure 1). Currently, the QuantiFERON®-TB Gold In-tube Test (QFT-G) and T-Spot are two approved IGRAs in the United States. Either the TST or an IGRA should be performed during the domestic refugee medical screening examination, unless overseas testing results are available. There is no reason to repeat a TST if a documented previous positive TST result is available. The TST should be repeated if no documentation of a result (in mm induration) is available; however, if the refugee reports a history of a previous severe reaction to a TST (e.g. blistering, ulceration), repeating the TST is contraindicated.

Skin testing:

Interpreting the results of the TST depends on the patient's risk factors (Table 2). In otherwise healthy refugees from areas of the world where TB is common, $\geq$ 10-mm induration is considered positive. A cutoff of $\geq$ 5-mm induration is considered positive in persons with HIV infection, those with recent close contact with a known case of infectious TB, persons with fibrotic changes in chest radiogram consistent with prior TB, persons with organ transplants, and other immunosuppressed persons. Many refugees from TB-endemic areas will have been vaccinated against TB with BCG vaccine. Although previous BCG may influence the results of the TST, especially in infants, a history of vaccination with BCG should not influence interpretation of the TST. The clinician must provide a thorough explanation to the patient of the reasons for not considering the BCG in the interpretation of the test. A positive result by TST demands further evaluation to exclude TB disease (Figure 1).

TST testing can be performed in all persons, including children and pregnant women. False-negative results may be more frequent in young children and in persons with a compromised immune system. False negatives also may occur more commonly in persons at high-risk for TB (a high pre-test probability). A TST should be administered and read by a trained health-care provider. For additional information about performing a TST, visit www.cdc.gov/tb/pubs/tbfactsheets/skintesting.pdf.

IGRA:

The interferon-gamma release assays (IGRAs) utilize *M. tuberculosis* complex-specific antigens to stimulate patient T- lymphocytes. Importantly, IGRAs do not cross react with antigens related to the *M. tuberculosis* BCG. Sensitized cells, in someone previously exposed to M. tuberculosis, will produce the cytokine interferon (IFN)-γ. The QFT-Gold test and third-generation QFTgold in-tube test (Cellestis, Victoria, Australia) are based on the quantification of IFN-γ produced by T-lymphocytes in whole blood stimulated by *M. tuberculosis* complex-specific antigens (e.g. ESAT-6, CFP-10 and TB7.7). The T-Spot TB Test (Oxford Immunotec, Marlborough, MA) measures the number of T-lymphocytes producing IFN-γ when stimulated by *M. tuberculosis* complex-specific antigens. IGRAs are being increasingly used by physicians and health departments for evaluation of tuberculosis infection. Clinicians should perform and interpret these tests as recommended in national guidelines (5). It should be noted that

these tests are currently not recommended in those < 5 years of age (5). A positive result by an IGRA (indicating infection with the TB mycobacterium) demands further evaluation to exclude TB disease (Figure 2).

Diagnostic evaluation

Chest Radiography: A chest radiograph should be performed for all refugees with a positive TST or IGRA test, either prior to immigration or on domestic refugee medical screening; a previous history of tuberculosis disease, including those with a Class A or B TB designation from an overseas examination; or symptoms consistent with TB disease, regardless of TST or IGRA results. A negative TST and/or IGRA does not eliminate TB disease from the differential diagnosis of a symptomatic patient. Pregnant women with a positive TST or IGRA should have a shielded chest radiograph. If the pregnant woman is asymptomatic and in the first trimester of pregnancy, the chest radiograph may be postponed until the second trimester. A posterior-anterior (PA) radiogram should be performed. In addition to the PA, a lateral radiograph is recommended in young children less than 11 years of age, since one of the most common findings is hilar adenopathy, which is poorly visualized on a PA film.

Specimen collection and mycobacterial culture: In the event that a refugee is symptomatic and/or has chest radiogram findings or physical findings (such as lymphadenopathy) suggestive of TB disease, attempts should be made to collect specimens for acid-fast smear (AFB) and mycobacterial culture. If pulmonary disease is suspected, three sputum samples should be collected at least 8-24 hours apart, with at least one being an early morning specimen. In addition, current CDC guidelines recommend nucleic acid amplification testing be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities (6). Sputa should be induced in persons unable to expectorate spontaneously. Specimens should be collected in either a well-ventilated area or a sputum collection booth or room with negative pressure. Collection of early morning specimens is preferred because of the overnight accumulation of secretions. Sputum should be collected under direct observation. This is to ensure that the patient is being properly coached and is giving a good coughing effort, as well as to ensure that uncooperative patients are producing their own sputum for examination. Children are often unable to expectorate voluntarily, so gastric aspirates or hypertonic saline-induced sputum may need to be obtained in lieu of a standard sputum sample. Children frequently must be hospitalized to collect adequate samples. Since diagnosis and management of children can be very challenging, consultation with an experienced and knowledgeable expert in pediatric TB is encouraged.

In the setting of suspected extrapulmonary disease, consideration should be given to obtaining one or more specimens of body fluid or tissue of the suspected site of disease if this can be done with an acceptable risk of complications. In general if there are multiple options for obtaining a specimen, the least invasive method should be used first (e.g., obtain urine before performing a renal biopsy).. Because of the increased risk for drug-

resistant TB among many refugees, strong efforts should be made to obtain adequate specimens for AFB culture, so that drug-susceptibility testing may be performed. At least one culture-positive specimen from each patient should have conventional drug-susceptibility testing. Rapid drug-susceptibility testing of positive culture isolates can be obtained from CDC after consultation with the state health department and may be particularly useful in some circumstances (e.g. suspect MDR, or history of previous treatment). In addition, some state health department laboratories offer rapid drug-susceptibility testing of direct specimens from patients who are at high risk for drug resistance.

Summary of diagnostic classifications

Diagnosis is based on the results of the clinical evaluation, chest radiograph, screening tests, and overseas exam. All refugees will meet one of the following categories.

Latent TB infection, no disease

Asymptomatic refugee with a positive TST or QFT-G and a negative chest radiograph and physical examination. Refugee should be offered treatment for LTBI if not previously treated for TB disease or LTBI and no contraindications to LTBI treatment. CDC guidelines for LTBI treatment and monitoring should be followed (7).

TB, not clinically active:

- *Old, healed, not previously treated TB*
  Asymptomatic refugee with a chest radiograph that indicates old, healed, no TB disease (stable chest radiogram) and no history of having received previous TB treatment. Refugee should be offered treatment for LTBI as above.
- *Old, healed, previously treated TB*
  A refugee with no current clinical symptoms who has a chest radiograph that has findings consistent with old/healed TB who has a documented history of receiving treatment for TB in accordance with current ATS/IDSA/CDC guidelines. No treatment needed.

Suspect or Confirmed TB disease

Screening results indicate suspected or confirmed TB disease. The results may include a combination of a positive TST or QFT-G, abnormal chest radiograph or CT scan, pathology findings consistent with TB disease (e.g., caseating granuloma), signs and symptoms consistent with either pulmonary or extrapulmonary disease, and sputum or tissue smear positive for AFB or a culture positive for *M. tuberculosis*. Immediate follow-up is needed for

definitive diagnosis and treatment. All suspect or confirmed cases (pulmonary or extrapulmonary) should be reported to the local health authorities within 24 hours of determination so that appropriate public health measures can be implemented. Cases of suspect TB disease should be reported promptly—do not wait for culture confirmation to report suspected TB disease. When pulmonary or laryngeal TB is suspected, the patient should be isolated in an appropriate setting to prevent spread of infection until the infectious potential is evaluated.

Overview of Treatment

All treatment should be administered in accordance with the ATS/CDC/IDSA guidelines for treatment of TB:
www.cdc.gov/nchstp/tb/pubs/mmwrhtml/Maj_guide/Treatment.htm.

Latent Tuberculosis Infection (LTBI)

Standard treatment for latent TB consists of oral isoniazid (INH) for 9 months for all ages. If INH is contraindicated alternative regimens are available at http://www.cdc.gov/tb/publications/LTBI/treatment.htm. When utilizing INH, unless the patient has underlying medical conditions increasing the risk of liver problems, there is no need to check baseline liver function tests (LFT's). However, baseline laboratory testing in patients whose initial evaluation suggests a liver disorder is indicated. Baseline hepatic measurements include serum aspartate aminotransferase (serum glutamic oxaloacetic transaminase) (AST [SGOT]) or alanine aminotransferase (serum glutamic pyruvic transaminase) (AST [SGPT]) and bilirubin. Baseline testing is also indicated for patients with HIV infection, pregnant women, and women in the immediate postpartum period (i.e., within 3 months of delivery), persons with chronic liver disease (e.g. hepatitis B of C, alcoholic hepatitis, or cirrhosis), persons who use alcohol regularly, and persons at risk for chronic liver disease. For patients who do need liver testing, treatment should be discontinued if a) liver function tests rise to 3 times the upper limit of normal if there are signs and symptoms of hepatitis, or b) if LFTs rise to 5 times the upper limit of normal if asymptomatic. DOT may be prudent for children less than 5 years of age who are close contacts of persons with TB disease. For dosing and monitoring guidelines, please see the national LTBI treatment guidelines at
www.cdc.gov/mmwr/PDF/rr/rr4906.pdf and for special considerations see www.cdc.gov/tb/publications/LTBI/treatment.htm.

Tuberculosis Disease

National treatment guidelines state that a provider undertaking to treat a patient with TB disease is assuming a public health function that includes not only prescribing an appropriate regimen but also ensuring adherence to the regimen until treatment is completed. TB disease should be treated in consultation with the public health department and a medical expert in the treatment of TB. All patients with TB disease should receive therapy under DOT.

References

1. Centers for Disease Control and Prevention. Trends in tuberculosis. Morbid Mortal Wkly Rep 2008;57(11):281-285.
2. Oeltmann JE, Varma JK, Ortega L, et al. Multidrug-resistant tuberculosis outbreak among US-bound Hmong refugees, Thailand, 2005. Emerg Infect Dis 2008;14(11). Electronic version, accessed Nov. 10, 2008: www.cdc.gov/eid/content/14/11/1715.htm.
3. Lillebaek T, Andersen AB, Dirksen A, et al. Persistent high incidence of tuberculosis in immigrants in a low-incidence country. Emerg Infect Dis 2002;8(7):679-684.
4. Centers for Disease Control and Prevention. Notice to readers: revised technical instructions for tuberculosis screening and treatment for panel physicians. Morbid Mortal Wkly Rep 2008; 57(11):292-3.
5. Mazurek GH, Jereb J, Vernon A, et al. Updated guidelines for using the interferon gamma release assays to Mycobacterium tuberculosis infection—United States, 2010. Morb Mortal Wkly Rep 2010;59(5):1-25.
6. CDC. Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. Morb Mortal Wkly Rep 2009;58(1):7-10.
7. CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. ATS/CDC Statement Committee on Latent Tuberculosis Infection. Recommendations and Reports. Morb Mortal Wkly Rep 2000;49(6):1-54.

Table 1. Comparison of 2007 Technical Instructions for Tuberculosis Screening and Treatment with 1991 Technical Instructions

Category	1991	2007
Validity of tuberculosis screening examination	12 months if normal; 6 months if Class A condition or Class B1 or B2 TB condition	6 months if no tuberculosis classification or only Class B2 TB or Class B3 TB. 3 months if Class B1 TB, Pulmonary or Class B1 TB, Extrapulmonary or for applicants who have HIV infection.
Tuberculosis history	Required	Required
Physical examination	Required	Required
CXR	Persons ≥15 years: PA; Persons <15 years: PA and lateral views in specific circumstances	PA required for all applicants ≥15 years. Applicants <15 years receive CXR if they have a TST ≥5 mm (when required based on estimated tuberculosis incidence rate in country of origin) or have signs and symptoms suggestive of tuberculosis, but see 42 CFR 34.3 (b)(v).
TST	Not routine; used infrequently in specific circumstances	All applicants 2-14 years of age living in countries with a WHO-estimated incidence rate ≥20 per 100,000. All applicants who are contacts of a known tuberculosis case.
Tuberculosis laboratory screening	Persons >15 years with CXR and/or symptoms suggestive of active disease (or children <15 years of age who are contacts, have history of tuberculosis disease, or signs or symptoms): AFB smears x 3	Persons with tuberculosis symptoms, abnormal physical examination, or CXR suggestive of tuberculosis disease, or who are HIV positive: sputum for AFB smear x 3 plus tuberculosis cultures and DST (for persons who cannot produce sputum: specimen collection by other means such as induced

		sputum or gastric aspirates).
Initial patient management prior to laboratory results	Not applicable	Consider treatment for other lower respiratory infection (no fluoroquinolones) if applicable; follow-up CXR for immigration medical screening not to be performed until 8 weeks after treatment.
Management of persons with positive TST	Not applicable	Applicants 2-14 years of age or contacts who have a TST ≥10 mm but who otherwise have a negative evaluation for tuberculosis will be classified for U.S. follow-up as Class B2 TB, LTBI Evaluation, with TST results and treatment status documented.
Tuberculosis treatment and management	Tuberculosis treatment guidance outdated, and minimal guidance for drug-resistant tuberculosis	Treating physicians should follow ATS/CDC/IDSA guidelines. For drug-resistant patients, treating physicians refer also to written guidance from the Francis J. Curry National Tuberculosis Center and California Department of Health Services, 2004: Drug-Resistant Tuberculosis: A Survival Guide for Clinicians; MDR TB expert consultations and CDC consultations recommended. Treatment of drug-resistant and MDR TB should be done by or in close consultation with experts in the management of such cases and in coordination with the Division of Global Migration and Quarantine (DGMQ).
Category	**1991**	**2007**
Sources of tuberculosis drugs	Source not specified	Quality-assured drugs: WHO Global Drug Facility for first-line drugs and International Dispensary Association and WHO Green Light Committee for second-line drugs.
Laboratory monitoring during tuberculosis treatment	No monitoring after AFB smear becomes negative	Drug susceptible, drug resistant (but not MDR) TB: two sputum specimens should be collected and submitted for AFB microscopy and mycobacteria culture each month of therapy until cultures are negative for 2 consecutive months. MDR TB: two sputum specimens should be collected and submitted for AFB microscopy and mycobacteria culture each month of therapy. No drug-susceptibility testing results (culture negative): one sputum specimen should be collected and submitted for AFB microscopy and mycobacteria culture each month of therapy.
Laboratory monitoring after tuberculosis treatment	Not applicable	All applicants to have two sputum specimens collected and submitted for AFB microscopy and mycobacteria culture at the end of therapy.
Management of known tuberculosis contacts	Not applicable	All contacts should have a TST. If the TST is ≥5 mm (or ≥10 mm in foreign-born persons from high-prevalence countries), the contact should be further evaluated with medical

		history, physical examination, and CXR. If the contact is not started on LTBI therapy, he or she should receive an evaluation with medical history, physical examination, and CXR every 3 months until departure. If the TST is <5 mm and the contact is not placed on prophylaxis, the TST should be repeated every 3 months until ≥8 weeks after contact ends, the index case has negative sputum cultures for 2 consecutive months, or TST becomes ≥5 mm. Children <4 years of age and applicants with impaired immunity who are contacts of a known tuberculosis case (that is not isoniazid resistant) and who have a negative evaluation for tuberculosis disease, should begin DOPT. Preventive therapy should be discontinued if TST is <5 mm 8 weeks after conclusion of exposure to the infectious case. Contacts cleared for travel should receive a Class B3 TB, Contact Evaluation classification.

Category	1991	2007
Pre-departure clearance examination	Not applicable	Additional screening immediately prior to departure (pre-departure evaluation) may be required in the event of an outbreak of tuberculosis disease or in the setting of extremely elevated rates of tuberculosis disease. When required, pre-departure screening would occur within 3 weeks of departure for all applicants with findings suggestive of tuberculosis disease on medical history, physical examination, or CXR but had negative sputum smears and negative cultures. Pre-departure screening would consist of medical history, physical exam, CXR, and at least 3 sputum smears for AFB microscopy (cultures not required).
Information transfer to CDC and state and local public health	Paper: DS medical forms travel with refugees and are processed at port of entry	Paper: DS medical forms and additional information on tuberculosis treatment travel with applicants and are processed at port of entry. Electronic data transfer of DS medical forms, including tuberculosis screening, diagnosis and treatment, when available. Class A and B1 cases reported to U.S. Embassy upon detection.

Category	1991	2007
Tuberculosis Classifications		
No TB Classification	Applicants with normal tuberculosis screening examinations	Applicants with normal tuberculosis screening examinations
Class A	"Tuberculosis, infectious." Abnormal CXR and one or more positive sputum smears.	Applicants who have tuberculosis disease diagnosed (sputum smear positive or culture positive) and require treatment overseas but who have been granted a waiver to travel prior to the completion of therapy.
Class B1 - Pulmonary	"Tuberculosis clinically active, not infectious." Abnormal CXR and sputum smears negative	No treatment: Applicants who have medical history, physical exam, or CXR findings suggestive of pulmonary tuberculosis but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis or can wait to have tuberculosis treatment started after immigration. Completed treatment: Applicants who were diagnosed with pulmonary tuberculosis and successfully completed DOT prior to immigration
Class B1 - Extrapulmonary	"Extrapulmonary tuberculosis, clinically active, not infectious." Radiographic or other evidence of extrapulmonary tuberculosis, clinically active	Evidence of extrapulmonary tuberculosis

Class B2	"Tuberculosis, not clinically active." Abnormal CXR suggestive of tuberculosis, not clinically active. No sputum smears required.	**LTBI Evaluation.** Applicants who have a tuberculin skin test ≥10 mm but who otherwise have a negative evaluation for tuberculosis.
Class B3	"Consistent with tuberculosis, old or healed." Abnormal CXR; only abnormality is calcified hilar lymph node, primary complex, or granuloma. No sputum smears required.	**Contact Evaluation.** Applicants who are a contact of a known tuberculosis case.

* AFB, acid-fast bacilli; ATS, American Thoracic Society; CXR, Chest radiograph; DGMQ; Division of Global Migration and Quarantine; DOPT, directly observed preventive therapy; DS, Department of State; DST, drug-sensitivity testing; HIV, human immunodeficiency virus; IDSA; Infectious Diseases Society of America; LTBI, latent tuberculosis infection; MDR TB; multidrug-resistant tuberculosis; PA, posterior-anterior; TST, Tuberculin Skin Test; WHO, World Health Organization

Table 2: TST Testing Interpretation Guidelines for Refugees

Induration of $\geq$ **5 mm** is considered positive in - refugees with HIV - refugees known to have been recently in close contact with someone with infectious TB - refugees with changes on chest X-ray consistent with prior TB - refugees with organ transplants and other immunosuppressed patients Induration of $\geq$ 10 mm is considered positive - all other refugees

Sources of Additional Information: Additional information regarding screening of refugees for tuberculosis and other infectious diseases can be obtain by visiting the CDC website at http://www.cdc.gov/ncidod/dq/panel.htm and http://www.cdc.gov/ncidod/dq/health.htm or at the WHO website at http://www.who.int/tb/surveillanceworkshop/

Appendix A: Summary of Primary Pulmonary and Reactivation Tuberculosis

Primary pulmonary tuberculosis: Adults with primary pulmonary TB classically present with fever, extensive pulmonary infiltrates, and hypoxia. This presentation should be uncommon during the domestic refugee medical screening examination, since the overseas medical examination should prevent those with TB disease from traveling. However, children and immunocompromised hosts may not have these classic symptoms or radiograph findings of TB. Therefore, special attention should be paid when evaluating these populations. Children, in particular, may have very subtle findings on chest radiogram and may be asymptomatic despite having TB disease. They may also present with such symptoms as malaise, failure to thrive or weight loss, or a history of recurrent pneumonias.

Reactivation TB (post-primary tuberculosis): Reactivation of tuberculosis is the clinical scenario most likely to be encountered during a refugee screening exam. Reactivation disease often manifests years after initial infection and may either be pulmonary or extrapulmonary. Progression from TB infection to disease is more likely to occur in older persons or those with comorbid conditions, including malnutrition, immunocompromised states (HIV, malignancy, diabetes mellitus, immunosuppresent medications), substance abuse and in those who smoke tobacco. Other factors common in refugees that may increase the risk of reactivation include stress (e.g., stress of immigration) and vitamin D deficiency.

Glossary of Abbreviations

ATS	American Thoracic Society
BCG	bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention, United States
CXR	Chest radiograph
DGMQ	Division of Global Migration and Quarantine
DOT	Directly observed therapy
DTBE	Division of Tuberculosis Elimination
FDA	U.S. Food and Drug Administration
EDN	Electronic disease notification
HIV	Human immunodeficiency virus
IDSA	Infectious Diseases Society of America
IGRA	Interferon-gamma release assays
LTBI	Latent tuberculosis infection
MDR TB	Multidrug-resistant tuberculosis
PPD	Purified protein derivative
TB	Tuberculosis
TI	Technical instructions
TU	Tuberculin units
TST	Tuberculin skin test
QFT	Quantiferon test
WHO	World Health Organization