



CTCA

CALIFORNIA TUBERCULOSIS
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C T C A G U I D E L I N E S

***Guidelines for
Tuberculosis (TB) Screening and
Treatment of Patients with
Chronic Kidney Disease (CKD),
Patients Receiving Hemodialysis (HD),
Patients Receiving Peritoneal Dialysis (PD),
Patients Undergoing Renal Transplantation
and Employees of Dialysis Facilities***

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Introduction

Tuberculosis (TB) among patients with compromised kidney function is an important public health concern. Patients with chronic kidney disease (CKD) or end stage renal disease (ESRD) have immune dysfunction manifested by depressed cell-mediated immunity (CMI). This impairment of CMI makes infection with *M. tuberculosis* (*M.tb*) more difficult to detect and more likely to progress to TB disease than in immune competent individuals. Multiple studies have demonstrated cutaneous anergy rates of 30 to 80% in patients with ESRD. The lack of reactivity is at least as severe as that reported in HIV disease. The medical literature states that the risk of active TB in hemodialysis (HD) patients is 7-52 times higher than in the general population. HD units located in countries with high background TB prevalence have reported that up to 23% of their HD populations eventually develop active TB. While the U.S. has low TB prevalence overall, a large and increasing proportion of patients in HD units emigrated from countries with high rates of TB infection, with TB disease rates reflecting their countries of origin. Studies of dialysis patients in New Jersey and California showed TB rates 6-11 times greater than the overall population. Further complicating detection and treatment, only a minority of ESRD patients with active TB will present with typical pulmonary disease; they may often have extrapulmonary disease or an atypical pulmonary presentation. TB patients with ESRD are also more likely to die than other TB patients.

Many patients with CKD have additional risk factors for progression to active TB disease. In this patient population, the most prevalent risk factor is diabetes, but the use of immunosuppressive drugs to treat rheumatologic disorders and to maintain kidney transplants is also common.

Most data on impairment of CMI are from patients in CKD stage 5 (GFR < 15 ml/min) or stage 6 (ESRD on dialysis). Many of the non-immune manifestations of nephron loss, such as anemia and hyperparathyroidism, become clinically apparent by the time a patient reaches CKD stage 4 (GFR < 30 ml/min). Although little specific information is available in the medical literature, it is reasonable to assume that impairment of CMI likewise progresses as a patient's kidney function worsens. Since screening tests for TB depend on CMI, early testing is less likely to be affected by anergy. Thus, baseline screening ideally should be accomplished before the patient reaches CKD stage 4, with GFR above 29 ml/min.

Prevention of progression to active TB among those patients with latent TB infection (LTBI) and early detection of active TB disease are a high priority because of the grave consequences of active TB in a congregate dialysis setting and the difficulty in treating TB in CKD patients. Therefore, all patients who are known to have advanced CKD, those who are on dialysis, and those with a transplant should be screened for TB. This screening should ideally occur at the time of diagnosis of CKD, prior to entering a HD unit where there is potential for transmission among other immunocompromised patients, and/or prior to receiving iatrogenic immunosuppression.

These guidelines will refer to the five stages of chronic kidney disease (CKD) as recommended by the Kidney Disease Outcome Quality Initiative (KDOQI) of the National Kidney Foundation (see table 1 below). However, it is impossible to avoid completely the use of prevalent and historically-entrenched terminology such as end stage renal disease (ESRD).

TABLE 1: STAGES OF CHRONIC KIDNEY DISEASE

Stage	Description	GFR (mL/min/1.73m ²)	ICD-9-CM Code
1	Kidney damage with normal or increased GFR	≥90	585.1
2	Kidney damage with mild decrease in GFR	60–89	585.2
3	Moderate decrease in GFR	30–59	585.3
4	Severe decrease in GFR	15–29	585.4
5	Kidney failure	<15	585.5
6	End stage renal disease, on dialysis	-----	585.6

Note: Stages 1-5 are derived from *K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification*. Am J Kidney Dis 39:S1-S000, 2002 (suppl 1). Stage 6 is not part of the original KDOQI™ classification. It was separated from Stage 5 for administrative purposes with revision of the ICD-9-CM in 2005.

These guidelines provide recommendations for TB screening and treatment of patients with CKD and of employees in the dialysis unit setting. Recommendations are made for patients at the time of diagnosis of CKD, at the initiation of dialysis, annually during established dialysis and prior to renal transplantation.

Local health department (LHD) TB program staff members are encouraged to form liaisons with, and provide expert consultation to, those personnel in dialysis facilities responsible for infection control.

Part I of these guidelines provides recommendations for TB screening of patients with CKD when first diagnosed, at initiation of dialysis, during established dialysis (periodic screening) and prior to renal transplant. **Part II** provides recommendations for diagnosis and treatment of LTBI in patients with CKD and/or those receiving dialysis. **Part III** provides recommendations for diagnosis and treatment of active TB in patients with CKD and/or those receiving dialysis. **Part IV** of these guidelines provides requirements for reporting active TB disease in patients with CKD. **Part V** defines the role of the LHD in the care of these complicated patients. **Part VI** provides recommendations for TB screening of employees of dialysis units.

What is TB? (See Appendix H for a glossary of terms)

In TB disease, living TB bacteria are present in the body and the disease is clinically active. Bacilli from TB disease of the lungs or larynx can be transmitted when a person with the disease coughs, sings, laughs, speaks, or breathes. Persons with TB disease have symptoms and often have a positive tuberculin skin test (TST). The symptoms of TB disease include, but may not be limited to the following:

- Persistent cough, generally productive, lasting 3 weeks or longer
- Fever
- Night sweats
- Fatigue or weakness
- Unexplained weight loss and/or loss of appetite
- Hemoptysis (coughing up blood)

TB disease should be considered in a patient with a diagnosis of recurrent pneumonia, or a pneumonia that does not improve within 2 weeks after antibiotic therapy is initiated.

If a person has latent TB infection (LTBI), living tubercle bacilli are present in the body without clinical disease. TB infection without TB disease cannot be transmitted. Persons with LTBI have no symptoms of TB disease, but do generally have a positive TST or QuantiFERON® (QFT); (see below); however, patients with CKD or ESRD often have false negative TST or indeterminate QFTs due to anergy.

Chronic Kidney Disease (CKD) greatly increases the risk of progression to TB disease in those with latent TB infection (LTBI).

For years the TST has been the basic screening test for TB infection. It involves the intradermal injection of a purified protein derivative (PPD) containing tuberculosis antigens, which generates a cell-mediated delayed sensitivity response. Limitations of the TST include the need to measure the response 48-72 hours after, and inaccuracies and errors in both placement and measurement. The QuantiFERON®-TB test, a whole blood interferon gamma release assay (IGRA) test for TB infection, has been licensed since 2001. The second generation test, QuantiFERON®-TB Gold (hereafter referred to as "QFT") was licensed in 2005 and is

currently the only FDA-approved TB interferon gamma release assay available in the US. Advantages over the TST include the need for just a single visit, elimination of reader inaccuracies, and elimination of false positive results due to BCG. Limitations of the QFT include the need to draw blood and process it within 12 hours after collection, and limited (as of 2006) laboratory and clinical experience with the test. Guidelines for using the test are available from the CDC (MMWR, 12/16/05/Vol 54/No. RR-15). Use of the QFT for screening employees would require a grant of Program Flexibility from Licensing and Certification (L&C), since the use of only the TST is currently required by regulation (CCR 22 72535). Use of the QFT for screening patients on admission to HD units requires approval of the patient care policy committee of the unit, while subsequent TB screening procedures are determined by the attending physician (CCR 22 52523 (c) (2) (C)).

Part I

Recommendations for TB Screening for Patients at Diagnosis of CKD, Patients Receiving HD and Patients Undergoing Renal Transplantation

1.1 Baseline screening (or upon admission) and periodic screening

Patients with ESRD should have baseline TB screening performed. TB screening should also be performed at least annually. The table below summarizes the minimum baseline and annual screening recommendations for these patients. Following the table is a detailed description about each of the TB screening tests.

**TABLE 2:
RECOMMENDATIONS FOR TUBERCULOSIS SCREENING OF
PATIENTS WITH END STAGE RENAL DISEASE**

POPULATION		TB SYMPTOM REVIEW ¹	CXR	TST/QFT
CKD Stages 3-5	No Hx of or Neg TST or QFT	At diagnosis	At diagnosis	At diagnosis
	Hx Pos TST or QFT in past	At diagnosis	At diagnosis	Not indicated
Transplant Candidate	No Hx of or Neg TST or QFT	Within 30 days prior to transplant ²	Within 30 days prior to transplant ²	Within 30 days prior to transplant ²
	Hx Pos TST or QFT in past	Within 30 days prior to transplant ²	Within 30 days prior to transplant ²	Not indicated
Initiation of dialysis	No Hx of or Neg TST or QFT	Within 30 days prior ²	Within 30 days prior ²	Within 30 days prior ²
	Hx Pos TST or QFT in past	Within 30 days prior ²	Within 30 days prior ²	Not indicated
Established dialysis or post-transplant	No Hx of or Neg TST or QFT	Annual ³	Annual ³	Annual ³
	Hx Pos TST or QFT in past	Annual ³	Annual ³	Not indicated

1. Screen for TB symptoms using the TB Risk Assessment Questionnaire (RAQ) in Appendix B
2. Or within 5-7 days after emergent initiation of dialysis or unscheduled transplantation
3. More frequent testing may be necessary if TST or QFT conversions are observed in patients or employees or a known exposure to an infectious TB patient has occurred. They should also be reminded to report any symptoms suggestive of TB developing between screenings (See 1.1.1 TB symptom screen).

1.1.1 TB Symptom Screen

For each patient, at the time of diagnosis of CKD, at the time of initial admission to the dialysis unit, and prior to scheduled renal transplantation, the dialysis center staff or other healthcare provider should administer the TB RAQ, document responses and, if symptomatic, ensure follow-up by the medical provider. The purpose of this screening process is to detect TB symptoms such as:

- Persistent cough, generally productive, lasting 3 weeks or longer
- Fever
- Night sweats
- Fatigue or weakness
- Unexplained weight loss and/or loss of appetite
- Hemoptysis (coughing up blood)

In most published series, fever, weight loss and malaise are the most common symptoms of active TB in patients with renal insufficiency. Cough may also be present.

Symptomatic Patients

All patients who have symptoms suggestive of active TB should be evaluated as described in the section below (3.1: Patients with CKD Suspected of having Active TB). Patients suspected of having TB disease need to be reported to the LHD within one working day (California Code of Regulations Title 17, Section 2500 (b)).

1.1.2 Tuberculin Skin Test (Mantoux Tuberculin Skin Test) or QFT

a. No Documented or Documented Negative TST/QFT

All patients who have written documentation of a prior negative TST or have unknown or undocumented previous TST/QFT results should be screened with a two-step TST or single QFT at the time of diagnosis of CKD, within 30 days prior to admission into HD unit (or within 5-7 days after initiating HD in emergent situations) or within 30 days prior to undergoing scheduled renal transplantation. A TST should consist of 0.1 ml of 5TU purified protein derivative (PPD) given intradermally onto the dorsal or volar surface of the forearm. The TST should be placed by a licensed healthcare professional specifically trained to apply and interpret the result. Skin test results should be read in 48-72 hours, and recorded in millimeters (mm) of induration. The TST is considered positive in dialysis populations when the area of induration at 48-72 hours \geq 10mm. However, in higher risk populations including HIV patients, people with solid organ transplants, and patients with recent TB exposure, 5 mm is used as the cut-off point. While 15 mm of induration is considered positive in normal, healthy people in other areas of the country, due to the high incidence of TB and low incidence of nontuberculous mycobacterial infection in California, the 15 mm cutoff is not used in California. Patients may not read their own TST results.

A QFT is performed on 5-10 ccs of whole blood drawn into a lithium heparin tube; blood draw should occur before dialysis starts to avoid excess heparinization of blood. If an indeterminate result occurs, QFT should be repeated, but if a second indeterminate result is obtained, then skin testing should be performed.

b. Two-Step Testing

Two-step, or boosted, testing is used to detect individuals with TB infection acquired in the remote past who may now have diminished TST reactivity. This procedure reduces the likelihood that a boosted reaction will later be interpreted as new infection in patients who are periodically tested. Two step testing is not necessary if QFT is used.

- Two-step testing should be performed on all newly identified CKD patients who do not have written documentation of a negative TST in the preceding 12 months and have an initial negative TST result at the time of screening.
- The second TST is placed 1-3 weeks after the initial test.
- Asymptomatic patients with a positive (boosted) reaction to the second TST are considered previously infected. The patient should have a good quality posterior-anterior (PA) chest radiograph (CXR). If the symptom review is positive or the chest radiograph is abnormal and not definitely related to a non-TB etiology, further investigation to rule out TB disease should be pursued; refer to the section below (3.1: Patients with CKD Suspected of having Active TB). If the symptom review is negative, and the CXR normal or not indicative of TB, please refer to the section below (LTBI Treatment Regimens 2.2).

c. New and Prior Documented Positive TST or QFT

Patients with a newly documented positive TST or QFT or prior documented positive TST or QFT should have a TB symptom review using the TB RAQ and a good quality PA chest radiograph. If the symptom review is positive and/or the chest-radiograph is abnormal and not definitely related to a non-TB etiology, further investigation to rule out TB disease should be pursued; refer to the section below (3.1: Patients with CKD Suspected of having Active TB). If the symptom review is negative and the chest-radiograph normal, or not indicative of TB, refer to the section (LTBI Treatment Regimens 2.2).

If the patient has had a recent chest radiograph within 30 days prior to initiation of dialysis or scheduled renal transplantation, this chest radiograph can be used for screening unless new TB symptoms have developed in the interim period from the date of the chest film.

Due to the increased possibility of false negative TSTs in the population, CXR & symptom screening are important parts of the initial TB evaluation.

d. Anergy Testing

There are currently no indications for anergy testing during the assessment of LTBI. The interpretation of the controls in the anergy panel is not standardized and the results can be misleading.

e. BCG Vaccination

A history of previous vaccination with Bacillus of Calmette-Guerin (BCG) is not a contraindication for placement of a TST or QFT. All patients with a history of BCG vaccination should still have a TST or QFT according to the above criteria. Criteria for interpreting TST results are the same. QFT may be more specific for TB infection in that it is not affected by prior BCG vaccination, as the TST might be.

1.1.3 Chest-radiographs

In addition to a TB symptom review and a TST or QFT (if indicated), all patients should have a good-quality PA chest radiograph within 30 days prior to scheduled renal transplantation or initiation of dialysis given the increased possibility of false negative TSTs in this population. A portable chest radiograph may not be of sufficient quality to exclude active TB. **If a patient is emergently dialyzed and continues dialysis thereafter, a chest radiograph, TST or QFT (if indicated), and a TB symptom review need to occur no later than 5-7 days after admission to the HD unit.** Chest-radiographs are often done for a variety of reasons in patients with chronic renal insufficiency and the results of these films should be reviewed periodically.

In general, the activity of TB infection cannot be determined with a single chest radiograph, but must be judged clinically, with follow-up chest-radiographs and microbiologic samples. Chest-radiographs should be classified as normal, abnormal or non-TB abnormality. A chest-radiograph report with the interpretation of “old” TB or “inactive” TB cannot be relied upon to exclude current active TB. All chest-radiograph findings that are abnormal and not definitely related to a non-TB etiology require further investigation to rule out TB disease. Chest-radiograph findings typically associated with active TB disease include upper lobe patchy or nodular infiltrates with or without cavitory lesions, hilar/paratracheal lymphadenopathy, and/or pleural effusions; however, patients who are immunocompromised may have infiltrates not typical of TB in any region of the lung. **It is important to have a low threshold for obtaining acid fast bacillus (AFB) sputum smears and cultures in this patient population to exclude the diagnosis of active TB.**

CKD patients with TB symptoms or abnormal CXR should have further evaluation for TB disease.

If the chest-radiograph is abnormal, three sputum samples for AFB smear and culture should be collected 24 hours apart (with at least one, if not all specimens being an early morning specimen). Sputa samples should be obtained via induction if the patient’s cough is nonproductive. Any additional appropriate specimens (e.g. fine needle aspirate, bronchoscopy, pleural tap and biopsy) needed to make a diagnosis of TB should also be obtained. Latent TB infection (LTBI) cannot be diagnosed until the results of these cultures are final and active TB has been excluded.

Delays in TB diagnosis in patients with CKD occur, for example, when it is assumed that pleural effusions reflect volume overload and/or under-dialysis. If a pleural effusion persists despite vigorous attempts to remove fluid by dialysis, the patient should undergo a diagnostic thoracentesis. If the effusion is found to be exudative and persistent, strong consideration should be given to obtaining a pleural biopsy (open or closed) because of the poor diagnostic yield of AFB cultures of pleural fluid. Pleural fluid and/or biopsy specimen should be sent for AFB smear as well as AFB culture and susceptibility testing. A nucleic acid amplification test (NAAT) of the pleural fluid may be helpful, but a negative NAAT does not exclude pleural TB. Patients with persistent pleural effusions should have sputum (induced, if necessary) sent for AFB smear and culture to exclude pulmonary TB.

1.2 Documentation

TST/QFT

TB screening results should be placed in the medical record and in a readily accessible log within the dialysis unit (this applies to all results including chest-radiograph findings, TSTs or QFT’s, RAQs upon admission and annually). A log is recommended to facilitate risk assessment of transmission of TB in the unit. A sample log is included in Appendix E. A two-step TST is not required for subsequent annual testing.

1.3 TST or QFT Conversion

A TST conversion is defined as an increase in the area of induration after PPD testing by at least 10 mm compared with prior negative testing done within the previous two years. However, among contacts, a TST conversion is defined as a change from negative to positive (induration less than 5 mm to induration ≥ 5 mm). QFT conversion is not well defined, but at this time is considered as a change from a negative to a positive result. Any patient with a TST or QFT conversion or newly positive TST or QFT result should have a chest-radiograph within 1 working day and should be referred as soon as possible for evaluation and management. If a patient is noted to be a TB skin test converter or QFT converter without evidence of active TB, they should be strongly urged to begin treatment of LTBI (see LTBI Treatment Regimens 2.2)

Part II

Recommendations for Diagnosis and Treatment of LTBI in patients with CKD and in patients receiving HD

2.1 Diagnosis of LTBI

Patients with a positive TST or QFT who are asymptomatic and have normal CXRs and physical examinations can be reasonably assumed to have LTBI and need no further evaluation. If a patient is suspected of having active TB either due to symptoms or an abnormal CXR, please refer to the following section (3.1: Patients with CKD Suspected of having Active TB). Once active TB has been excluded, if indicated, patients with a positive TST or QFT, without adequate prior treatment, should be urged to complete a course of treatment for LTBI (see MMWR 2004, 49: RR-6 for guidelines regarding treatment and monitoring of LTBI).

2.2 LTBI Treatment Regimens

HD and PD patients who are believed to have LTBI are considered at high risk of developing active TB, and should generally be treated. Options for treatment of LTBI are the following:

- Isoniazid (INH) 300 mg po daily for a period of 9 months (270 doses) (9 months is preferred to previously recommended 6 months, given immunocompromised state)
- INH 300 mg po daily and rifampin (RIF) 600 mg po daily for a period of 4 months (120 doses) in patients classified as TB4 (with radiographic evidence of old inactive TB, positive TST or QFT and active disease ruled out)
- RIF 600 mg po daily alone for a period of 4 months (120 doses) if intolerant to INH or if known contact to an INH-resistant case (not as well studied)

Two months of rifampin and pyrazinamide should not be used. An MMWR (MMWR 2001; 50, no. 34) recommended against this option for treatment of LTBI given the risk of hepatotoxicity associated with this regimen.

Both INH and RIF are primarily metabolized by the liver and are not dialyzed. They should both be given after HD on the day of HD. No dose adjustments are necessary in CKD. Patients on INH should also receive 25 mg of Vitamin B6 (in addition to the Vitamin B6 contained in renal vitamin preparations) given the higher incidence of neuropathy related to INH in patients with CKD and diabetes. In patients with CKD, doses of Vitamin B6 in excess of 50 mg po qd have the potential to cause a neuropathy.

Because of drug-drug interactions, RIF should be avoided when possible in patients with LTBI taking warfarin, cyclosporine, tacrolimus, sirolimus, digoxin and other drugs metabolized by the cytochrome P450 system. If RIF is the only alternative, then blood tests or drug levels need to be carefully monitored and drug doses adjusted as needed (see 3.3 Drug-Drug Interactions Specific for Patients with CKD).

2.3 Directly Observed Therapy (DOT)

DOT, the process by which a health care worker observes the patient swallowing anti-TB medications, should be considered for patients with CKD being treated for LTBI because of the increased risk of progression from inactive to active TB in this patient population. If resources are available for DOT, health department staff can administer medications (INH 900 mg PO twice or thrice weekly) post-dialysis; for assistance, contact your local health department. DOT may be administered by hemodialysis facility staff after coordination with local health department TB Program.

2.4 Monitoring of Patients During LTBI Treatment

Liver function tests should be monitored according to the CDC/ATS LTBI treatment guidelines established in 2000. However, the provider should take into account the increased incidence of chronic hepatitis B and C infection as well as increased use of hepatotoxic medications (i.e., HMG-CoA reductase inhibitors) in this population when deciding whether baseline LFTs are needed and on the frequency of monitoring for hepatotoxicity.

Every effort should be made to accurately document that the patient takes and completes therapy. Patients should be monitored monthly according to published guidelines.

If treatment of LTBI is self administered, the treating provider should give no more than a thirty-day supply of medication. Monthly monitoring for adherence, medication side effects and TB symptoms should be performed. In patients who have successfully completed LTBI treatment, continued yearly symptom screening, using the TB RAQ, is advised.

Part III

Recommendations for the diagnosis and treatment of active TB disease in patients receiving dialysis and in patients with CKD

3.1 Patients with CKD Suspected of having Active TB

Patients with CKD and a positive TST/QFT or symptoms suggestive of TB should be evaluated for the presence of active TB. If the chest-radiograph is abnormal and/or the patient is symptomatic, three sputum samples should be collected 24 hours apart (with at least one specimen being an early morning specimen) for AFB smear and culture (induced if necessary) and any additional appropriate specimens (e.g. fine needle aspirate, bronchoscopy, pleural tap and biopsy) needed to make a diagnosis of TB should be obtained. Strong consideration should be given to transferring HD patients to an airborne-infection isolation room (AIIR) for further dialysis during the evaluation if there is strong suspicion for active TB.

Patients with CKD on dialysis strongly suspected of having clinically active TB should be placed on standard anti-TB therapy until final cultures and susceptibility results are available and the clinical response to empiric therapy assessed. If a diagnosis of active TB is made, refer to the following section (Treatment Regimens, 3.1.1).

AFB smear positive patients should be dialyzed in AIIR until 3 criteria are met: 1) patient is on an appropriate TB medical regimen for a minimum of 14 days, 2) 3 consecutive sputa specimens are smear negative and 3) patient shows signs of clinical improvement

Strong consideration should be given to transferring HD patients to an airborne-infection isolation room (AIIR) for further dialysis during the evaluation if there is strong suspicion for active TB.

3.1.1 Treatment Regimens

All patients with CKD Stage 4 or 5 and drug-sensitive TB (sensitive to all first line anti-TB drugs), including those patients receiving dialysis, should be treated with the following directly observed regimens: (see MMWR 2003, 52: RR-11 for more information on treatment)

Initial Phase (First two months):

- INH 300 mg po daily, dosed **after HD in patients undergoing HD** (56 doses)
- RIF 600 mg po daily, dosed **after HD in patients undergoing HD** (56 doses)
- Ethambutol (EMB) 15 mg/kg po thrice weekly, dosed **after HD in patients undergoing HD** (24 doses)
- Pyrazinamide (PZA) 25 – 35 mg/kg po thrice weekly, dosed **after HD in patients undergoing HD** (24 doses)
- Vitamin B6 25, mg po qd or 50 mg po thrice weekly (24 doses)

Continuation Phase (months 3-6):

- If drug-sensitive disease, administer INH and RIF daily until completion of therapy for total of 6 months. (180 doses)
- If necessary, the entire regimen can be given thrice weekly after the first two weeks of therapy (14 doses):
 - INH 900 mg po thrice weekly **after HD in patients undergoing HD** (72 doses)
 - RIF 600 mg po thrice weekly **after HD in patients undergoing HD** (72 doses)
 - EMB 15 mg/kg po thrice weekly **after HD in patients undergoing HD** (number of doses will depend on drug susceptibility)
 - PZA 25 - 35 mg/kg po thrice weekly **after HD in patients undergoing HD** (number of doses will depend on drug susceptibility)
 - Vitamin B6, 25 mg po daily or 50 mg po thrice weekly

Medications for TB should be dosed after HD, and EMB & PZA require dose adjustments in CKD.

Both INH and RIF are primarily metabolized by the liver and are not dialyzed. No dose adjustments are necessary for INH and RIF in CKD. The effect of PD on the removal of anti-TB medications has not been studied in the same manner as the effect of HD. However, the above regimens have been used successfully in this population. Patients who are status post-renal transplant should be treated with a regimen tailored to their current CrCl. An actual CrCl may need to be measured as they may have reduced renal function at baseline and their creatinine may need to be monitored closely throughout treatment.

If drug-resistant TB or multi-drug resistant TB (MDR-TB) is suspected or confirmed, it is strongly recommended that the patient be managed by TB experts familiar with the treatment of MDR-TB, because of the complex treatment issues and the high risk for treatment failure with further acquired resistance. In the event that the treating physician is not an MDR-TB expert, consultation with an MDR-TB expert must be sought immediately after multi-drug resistance is known. It is strongly recommended that written consultation be provided to the treating physician and local health department (LHD) TB program.

In addition, it is legally mandated (California Code of Regulations Title 17, Section 2500) that the treating physician notify the LHD as well as the CDHS Licensing & Certification (L&C) district office within one working day of diagnosis of TB or initiation of treatment for suspected TB. The LHD TB program can discuss management, follow up and public health aspects of the case.

3.1.2 Clinical Management

Patients diagnosed with TB disease, whether culture positive or negative, should be treated as outlined above. Baseline laboratory studies, including a complete blood count (CBC), liver function tests (LFTs), hepatitis B and C serologies and an HIV antibody test should be a routine part of the initial evaluation of the patient. Ethambutol (EMB) can be discontinued as soon as the isolate is known to be drug-sensitive. All patients with CKD taking EMB should have monthly vision checks. EMB is not removed by HD and ocular toxicity, which can occur while on EMB, is dose dependent. Consideration should be given to monitoring ethambutol levels in all patients on ethambutol and HD or PD. If this is felt to be necessary, consult your local Public Health Department TB Program for assistance in identifying a laboratory that can measure EMB levels.

PZA is significantly removed by HD. In patients hemodialyzed more often than thrice weekly, PZA needs to be dosed after each HD session. PZA should be discontinued after 8 weeks of therapy in drug-sensitive disease. Patients receiving PZA may show evidence of increased uric acid on laboratory monitoring, and PZA may precipitate gout, especially in post-transplant patients who have a higher incidence of gout secondary to other

medications. The patient should be monitored clinically for symptoms of gout and treated appropriately if gout is diagnosed. Discontinuing PZA as a result of gout should be the last resort after exhausting other methods to control symptoms. If PZA is discontinued before 8 weeks of therapy have been completed, a longer course of therapy may be needed; please consult a specialist in TB care for advice.

INH, PZA, and less commonly RIF may lead to drug-induced hepatitis. Many patients on HD have routine monthly labs drawn, but patients should also be monitored for the signs and symptoms of drug-induced hepatitis. Many TB medications can cause gastrointestinal symptoms unrelated to hepatitis, so if serious symptoms were to occur, consultation with a specialist in TB care is advised.

Patients on INH should also receive Vitamin B6 25 mg po daily or 50 mg po thrice weekly (in addition to the Vitamin B6 contained in renal vitamin preparations) given the higher incidence of neuropathy related to INH in patients with ESRD and diabetes. In patients with CKD, higher doses of Vitamin B6 have the potential to also cause a neuropathy.

3.1.3 Extrapulmonary TB

There is a high incidence of extrapulmonary TB and miliary TB in patients with active TB and ESRD. The most common forms of extrapulmonary disease are pleural and lymph node TB. Tuberculous peritonitis can occur in PD patients. Presentation may be indistinguishable from typical bacterial peritonitis with cloudy fluid, fever, and abdominal pain. Smear for AFB and culture for MTB are usually positive. However, delays in diagnosis often occur, and peritoneal biopsy showing caseating granulomas is sometimes needed for early diagnosis. Peritoneal catheter removal is sometimes necessary, although most patients respond to a standard 6 month treatment course.

The presence of pulmonary TB must be excluded in all patients with suspected/confirmed extrapulmonary TB. Medical evaluation (pulmonary TB symptom check, PA chest radiograph) should be performed and if respiratory symptoms and/or an abnormal chest radiograph is reported, three consecutive AFB sputum smears and cultures, collected 24 hours apart, with at least one specimen being an early morning specimen, should be obtained.

There is a high incidence of extra pulmonary TB in patients with CKD; pulmonary TB must be ruled out in these patients.

3.1.4 Length of Treatment

Standard short-course chemotherapy for a period of six months (please see 3.1.1 for # doses) is highly efficacious for both pulmonary and extrapulmonary drug-sensitive TB. In cases of TB meningitis, treatment should be extended to 12 months; treatment duration for bone/joint involvement may also need to be extended. Patients at higher risk for relapse or treatment failure (e.g., extensive disease, lack of culture conversion within two months, drug intolerance, cavitary disease, lapses in therapy, etc.) should be considered for a minimum of nine months of therapy. Drug resistant TB requires longer therapy; please consult with a specialist in TB for advice.

3.2 Monitoring During Treatment

Patients should have a face-to-face monthly medical evaluation, symptom review, and laboratory testing (i.e. CBC, electrolytes, BUN, creatinine, LFTs). Additional laboratory tests should be ordered as indicated by the patient's underlying medical history and medical regimen.

Patients with initially AFB smear-positive pulmonary TB should have sputum samples collected for AFB smear at least every two weeks until 3 consecutive negative AFB sputum smears obtained at least 24 hours apart have been documented. Patients should continue to be dialyzed in an All room until clinical improvement on standard multi-drug anti-TB therapy for a minimum of 2 weeks AND have 3 negative sputum smears (as above).

Hospitalization may be required if no appropriate outpatient AIIR dialysis setting is available. Once AFB sputum smears become negative, or for those patients with AFB smear-negative but culture-positive pulmonary TB, sputum samples should be collected monthly for AFB smear and culture until two consecutive negative cultures have been documented for at least two consecutive months. Sputum induction should be performed, if necessary, to collect adequate specimens. Collection of one to two sputum specimens for AFB smear and culture at the completion of therapy, is highly recommended, for all patients initially smear and/or culture positive, and especially for patients with a delay in response to therapy or a high risk of relapse (i.e., cavitary/extensive disease, lack of culture conversion for greater than two months, advanced HIV disease), or in patients who received thrice weekly rather than daily treatment.

Chest-radiographs should be performed every 3-6 months during treatment and an end of treatment chest-radiograph should be obtained to provide a new baseline for comparison with follow-up chest-radiographs.

3.3 Drug-Drug Interactions Specific for Patients with CKD

Rifamycins significantly interact with multiple drugs commonly taken by patients with CKD. A complete current medication list needs to be kept up to date and reviewed for all patients on TB therapy. Patients taking warfarin, cyclosporin A, tacrolimus, sirolimus, digoxin and other medications metabolized by the cytochrome P450 (CYP450) system need to have levels monitored closely and doses adjusted as necessary. Consider consultation with a pharmacologist if needed.

Rifamycins can have significant interactions with many medications; a current medication list should be reviewed.

Treatment regimens for patients with active TB who are post-renal transplant and on anti-rejection agents can be especially problematic. The interaction between rifampin and cyclosporin, tacrolimus and sirolimus causes metabolism of these medications to be accelerated. As a result, levels of these medications may decline precipitously, and there is a well-documented risk for organ transplant rejection. Levels of these medications should be monitored weekly, and doses adjusted accordingly until stabilized. Consideration can be given to treating with rifabutin (RBT) instead of rifampin, since RBT is a less potent inducer of CYP450, but

levels of potentially affected medications should still be monitored. Close communication between the physician treating the patient for TB and the transplant center coordinating the patient's transplant care is needed.

3.4 Directly Observed Therapy (DOT)

DOT, the process by which trained staff observes the patient swallowing anti-TB medications, should be considered a core management strategy for all patients with active TB. Because of the increased risk of transmission to other HD patients, it is imperative that HD patients with active TB receive their medications by DOT. All HD patients with active TB should be provided with DOT after HD at the HD unit by either HD staff or health department staff. It is essential that all HD units and their employees be educated and aware of the need for DOT.

If HD staff members are administering medications by DOT, the local health department should ensure adequate administration of DOT (e.g., by providing education to HD staff about the rationale for DOT, DOT protocols, periodic evaluation of HD staff's DOT practices through onsite observation of DOT administration and inspection of DOT records). A health department staff member should be able to provide DOT at the patient's home on non-dialysis days for the entire treatment period. For patients who have CKD who are not receiving HD, DOT should be arranged through mutual agreement between the public health case manager and the patient.

Accurate record keeping is essential. The local public health department TB Program can assist in providing training to HD unit staff as well as forms for recording DOT.

3.5 Airborne Isolation Requirements for Patients with Active TB

HD patients with AFB smear positive pulmonary TB should be dialyzed in an AIIR until they have completed a minimum of two weeks of anti-TB therapy, *and* are AFB smear negative on 3 consecutive specimens obtained at least 24 hours apart (with at least one specimen obtained in the early morning) *and* are showing clinical improvement with continued close medical supervision and adherence to treatment. The decision to release a patient out of AIIR should be made in conjunction with the Health Department. **It is critical that LHD and HD staff not confuse an AIIR with hepatitis B isolation stations for HBsAg-positive patients.** Confusion and miscommunication about different types of isolation have led to HD patients being exposed to infectious TB patients who were permitted to return to a HD facility prematurely because it was believed the facility had an AIIR when, in fact, only a hepatitis B isolation station was available.

Patients with active pulmonary TB who have always been AFB smear negative should be placed on anti-TB therapy and can be dialyzed in the main unit after having taken a minimum of four days of therapy.

Patients with known or suspected active pulmonary TB and who are thought to have high risk for drug-resistant disease should have TB regimens tailored to their drug resistance pattern and should continue being dialyzed in an AIIR until cultures and susceptibility testing are available to confirm that the patient is on appropriate therapy and the patient meets criteria outlined above. Risk factors for drug resistance include foreign-born status, previously treated TB, known contact to an MDR-TB case, and patients who are not responding well to the standard four-drug regimen of INH, RIF, PZA, and EMB (particularly if cultures remain positive after two months of DOT). Clearance to return to non-AIIR Room HD must be obtained from the local health department TB Control Program.

Patients with CKD not on HD, or patients on PD, can usually be treated on an outpatient basis by DOT if not critically ill or in a congregate residential setting. Isolation in a health care facility in an AIIR is indicated if the patient is smear-positive and in a high-risk living situation.

Part IV

Reporting Requirements

Patients with confirmed or suspected active TB disease (pulmonary or extrapulmonary) shall be reported to the local health department within one day (Title 17, Section 2500). Cluster(s) of TST or QFT conversions (2 or more test conversions within a 3 month time period) in employees or patients should be reported to the local health department within one working day.

Any patient being treated for active TB disease who defaults from therapy or discontinues the treatment regimen against medical advice should be reported to the local health department within one working day. Also, any patient being treated for active TB disease who becomes hospitalized for any reason must be reported to the local health department within one working day. All patients being treated for active TB disease who change their address or health care provider should notify the local health department of the change. These changes should also be reported to the local health department by the health care provider.

Public health departments are exempt from Health Insurance Portability and Accountability Act (HIPAA) constraints for purposes of public health investigation, which includes, but is not limited to, case finding, case contact investigation, source case investigation and access to records.

Part V

Role of the local health department

The local health officer has the responsibility and authority under the law to control TB in his/her jurisdiction (Health and Safety Code 120175). The local health department TB Control Program staff is an important source for expert consultation to HD unit personnel on TB infection control and medical issues.

In addition, each local health officer is legally mandated to use every available means to investigate all reported or suspected cases of active TB in the jurisdiction (Health and Safety Code 121365). The local TB Control Program will, upon report of a suspect or active TB case, initiate case contact investigations according to CDHS/CTCA guidelines. These investigations are performed in order to identify those persons who are at risk of infection due to exposure to a known case and to ensure adequate evaluation and/or treatment. It is critical for HD staff to cooperate with the local TB Control Program in these investigations, since there are often numerous high-risk patients exposed, and timely and complete evaluation and treatment of those infected is critical to detect or prevent secondary cases. Local health departments may also initiate investigations to identify any possible active case of TB when a cluster of TST or QFT conversions occur (CTCA, 2001).

State laws require reporting of any persons with known or suspected TB to the local health department as well as to the CDHS Licensing & Certification (L&C) district office within one working day. These requirements are summarized in Appendix C.

Part VI

Tuberculosis Screening of Employees

6.1 Employee TB Screening

All employees and volunteers (including permanent, temporary and contract staff), who have potential for exposure to tuberculosis patients should be screened for TB at hire, and at least annually thereafter by a TB symptom review (see Appendix B). In addition, a TST or QFT is required before hire and annually for employees who have no documented positive TST or QFT (22 CCR 7235(b)). Use of the QFT for screening employees requires a grant of Program Flexibility from Licensing and Certification (L&C), since the use of the TST is required by regulation (CCR 22 72535). Use of the QFT for screening patients on admission to HD units requires approval of the patient care policy committee of the unit, while subsequent TB screening procedures are determined by the attending physician (CCR 22 52523 (c) (2) (C)).

6.1.1 TB Symptom Screen

All employees and volunteers should be screened at hire and at least annually for TB symptoms which include:

- Persistent cough, generally productive, lasting 3 weeks or longer
- Fever
- Night sweats
- Fatigue or weakness
- Unexplained weight loss and/or loss of appetite
- Hemoptysis (coughing up blood)

6.1.2 Symptomatic Employees

Regardless of TST status, any employee or volunteer with a persistent cough, especially in the presence of other signs or symptoms of TB, should be evaluated promptly for TB. The individual will not return to work until the following criteria are met:

1. TB disease is ruled out based on physical exam, chest-radiograph, and bacteriology (if indicated),

OR

2. TB disease is diagnosed and treated, and the individual is determined to be non-infectious as defined below:

- Has 3 consecutive negative AFB sputum smears obtained 24 hours apart with at least one specimen being obtained early morning; *and*
- Has completed at least 2 weeks of multi-drug anti-TB therapy if any AFB sputum smear positive, *or* at least 4 days of multi-drug anti-TB therapy if always AFB sputum smear negative; and
- Exhibits clinical improvement; and
- Has continued close medical supervision; *and*
- Adheres to treatment regimen; *and*
- Has been reported to and cleared to return to work by the local TB Control Program

The employee should bring documentation of his/her evaluation and treatment and a letter from the local health department stating that the employee is cleared to return to work.

Employees or patients who are suspected or confirmed to have active TB must be reported to the local health department within one working day (CCR Title 17, Section 2500).

6.1.3 Mantoux Tuberculin Skin Test or Quantiferon

All employees and volunteers who have written documentation of a prior negative TST or QFT or unknown or undocumented previous TST or QFT results must have a TST or QFT administered and read prior to starting employment. This requirement may be waived for an employee who had a TST or QFT within the past 3 months (22CCR Section 72535(b)) and has written documentation of a negative result. The TST should consist of 0.1 ml of 5TU purified protein derivative (PPD) given intradermally.

If using TST for screening employees, two-step testing is needed for new hires.

The TST should be placed by a licensed healthcare professional specifically trained to apply and interpret the result.

Skin test results should be read in 48-72 hours. Employees may not self-read a TST result. Skin test results must be recorded in millimeters (mm) of induration. Erythema without induration is not measured. A TST result with no induration is recorded as 0 mm. See Appendix F for interpretation of TST results.

6.1.4 Two-Step Testing

Two-step testing is used to detect individuals with TB infection acquired in the remote past who may now have diminished skin test reactivity. This procedure reduces the likelihood that a boosted (see below) reaction will later be interpreted as new infection in employees who are periodically tested. Two-step testing should be performed on all new employees who do not have written documentation of a negative TST in the preceding 12 months and have an initial negative TST result at the time of employment. The second TST is placed 1 to 3 weeks after the initial test. Employees who have a negative reaction to the first test

and a negative TB symptom screen may start work before the second test is placed. Any employee with a persistent cough (3 weeks or longer), especially in the presence of other signs or symptoms compatible with TB, should be excluded from the workplace and promptly evaluated for TB. Asymptomatic employees with a positive (boosted) reaction to the second TST are considered previously infected. The employee will be given a baseline chest-radiograph and referred to the local health department or to the employee's health provider for consideration of treatment for LTBI. A two-step TST is not required for subsequent annual testing. Two-step testing is not required if the QFT is chosen as the test to screen for TB infection.

6.1.5 Employees with Prior Positive Tuberculin Skin Test or QFT

Employees and volunteers who have written documentation of a previous positive TST or QFT result are required to have a baseline chest-radiograph at hire or provide written documentation of a normal chest-radiograph taken within 3 months prior to hire (22CCR 72535(b)).

If the new employee is asymptomatic and radiographic findings show no evidence of active TB, the employee can be cleared to work. The new employee should be referred to his or her medical provider, or, in some areas, the local health department for medical evaluation and treatment of LTBI.

If TB symptoms are present or the chest-radiograph is abnormal, the new employee should be immediately referred to his/her primary care provider, the local health department, or the employee's occupational health provider for medical examination and evaluation for active disease and/or treatment of TB. The employee should not begin work until medically cleared as in section 6.1.2.

Employees with positive TST or QFT should be screened annually, via a TB symptom review questionnaire. This questionnaire will be completed whenever a TST or QFT would be required of an employee with a negative TST or QFT result. If the symptom screen reveals signs or symptoms of TB, the employee will be excluded from the workplace. A new chest-radiograph and medical evaluation is then required.

The California Department of Health Services (CDHS) L&C Program does not require HD unit employees known to be TST or QFT positive to have an annual chest-radiograph. The chest-radiograph should be repeated only if the employee develops signs or symptoms of TB detected upon the annual symptom review or self-reported between annual screening.

A copy of the chest-radiograph report should be included in the employee's health record.

6.1.6 Tuberculin Skin Test or QFT Conversions and Other Newly Positive TSTs or QFT's

A TST conversion is defined as an increase of at least 10 mm in the size of induration from less than 10 mm to 10 mm or greater within a 2-year period. A QFT conversion is not well defined, but at this time, is considered as a change from a negative to a positive. Other persons with newly positive TST or QFT may have had no prior TST or QFT, or a negative TST or QFT from more than 2 years earlier.

Any employee or volunteer with a TST or QFT conversion or a newly positive TST or QFT result should have a chest-radiograph within 1 week, and should be referred as soon as possible for evaluation and management. The referral may be to the local health department or to the employee's health provider. In addition to referral for evaluation and management, symptomatic employees should be excluded from work until cleared by a physician. If an employee is suspected of having active TB, please refer to the Employee with Suspected Infectious TB section (6.1.2).

Additional recommendations for TST or QFT converters are:

1. If an employee is noted to be a TST or QFT converter without evidence of active TB, his/her health care provider should offer therapy for LTBI.
2. An investigation should be conducted by the facility to try and determine the source of the employee's infection. If employee conversions exceed the average number per year for the facility, the local health department should be consulted regarding appropriate follow-up testing. It is important for the facility to maintain and monitor data on employee conversions.
3. Some local health departments require reporting of persons who convert their TST from negative to positive.

6.1.7 BCG Vaccination

A history of previous vaccination with Bacillus of Calmette-Guerin (BCG) is not a contraindication for placing a TST or obtaining a QFT test. Criteria for interpreting TST results are the same. Screening for TB infection with TST or QFT should not be influenced by BCG vaccine status, however, the QFT may be more specific for TB infection than TST.

6.1.8 Periodic TB screening

All employees must be screened for TB at least annually (22 CCR 72535 (b)). This can be done on the anniversary of the hire date. All employees, regardless of TST or QFT status, must complete the TB symptom review on a yearly basis. They should also be reminded to report any symptoms suggestive of TB developing between screenings. For employees without documented positive TST or QFT results, the annual TB screen must include a TST or QFT in addition to the symptom screen (22 CCR 72535(b)). Compliance with the TB screening program and post-exposure follow-up is mandatory for all employees and volunteers. Subsequent employee TB screenings should be completed within 30 days of employee hire anniversary date or be initiated within one week of a post-exposure contact investigation

More frequent testing will be necessary if TST or QFT conversions are observed in patients or employees or after a known exposure to an infectious TB patient or employee has occurred.

All employees must be screened for TB at least annually (22 CCR 72535 (b)).

6.1.9 Chest-radiographs

A single, PA baseline chest-radiograph is recommended for employees who:

- Convert their TST or QFT from negative to positive during the course of employment
- Are TST or QFT positive on initial employment and cannot provide a written report of a normal chest-radiograph taken within 3 months prior to the date of employment
- Present at any time with symptoms compatible with active TB disease (productive cough for greater than 3 weeks, fever, anorexia, weight loss, night sweats, etc.)

Those employees who require a chest-radiograph for evaluation should bring documentation of his or her evaluation and treatment and a letter from their health care provider and/or the local health department stating that the employee is cleared to return to work. This will be included in the employee's health record.

6.1.10 Employee with Suspected Infectious TB

If the symptom screen, history, physical examination, or chest-radiograph is consistent with TB disease, the worker will be excluded from the workplace until:

- A qualified physician rules out TB disease based on physical exam, chest x-ray, and bacteriology, or
- TB disease is diagnosed, treated, and the individual is determined to be non-infectious as defined above under Symptomatic Employees section (6.1.2).

State regulation mandates that any person diagnosed with known or suspected active TB be reported to the local health department within 1 working day of identification (17 CCR 2505). In addition, the California Department of Health Services Licensing and Certification (CDHS L&C) regional office must be notified within one working day of any employee being diagnosed with or suspected of having active TB disease (22 CCR 72541).

6.2 Employee Exposure and Follow-Up

Employees may be inadvertently exposed to TB during the course of their work.

6.2.1 Exposure Definition

An employee is considered exposed when the employee has significant contact, without the benefit of all appropriate exposure control measures, with a patient whose sputum culture or nucleic acid amplification test (NAAT) is positive for *M. tb*, and who has not met all criteria to indicate that the patient is non-infectious as previously defined.

Factors that affect the significance of contact include:

- Duration of contact
- Proximity of contact
- Use of control measures that are functioning appropriately at the time of exposure (e.g., employee wore a fit-tested N-95 respirator, TB patient was masked)

6.2.2 Screening Following Exposure

A post-exposure baseline TST or QFT (for TST-negative employees) and TB symptom review should be administered to exposed personnel within one week of TB exposure confirmation (i.e., positive sputum smear/culture or positive NAAT for *M. tb*). Employees who have had a negative TST result within the last 3 months may use that test and a new TB symptom review as a baseline. Baseline status of employees with past positive TST or QFT results should be established by completion of a TB symptom review.

**A TST of
≥ 5mm induration
is considered
positive in
individuals with
exposure to TB.**

If the post-exposure baseline TST or QFT result is negative, a second test should be performed 8-10 weeks after the date of the last known exposure. A TST of ≥ 5mm induration is considered positive in individuals with exposure to TB.

6.2.3 Evaluation of TST or QFT Conversion

Any employee or volunteer with a TST or QFT conversion or newly positive TST or QFT result should have a chest x-ray and symptom review within 1 week, and be evaluated by the local health department or the employee's private physician. Symptomatic employees should be restricted from work until cleared by a physician.

Treatment recommendations for recent close contacts to active TB are described in the CDHS/CTCA Joint Guidelines for Testing and Treatment of Latent Tuberculosis Infection in Adults and Children. (Revised 5/06 –www.ctca.org)

6.3 Employee Education

Upon hire and annually, all employees should be trained in methods to identify, prevent and control the transmission of TB. The training should be conducted by a healthcare professional using current literature such as guidelines published by the CDC or recommendations made by the local health department's TB Controller. The training should be appropriate to the educational level, literacy skills and language ability of each employee and should be provided during regular work hours. A sign-off sheet should be initialed by the employee at the end of the session to acknowledge understanding of information described in the learning objectives. Cal/ OSHA (8 CCR Section 3203(a)(7) requires the following topics to be included:

- Where to get a copy of the Exposure Control Plan (ECP) if desired
- Groups at risk for occupational TB, especially immunocompromised workers
- Modes of M. tb transmission
- Symptoms of infectious TB
- TB screening and preventive therapy for TB
- Multidrug resistant- TB (MDR-TB)
- Procedure for segregating or isolating a suspected or known infectious TB patient
- Employer and employee responsibilities under the TB Exposure control procedures
- Use and limitations of methods that will prevent TB exposure, including administrative and work-practice controls, engineering controls, and respirators
- Decontamination and disposal of personal protective equipment

Additional topics, although not required, might include the role of the health department in following patients and the importance of DOT in dialysis patients. The educational session should include an opportunity for questions and answers with the instructor.

6.4. Retention of Records

6.4.1 Educational Record Maintenance

Educational records should include the class topic, name and qualifications of the instructor, employee name, position, department, and date and time of educational program. A sign-off sheet should be initialed by the employee to document attendance. Records should be maintained for 3 years.

6.4.2 TB Screening Record Maintenance

All employees, physicians, and volunteers should receive written notification of their TST or QFT results and interpretations. In addition to the TST or QFT result the notification should include a statement such as the following: "HIV infection and other medical conditions may cause a TST or QFT to be negative, even though you may be infected with TB. Please consult with your health care provider should you have concerns".

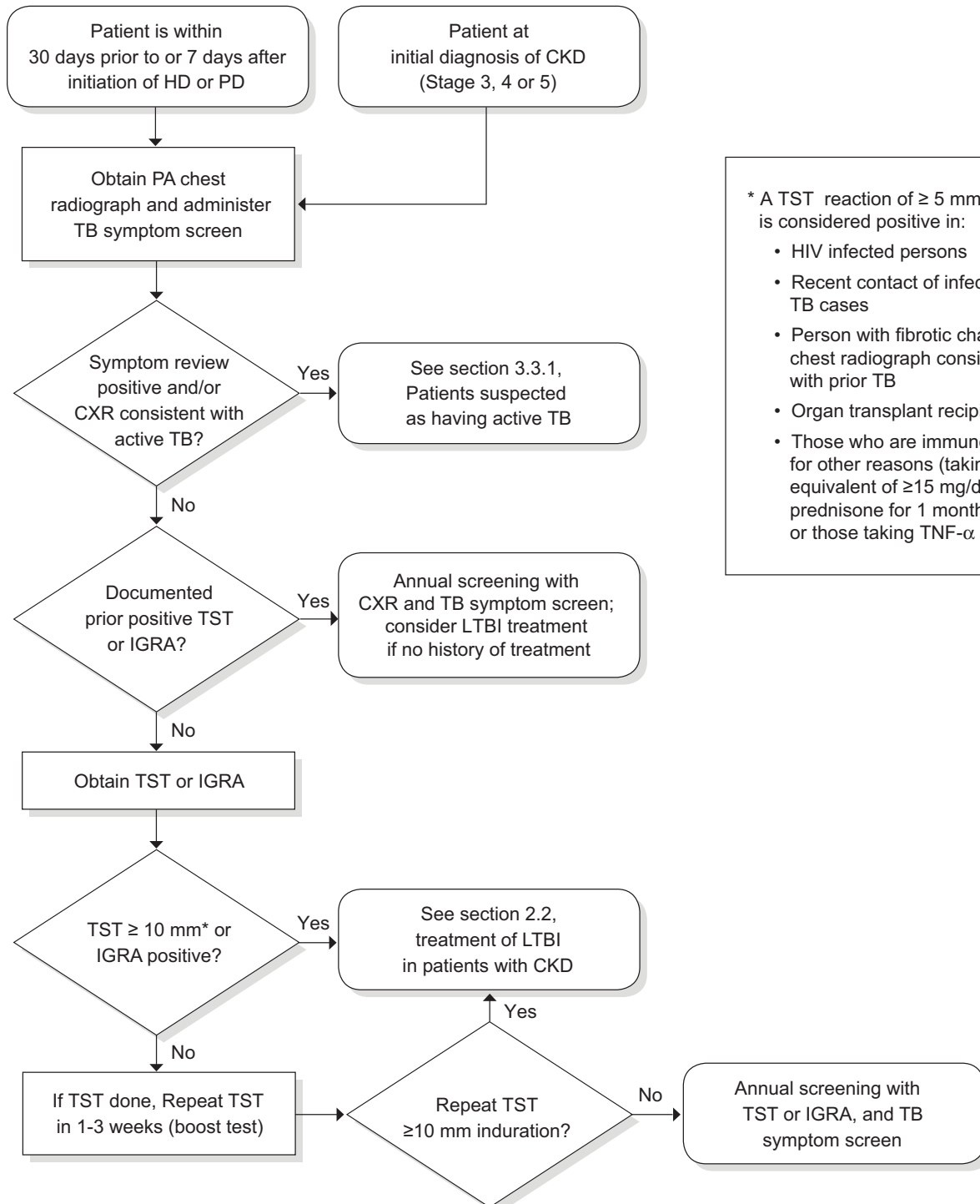
All employee TST or QFT conversions and confirmed TB cases should be recorded on the OSHA Log 200 unless substantiated as community-acquired.

6.4.3 Employee Health Record

The employee health record, maintained by the occupational provider, should be confidentially maintained for a period of thirty years following termination of employment. The facility's copy of the TST or QFT form is maintained in the employee's confidential health file.

Appendix A

Tuberculosis screening for patients at initiation of dialysis, or when first diagnosed with CKD stages 3-5. (See Section 1.1 for details)



* A TST reaction of ≥ 5 mm of induration is considered positive in:

- HIV infected persons
- Recent contact of infectious TB cases
- Person with fibrotic changes on chest radiograph consistent with prior TB
- Organ transplant recipients
- Those who are immunosuppressed for other reasons (taking equivalent of ≥ 15 mg/day of prednisone for 1 month or more or those taking TNF- α antagonists)

Appendix B

Sample TB Risk Assessment Questionnaire (TB-RAQ)

Name _____ Date _____

Medical Record or Employee Number: _____ Date of Birth _____

Department _____ Work Phone _____

Job Title _____ Signature _____

1. In the last year, have you had any of the following symptoms?

- | Yes | No | |
|--------------------------|--------------------------|---|
| <input type="checkbox"/> | <input type="checkbox"/> | Coughing up blood |
| <input type="checkbox"/> | <input type="checkbox"/> | Hoarseness lasting 3 weeks or more |
| <input type="checkbox"/> | <input type="checkbox"/> | Persistent cough lasting 3 weeks or more |
| <input type="checkbox"/> | <input type="checkbox"/> | Unexplained, excessive fatigue |
| <input type="checkbox"/> | <input type="checkbox"/> | Unexplained, persistent fever lasting 3 weeks or more |
| <input type="checkbox"/> | <input type="checkbox"/> | Unexplained, excessive sweating at night |
| <input type="checkbox"/> | <input type="checkbox"/> | Unexplained weight loss |

IF YOU ANSWERED YES TO ANY ITEM IN 1, PLEASE ANSWER THE FOLLOWING QUESTIONS.

In the last year:

2. Have you been told by a health care provider that your immune system is not working right, or that you cannot fight infection?

- Yes No Don't Know

3. Have you worked in a location where patients with active TB receive care or services?

- Yes No Don't Know

4. Have you lived with or had close contact with someone who has TB disease?

- Yes No Don't Know

5. Have you had an abnormal chest x-ray?

- Yes No Don't Know

6. Have you worked, volunteered, or lived in any institution such as another medical facility, jail, group home, or homeless shelter?

- Yes No Don't Know

7. Have you traveled outside the United States?

- Yes No Don't Know If yes, where? _____

Appendix C

Requirements for Reporting Known or Suspected Cases of Active TB Disease in a Patient or Employee

Sources: California Code of Regulations (CCR)

Health and Safety Code (HSC)

1. Within 1 working day of diagnosis of known or suspected TB, report to
 - The local health department (17 CCR 2505).
 - CDHS Licensing and Certification district office (22 CCR 72541).
2. Report to LHD when persons with known or suspected TB change or cease treatment regimen, change provider, or move to a new address.(HSC 121362).
3. Prior to discharging a known or suspected TB patient from a HD unit or hospital, health facilities must notify and provide a written treatment plan to the local health officer (HSC 1213612). The patient can be discharged only after the health officer approves the written treatment plan.

Exception: when the patient is being transferred to a general acute care hospital due to an immediate need for a higher level of care, notification and a written treatment plan must be submitted to the health officer, but the transfer can occur prior to obtaining written health officer approval.

Appendix D

Sample Patient TST or QFT Log

Patient Name					
Date of Birth					
Admission date/Discharge Date	A:	A:	A:	A:	A:
	D:	D:	D:	D:	D:
Date & Result of admission First step TST (or QFT)	Date:	Date:	Date:	Date:	Date:
	Result: mm	Result: mm	Result: mm	Result: mm	Result: mm
Date & Result of admission second step TST	Date:	Date:	Date:	Date:	Date:
	Result: mm	Result: mm	Result: mm	Result: mm	Result: mm
Date & result of admission CXR	Date:	Date:	Date:	Date:	Date:
	Result:	Result:	Result:	Result:	Result:
Date and result of periodic TST or QFT	Date:	Date:	Date:	Date:	Date:
	Result: mm	Result: mm	Result: mm	Result: mm	Result: mm
Date and result of periodic TST or QFT	Date:	Date:	Date:	Date:	Date:
	Result: mm	Result: mm	Result: mm	Result: mm	Result: mm
Date and result of periodic TST or QFT	Date:	Date:	Date:	Date:	Date:
	Result: mm	Result: mm	Result: mm	Result: mm	Result: mm

Appendix E

Division of Occupational Safety and Health Policy and Procedures Manual Interim Tuberculosis Control Enforcement Guidelines

P&p c-47

Issue Date: 12/1/92

Revised: 8/1/94, 7/1/95, 4/11/97

AUTHORITY: California Labor Code §§6305, 6309, 6317, 6400, 6401, 6401.7, 6402, 6403 and 6404 and Title 8 California Code of Regulations §§332.2, 3203, 5079, 5141, 5143, 5144 and 14301.

POLICY: It is the policy of the Division of Occupational Safety and Health to ensure that compliance District Offices make a record of, and respond to, any complaint alleging employee exposure to tuberculosis, conduct an appropriate investigation of tuberculosis exposure, work cooperatively with Cal/OSHA Medical Unit consultants, local public health officers and tuberculosis controllers, as well as with the Tuberculosis Control Branch of the California Department of Health Services, and issue citations, notices or Special Orders based on sound evidentiary evaluation of the work setting where a tuberculosis hazard is alleged to exist.

Appendix F

Interpreting the Results of the TST or QFT

(see CDHS / CTCA Joint Guidelines for Testing and Treatment of Latent Tuberculosis Infection in Adults and Children)

A reaction of 5 mm or more of induration is considered positive if the resident or employee meets any of the following criteria:

- Is known or suspected to have HIV infection
- Recent contact to an active case of pulmonary or laryngeal TB
- Has an abnormal chest-radiograph consistent with TB disease
- Is immunosuppressed

A reaction of 10 mm or more of induration is considered positive for all other persons.

For interpretation of QFT-G results, please refer to CDC Guidelines

Appendix G

Risk Factors for TB Disease

(see CDHS / CTCA Joint Guidelines for Testing and Treatment of Latent Tuberculosis Infection in Adults and Children)

About 10% of previously infected persons will develop active disease at some point in their adult life. The progression from latent infection to active disease is more likely to occur in people with any of the following conditions:

- Recent (within 2 years) infection with *Mycobacterium tuberculosis*
- HIV infection
- Injection drug use, regardless of HIV serostatus
- Diabetes mellitus (especially insulin-dependent)
- Silicosis
- End-stage renal disease
- Chronic immunosuppression (such as transplant recipients, prolonged corticosteroid treatment, or other immunosuppressive therapy, such as TNF- α antagonists)
- Hematologic or reticuloendothelial diseases (e.g. leukemia and Hodgkin's disease)
- Malnutrition and clinical situations associated with rapid weight loss such as cancers of the head and neck, intestinal bypass or gastrectomy, chronic malabsorption, low body weight (>10% below ideal body weight)
- Radiographic findings consistent with old TB

Appendix H

Glossary

acid-fast bacilli (AFB) smear

A laboratory test that involves gross microscopic examination of a stained smear (usually of sputum) to determine if mycobacteria are present. Mycobacteria are a type of bacteria that includes *Mycobacterium tuberculosis*. A presumptive diagnosis of pulmonary TB can be made with a positive AFB sputum smear result; however, about half the patients with TB of the lungs have negative AFB sputum smears.

airborne infection isolation room (AIIR) (formerly called a negative pressure isolation room)

A single-occupancy room used to isolate persons with suspected or confirmed infectious TB. The room's ventilation system will be designed to provide

- Negative pressure in the room (so that air flows under the door gap into the room); and
- Air flow rate of 6 to 12 air changes per hour; and
- Direct exhaust of air from the room to the outside of the building or recirculation of air through a high efficiency particulate air (HEPA) filter

Bacillus of Calmette-Guérin (BCG) vaccine

A live attenuated TB vaccine used in many parts of the world. BCG is rarely used in the United States.

baseline tuberculin skin test

A TST provided to employees or residents to determine if the person was previously infected with *M. tuberculosis*

boosted tuberculin skin test (TST)

A phenomenon in which some persons who receive a TST many years after acquiring latent TB infection have a negative reaction on an initial test, followed by a positive TST reaction on a subsequent test. Waned sensitivity to tuberculin on the first test is "boosted" by the second test. See two-step tuberculin skin testing (TST).

clinical examination

An in-person evaluation of the clinical status of a patient by a physician or equivalent licensed practitioner. Purposes can include to diagnose TB disease or latent TB infection, to select treatment, and to assess response to therapy. The evaluation may include the following:

- Medical history and TB symptom review
- Clinical and/or physical examination
- Screening and diagnostic tests (such as tuberculin skin tests, QFT, chest x-rays, bacteriological examination, and HIV testing)
- Counseling
- Treatment referrals

Glossary *(continued)*

cluster

Two or more tuberculin skin test conversions occurring within a 3-month period, which suggest transmission within the facility.

contact

A person who has experienced a TB exposure incident.

contact investigation

Procedures that occur when a patient with infectious TB is identified, including elicitation of people (contacts) exposed to the patient, testing and evaluation of contacts to identify latent TB infection or TB disease, and treatment of these individuals.

conversion

See tuberculin skin test (TST) conversion.

culture

See Mycobacterium tuberculosis culture

directly observed therapy (DOT)

Therapy in which a healthcare worker or a health department employee observes the patient swallow each dose of TB medication.

environmental control measures

Physical or mechanical measures (as opposed to administrative control measures) used to reduce the risk of TB transmission. Examples include ventilation, filtration, ultraviolet lamps, airborne infection isolation rooms, and local exhaust ventilation devices.

exposure incident

A situation in which staff, patients, or visitors have had significant exposure to an individual with suspected or confirmed TB disease (or to air containing TB bacteria) during the determined infectious period, without the benefit of appropriate environmental control measures or personal protective equipment, such as an N-95 particulate respirator.

False-negative tuberculin skin test (TST)

TST result that fails to identify TB infection when present.

False-positive tuberculin skin test (TST):

TST result that incorrectly identifies TB infection when TB infection is not present.

HEPA filter unit

A self-contained device consisting mainly of a HEPA filter, pre-filter, and fan. These devices can be used to provide clean air to supplement a building ventilation system.

high efficiency particulate air (HEPA) filter

A filter that removes all airborne particles in the size range of particles that contain the TB bacterium. HEPA filters may be either portable or stationary. Use of HEPA filters in building ventilation systems requires expertise in installation and maintenance.

human immunodeficiency virus (HIV) infection

Infection with the virus that causes acquired immunodeficiency syndrome (AIDS). HIV infection is the most important risk factor for the progression of latent TB infection to active TB disease.

immunosuppression

A condition in which the immune system is not functioning normally. Immunosuppressed individuals are at greatly increased risk of rapidly progressing from latent tuberculosis infection to active TB disease.

index case

A person with suspected or confirmed infectious TB who is the first patient with TB to be identified and who may be the source of exposure in other persons.

induration

Swelling that can be palpated (felt) at the site of the TST, measured and recorded in millimeters (not erythema/redness)

infectious period

Time period during which the TB case may have transmitted TB to others, marked by the date(s) of symptom(s) onset or the date of the first positive finding consistent with respiratory tract TB (positive smear or culture, or chest x-ray showing abnormality consistent with TB), until the time as the patient has converted to sputum smear negativity and has been on antituberculosis treatment sufficient to render the patient no longer infectious.

Interferon Gamma Release Assay (IGRA) for TB

Blood test for the diagnosis of TB. Uses TB specific antigens to stimulate lymphocytes in vitro, and measures interferon response to TB antigens compared to positive and negative controls; does not differentiate between TB infection and disease.

intra-dermal

Injection of purified tuberculin in the dermis of the skin used in Mantoux tuberculin skin testing

latent TB infection (LTBI)

A condition in which living *Mycobacterium tuberculosis*, the bacterium that causes TB disease, is present in the body without producing clinical disease. Persons with LTBI are not contagious, have no symptoms, and generally have a positive tuberculin skin test or positive IGRA.

Glossary *(continued)*

mask

A device worn over the nose and mouth of a person with suspected or confirmed infectious TB disease to prevent infectious particles from being released into room air.

Mycobacterium tuberculosis (M. tb)

The bacterium that causes latent TB infection and TB disease.

Mycobacterium tuberculosis culture

A laboratory test to determine the presence of Mycobacterium tuberculosis. A positive culture confirms the diagnosis of TB disease.

negative pressure isolation room

See airborne infection isolation room.

purified protein derivative (PPD)

A purified tuberculin preparation used in Mantoux tuberculin skin test.

QuantiFERON®TB-Gold (QFT-G)

A blood test to identify tuberculosis infection. It is an interferon- γ release assay (IGRA). As of this writing, the QuantiFERON®TB -Gold (QFT-G) test is the only FDA-approved interferon gamma release assay.

Respirator

A device worn by an individual to prevent the wearer from inhaling airborne contaminants.

smear

See acid-fast bacilli (AFB) smear

sputum

Secretions coughed up from deep within the lungs (to be distinguished from saliva and nasal secretions).

sputum induction

A medical procedure used to obtain sputum from a patient who is unable to cough up a specimen spontaneously. The patient inhales a hypertonic saline mist, which stimulates a cough from deep within the lungs. This procedure is commonly used to obtain sputum specimens from patients with suspected or confirmed TB disease.

symptoms of TB of the lungs or larynx

A cough lasting longer than 3 weeks, persistent fatigue, unexplained weight loss, fever, night sweats, and coughing up blood.

TB disease (active TB disease)

Clinically active disease caused by *Mycobacterium tuberculosis*. Persons who have active TB usually have symptoms, and about 80% have a positive tuberculin skin test. TB disease of the lungs or larynx can be transmitted when a person with the disease coughs, sings, laughs, speaks, or breathes. Extrapulmonary TB can occur in any organ and, with the exception of laryngeal TB, is generally not considered transmissible.

TB exposure incident

A situation in which staff, patients, or visitors have been exposed to an individual with confirmed or suspected infectious TB (or to air containing TB bacteria) without the benefit of appropriate infection control measures.

tuberculin skin test (TST)

An intradermal Mantoux test with 0.1 mL purified protein derivative (PPD) tuberculin containing 5 tuberculin units, used to determine the presence of latent TB infection.

tuberculin skin test (TST) conversion

A change in tuberculin skin test results in which induration increases at least 10 millimeters (mm) from less than 10 mm to 10 mm or greater within a 2-year period, regardless of age. For contacts to a TB case, a TST conversion is defined as a change from less than 5 mm induration on the initial TST to a reaction of greater than or equal to 5 mm on the second test, 8 to 10 weeks after exposure has ended.

tuberculin skin test (TST) reactor

A person with a positive TST.

two-step tuberculin skin testing (TST)

A procedure for baseline testing of persons who will receive periodic TSTs to reduce the likelihood of mistaking a boosted reaction for a new infection. If the result of the first TST is negative, a second test is given 1 to 3 weeks later. If the result of the second TST is positive, it likely indicates a boosted reaction due to latent TB infection acquired in the remote past. If the second test result is negative, the subject is classified as uninfected. Two-step testing reduces the likelihood of misinterpreting a boosted TST reaction that indicates a past latent TB infection as a newly acquired infection. This distinction is important in determining whether TB transmission has likely occurred in the facility and in recommending treatment for latent TB infection in an individual. Two-step TST is also used for patients on intake into dialysis in order to establish a valid baseline TB status.

transmission

Spread of *M. tuberculosis* organisms through the air when a person with active TB disease coughs, sings, laughs, speaks or breathes.

Additional reading

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