

## Tuberculosis: Infection Control/Exposure Control Issues for Oral Healthcare Workers

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### Abstract

**Aim:** The aim is to present the essential elements of an infection control/exposure control plan for the oral healthcare setting with emphasis on tuberculosis (TB).

**Methods and Materials:** A comprehensive review of the literature was conducted with special emphasis on TB infection-control issues in the oral healthcare setting.

**Results:** Currently available knowledge related to TB infection-control issues is supported by data derived from well-conducted trials or extensive controlled observations. In the absence of supportive data the information is supported with the best-informed, most authoritative opinion available.

**Conclusion:** Essential elements of an effective TB infection-control plan include a three-level hierarchy of administrative, environmental, and respiratory-protection controls.

**Clinical Significance:** Standard precautions provide the fabric for strategies to prevent or reduce the risk of exposure to bloodborne pathogens and other potentially infectious material. However, standard precautions are inadequate to prevent the spread of organisms through droplet nuclei 1-5 micron in diameter and additional measures are necessary to prevent the spread of *Mycobacterium tuberculosis*. Oral healthcare settings have been identified as outpatient settings in which patients with suspected or confirmed infectious TB disease are expected to be encountered. Therefore, oral healthcare settings must have a written TB infection-control program.

**Keywords:** Tuberculosis, latent TB infection, TB disease, TB infection-control

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## Introduction

In 2005, the Centers for Disease Control and Prevention (CDC) published new guidelines for preventing the transmission of *Mycobacterium tuberculosis* (MBT) in healthcare facilities.<sup>1</sup> These guidelines replace all previous CDC guidelines for tuberculosis (TB) infection-control in healthcare settings and apply to all settings in which healthcare workers (HCWs) might either share air space with persons with infectious TB disease or have contact with clinical specimens containing MBT. The magnitude of the risk varies by setting, occupational group, prevalence of TB in the community, patient population served in the setting, procedures performed, and effectiveness of TB infection-control measures. However, every setting in which services are provided to persons who have suspected or confirmed TB disease should have a TB infection-control plan. The 2005 guidelines explicitly identify oral healthcare facilities as outpatient settings in which patients with suspected or confirmed infectious TB disease are expected to be encountered.



the exposure to a person with infectious TB disease.<sup>1</sup> Environmental factors such as exposure in confined spaces, inadequate ventilation, and recirculation of air containing infectious droplet nuclei further increase the likelihood of transmission.<sup>6</sup> The persons at highest risk for exposure to an infection with MBT are close contacts of persons who share air space in a household or other enclosed environment with a person with pulmonary tuberculosis (Table 1).<sup>6</sup>

When susceptible hosts inhale droplet nuclei, the bacilli travel through the mouth or nasal passages, the upper respiratory tract, and bronchi to the alveoli where a local infection is established.<sup>7</sup> The immune response to such infections is predominantly cell-mediated, involving both CD4+ and CD8+ T-cells.<sup>8</sup> Pulmonary macrophages process the antigens and present them to both major-histocompatibility-complex (MHC) class II molecules, which activate CD4+ cells; and to MHC class I molecules, which activate CD8+ T cells. Within two to ten weeks following exposure the immune response will limit further multiplication of MBT. However, if the quantity or virulence of the TB bacilli is such that they overwhelm the immune response, the bacilli may disseminate throughout the body by lymphatic and hematogenous spread.<sup>9,10</sup>

## Etiology and Epidemiology

Robert Koch first described MBT, the causative organism for tuberculosis, in 1882.<sup>2</sup> MBT is carried in airborne particles called droplet nuclei that are generated when persons with infectious TB disease cough, sneeze, shout, sing, or talk (Figure 1).<sup>3,4</sup>

These droplet nuclei are between 1-5 microns in size, which can remain suspended in air for hours and can be carried in normal air currents throughout a room or building.<sup>5</sup> The probability of a person exposed to MBT becoming infected depends on the concentration of infectious droplet nuclei in the air and the duration of



**Figure 1.** MBT is carried in airborne particles called droplet nuclei that are generated when persons with infectious TB disease coughs, sneezes, shouts, sings, or talks.

**Table 1. Persons at highest risk for exposure to an infection with MBT.<sup>6</sup>**

Population	Examples
Foreign-born persons from countries with a high incidence of TB disease who arrived in the U.S. within the past five years	Africa, Asia, Eastern Europe, Latin America, and Russia
Persons who frequently travel to countries with a high incidence of TB disease	
Residents and employees of settings that are high risk	Correctional facilities, long-term care facilities, and homeless shelters
Populations at high risk who are defined locally as having an increased incidence of TB disease	<ul style="list-style-type: none"> <li>• Foreign-born persons</li> <li>• Hispanics</li> <li>• Blacks</li> <li>• Asians</li> <li>• Patients untreated for latent TB infection</li> <li>• HIV-infected patients</li> <li>• Patients receiving immunosuppressive therapy</li> </ul>
Populations at high risk who are defined locally as medically underserved and who have low income	
Infants, children, and adolescents exposed to adults in high-risk categories	
HCWs who serve patients who are at high risk	
HCWs with unprotected exposure to a patient with TB disease	

TB is recognized worldwide as the leading cause of death from an infectious disease, responsible for approximately two million deaths annually.<sup>11</sup> In the United States, a total of 14,097 TB cases were reported to the CDC in 2005, which represented a 2.9% decrease from 2004 and the TB case rate of 4.8 per 100,000 in 2005 represented a 3.8% decline compared with 2004.<sup>12</sup> The decrease in the annual case rate slowed, from an annual average of 5.6% for 1993 through 2002 to an average of 3.1% for 2003 through 2005.<sup>12</sup> The rate of TB in foreign-born persons was 8.7 times that of those born in the United States. In addition, Hispanics, Blacks, and Asians had TB rates 7.3, 8.3, and 19.6 times higher than whites, respectively. Moreover, the number of multidrug-resistant (MDR) cases of TB increased by 13.3% compared to 2003 (the most recent year for which complete drug-susceptibility data are available). The slower deceleration

of TB rate nationally, the disparity of TB rates between whites and racial/ethnic minorities, and the increased incidence of MDR cases all threaten progress toward the goal of eliminating TB in the United States.

### Clinical Manifestations

#### Latent TB infection (LTBI)

The immune response to MBT culminates in the formation of tuberculous granulomas at foci of infection. Consequently, not all bacilli are eliminated from the body and those incarcerated in granulomas can remain viable for many years.<sup>13,14</sup> At this stage, the person infected is said to have LTBI. Although immunological test results for MBT are positive, these patients have no symptoms, no radiographic abnormalities compatible with tuberculosis, and all bacteriologic studies are negative. Patients with LTBI are not contagious.

**Table 2. Diseases and conditions that increase the risk of progression from LTBI to TB Disease.**<sup>1,15,16</sup>

<ul style="list-style-type: none"> <li>• HIV infection</li> <li>• History of infection with MBT within the past two years</li> <li>• History of untreated or inadequately treated TB disease</li> <li>• Infants and children aged &lt;4 years</li> <li>• Diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic renal failure</li> <li>• Immunosuppressive therapy</li> <li>• Silicosis</li> <li>• Malignancies (carcinoma of the head, neck, lung; leukemia; lymphoma)</li> <li>• Intestinal bypass or gastrectomy</li> <li>• Body weight <math>\geq 10\%</math> below ideal weight</li> </ul>
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### **Tuberculosis (TB disease)**

Approximately 5-10% of the people who become infected with MBT and who are not treated for LTBI will develop TB disease during their lifetime (Table 2).<sup>1,15,16</sup>

The lung is the most common site for TB disease. Classic symptoms include chronic ill health, coughing with hemoptysis, low-grade fever, weight loss, and night sweats. About 15% of patients with TB disease present with an extrapulmonary site of infection. This is especially common in patients who have both TB and an HIV infection. Expectoration of the infected sputum may cause tuberculous tracheitis, laryngitis (hoarseness, coughing, and pain), and tuberculous ulcers on the tonsils (dysphagia) and nasal cavity (obstruction, perforation, nasal discharge).<sup>17,18</sup> When the cervical lymph nodes are involved, they may caseate forming tuberculous abscesses or undergo fibrosis and calcification.<sup>17,18</sup> Swallowing of the infected sputum may result in tuberculous ulceration of the ileum. In a few instances, there is rapid pathologic progression and the tubercle bacilli spread via the bloodstream to many organs giving rise to miliary tuberculosis.<sup>19</sup>

### **Oral Manifestations of TB**

The estimated prevalence of oral tuberculous lesions ranges from 0.05 to 5%.<sup>20,21,22</sup> Oral lesions are usually secondary, reflecting oral inoculation with infected sputum or as a result of hematogenous spread.<sup>20,23,24</sup> Rare cases of primary tuberculous involvement of oral structures have been reported.<sup>20,25-28</sup> In a recent study evaluating patients with TB and a co-infection with HIV, the prevalence of oral tuberculous lesions was found to be 1.33%.<sup>24</sup> Oral tuberculous lesions are



**Figure 2.** Oral tuberculous lesion of the dorsum of the tongue in a patient with both TB disease and HIV infection.

nonspecific in their clinical presentation, and their consideration in the differential diagnosis requires a high degree of awareness.<sup>24,29-34</sup> While all oral tissues may be affected, in the cohort of patients with both TB disease and HIV-infection, the palate and dorsum of the tongue (Figure 2) were the most frequent sites of oral involvement.<sup>20,24,28</sup> These data are in agreement with those reported by other investigators in patients with TB disease without an HIV-infection.<sup>35,36,20,24,28</sup> Pain and cervical lymphadenopathy are common but not universal findings.<sup>24</sup> A rare case of tuberculous osteomyelitis of the mandible and several cases of tuberculous parotitis have been documented.<sup>37-40</sup>

### **Diagnosis**

Early diagnosis of infection with MBT is important because of the nature of the disease. The tuberculin skin test or a blood assay for *Mycobacterium tuberculosis* are useful for screening groups of people for LTBI with exposure rates that substantially exceed those of the general population (Table 1).<sup>1</sup>



Table 3. Interpreting the tuberculin skin test reaction.<sup>1</sup>

Induration of $\geq 5$ mm	Induration of $\geq 10$ mm	Induration of $\geq 15$ mm
People with HIV infection	Foreign-born persons	People with no risk factors for TB
Close contacts of people with TB	HIV-negative persons who use illicit drugs People with no risk factors for TB	
People who have had TB disease before	People in residential facilities	
Illicit drug users	Children $\leq 4$ years of age	

### Latent TB Infection

The tuberculin skin test (TST), which is the Mantoux intradermal test, using 5 tuberculin units of tween-stabilized purified protein derivative (PPD)-tuberculin is the traditional method of diagnosing LTBI.<sup>1</sup> The antigen is injected intracutaneously into either the volar or dorsal surface of the forearm. In patients with LTBI, the TST evokes a delayed hypersensitivity reaction to the tuberculin mediated by T-lymphocytes producing an area of redness and swelling. The test is read at 48 to 72 hours. Erythema is disregarded, and the diameter of the induration is measured (Table 3).

While the relative specificity of the TST skin test is high, both false positive and false negative reactions have been reported.<sup>41</sup> False-positive reactions may be due to previous sensitization with mycobacterial antigens, as may be seen following vaccination with Bacille Calmette-Guerin

(BCG).<sup>42</sup> False-negative reactions to the TST have been reported in immunocompromized patients, in patients with recent exposure to MBT, and in very young children.<sup>41-42</sup>

The CDC recommends persons with a positive TST undergo further evaluation.<sup>43</sup> In recent years a number of *in vitro* diagnostic tests in the form of blood assays for *Mycobacterium tuberculosis* (BAMT) have been developed. One of these tests approved by the Food and Drug Administration (FDA) for the detection of latent TB infection is the QuantiFERON®-TB Gold (QFT-G) test.<sup>44</sup> This test detects the release of interferon-gamma in fresh heparinized blood from sensitized persons when it is incubated with mixtures of synthetic peptides representing two proteins present in MBT. The sensitivity of QFT-G is statistically similar to that of TST for detecting TB infection. However, the QFT-G measures cell-mediated response to peptides from two MBT proteins not present in

any BCG vaccine strains and absent from the majority of mycobacteria other than MBT. Hence, the QFT-G has greater selectivity.

### TB Disease

Although the history, physical examination, TST and/or QFT-G data, and other studies such as chest radiographs are helpful and at times may strongly suggest TB disease, definitive diagnosis usually requires the demonstration of MBT in the patient's tissues or secretions.<sup>1</sup> Bacteriologic examination, which includes obtaining a specimen of sputum, detection of acid-fast bacilli (AFB) in stained (Ziehl-Neelsen method) smears examined microscopically, may provide the first bacteriologic clue to TB disease. However, not all AFB are tubercle bacilli, therefore, a positive bacteriologic culture for MBT is essential to confirm the diagnosis. DNA probes specific for the genus *Mycobacterium* now are used routinely to identify specific mycobacterium. When the presence of MBT has been confirmed, it is then necessary to perform drug susceptibility testing on positive cultures.

## Principles of Medical Management

### Prevention

Immunization with viable *Mycobacterium bovis* BCG is the most widely used preventive measure to control tuberculosis worldwide. Administered to newborns in a single dose, it prevents severe disease and reduces mortality among children from miliary and meningeal disease.<sup>45,46</sup> However, BCG does not protect against pulmonary tuberculosis in children or adults.<sup>45,46</sup> As mentioned earlier, optimal immune response to MBT infection appears to involve both CD4+ and CD8+ T-cells.<sup>8</sup>

BCG activates CD4+ T-cells by being taken up by macrophages and residing within phagosomes which are membrane-enclosed vacuoles. These antigens, once processed in the phagosomes, then readily interact with MHC class II molecules. However, the ability of the bacillus to block acidification of the phagosomes precludes its release into the cytoplasm and for an antigen to bind to MHC class I molecules it must be processed in the cytoplasm of the infected cells. Consequently, BCG fails to elicit a CD8+ T-cell response. A recently developed recombinant

bacillus with an impaired ability to counter the acidification of phagosomes will soon enter phase 1 clinical trials.<sup>47</sup> This new vaccine is likely to be more effective because it targets both CD4+ and CD8+ T-cells.

### Treatment of Infection with MBT

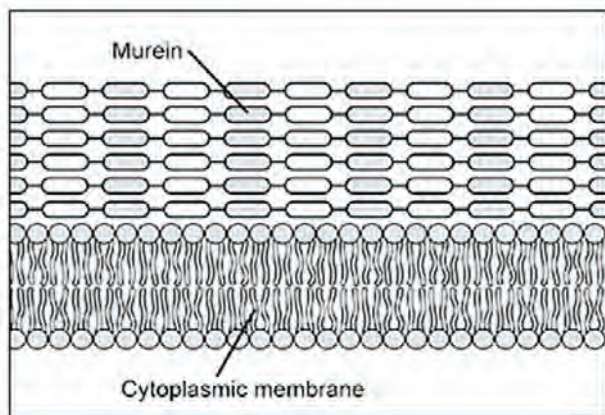
The goal of antibacterial chemotherapy is to induce selective toxicity. Selectivity can be realized by attacking targets:

- Unique to the pathogen
- In the pathogen that are similar to but not identical to those of the host
- In the pathogen that are shared by the host but that vary in importance between pathogen and host

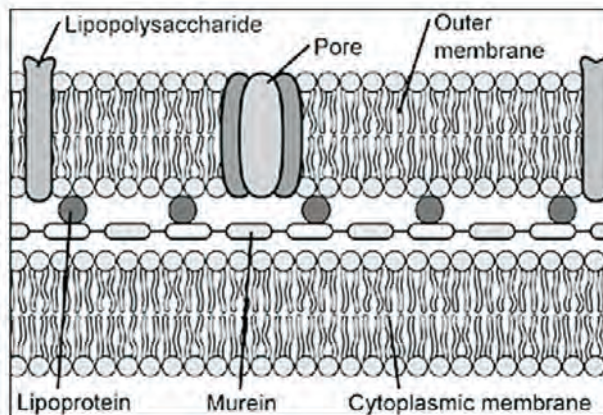
One target is the bacterial cell wall, a structure that is both unique and essential for the survival of most pathogenic bacteria.<sup>48</sup> The bacterial cell wall is a three-dimensional meshwork of peptide-crosslinked sugar polymer (peptidoglycan or murein) surrounding the cell just outside its cytoplasmic membrane.

Bacteria may be conveniently divided into two groups, Gram-positive and Gram-negative, based on the relative abilities of bacteria to retain purple Gram-stain after being washed with an organic solvent such as acetone. Gram-positive bacteria retain the stain and appear purple, whereas Gram-negative bacteria lose the stain and appear pink. The ability to retain stain results from two distinguishing characteristics of cell wall architecture. In Gram-positive bacteria, the cell wall is composed of a thick layer of murein (Figure 3A). The murein layer in Gram-negative bacteria is thinner but it is surrounded by a second, outer lipid bilayer membrane (Figure 3B). The cell wall of mycobacteria, which include the causative agent of tuberculosis, is similar to that of Gram-negative bacteria (Figure 3C).

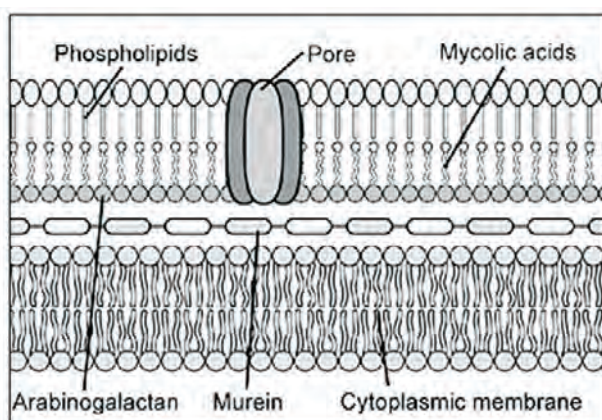
Both are enclosed by an inner cytoplasmic membrane, a thin murein layer, and an outer membrane. The main difference is that, in mycobacteria, the outer membrane is thick, composed of two leaflets that are asymmetrical in size and composition.<sup>49</sup> The inner leaflet is composed of arabinogalactan and mycolic acid, and the outer leaflet is composed of extractable



**Figure 3A.** In Gram-positive bacteria, the cell wall is composed of a thick layer of murein.



**Figure 3B.** The murein layer in Gram-negative bacteria is thinner but it is surrounded by a second, outer lipid bilayer membrane.



**Figure 3C.** The cell wall of mycobacteria, which includes the causative agent of tuberculosis, is similar to that of Gram-negative bacteria. The main difference being mycobacteria has a thick outer membrane composed of two leaflets that are asymmetrical in size and composition.

phospholipids. Cell wall biosynthesis takes place in the following three major steps:

1. Synthesis of murein monomers from amino acids and sugar building blocks (N-acetylglucosamine [NAG] and N-acetylmuramic acid [NAM]).
2. Polymerization of the monomers into linear peptidoglycans.
3. Crosslinking of the polymers into a three-dimensional meshwork.

In mycobacteria the NAM residues of the cell wall are modified by the addition of a long chain consisting of a NAG-arabinogalactan

linker topped with mycolic acid. The addition of arabinose units is catalyzed by the enzyme arabinosyl transferase. The synthesis of mycolic acid includes the formation of saturated hydrocarbon chains catalyzed by the enzyme fatty acid synthetase 1 (FAS1), which are then linked by the enzyme fatty acid synthetase 2 (FAS2). The linked products undergo further enzymatic transformations to become mycolic acid.

Standard antimycobacterial treatment regimens include antibiotics that target unique targets such as the synthesis of NAG-arabinogalactan and the early steps in mycolic acid synthesis (Table 4).

Table 4. Antimycobacterial agents.<sup>1,51</sup>

First-line Drugs		
Drug	Mechanism of Action	Adverse Drug Effects
Ethambutol	Inhibits arabinosyl transferase	Optic neuritis Loss of visual acuity
Pyrazinamide	Inhibits fatty acid synthetase <sup>1</sup>	Morbilliform rash Arthralgias Hyperuricemia
Isoniazid	Inhibits fatty acid synthetase <sup>2</sup>	Hepatitis Peripheral neuropathy Inhibits CYP450 enzymes
Rifamycins: Rifampin Rifabutin Rifapentin	Bind to RNA polymerase and inhibit transcription	Hepatitis Flu-like symptoms Morbilliform rash GI disturbances Induce CYP450 enzymes
Second-line Drugs		
Cycloserine	Inhibits monomer synthesis	Psychosis Seizures Peripheral neuropathy
Ethionamine	Inhibits fatty acid synthetase <sup>2</sup>	Hepatitis Hypothyroidism
Aminoglycosides: Streptomycin Capreomycin Kanamycin Amikacin	Bind to the 30S ribosomal subunit and inhibit translation	Ototoxicity Nephrotoxicity Neuromuscular blockade
Fluoroquinolones: Ciprofloxacin Ofloxacin Gatifloxacin Levofloxacin Moxifloxacin	Inhibit topoisomerase II (DNA gyrase), thereby releasing DNA with staggered double-stranded breaks	Nausea Abdominal pain Restlessness Confusion
Aminosalicylic acid	Competitive para-aminobenzoic acid antagonist	GI disturbances
Combination Drugs		
Rifamate	isoniazid + rifampin	
Rifater	isoniazid + rifampin + pyrazinamide	

Antimycobacterial agents are almost always used in combination. The frequency of resistance mutations and the number of bacteria present in a clinical infection dictate this therapeutic strategy.<sup>50</sup>

Each tuberculous lesion in an infected lung can contain 10<sup>8</sup> bacteria. The frequency of mutant resistance to any single antimycobacterial drug is about one in 10<sup>6</sup> bacteria. This means in each tuberculous lesion an average of about 100 bacteria are resistant to an antimycobacterial drug even before that drug is administered. Combination therapy with two drugs reduces the likelihood of encountering pre-existing resistance to about one bacterium in 10<sup>12</sup>. Treatment with four drugs further lowers this possibility to one in 10<sup>24</sup>. Resistance to antimycobacterial agents is primarily chromosomal. The treatment of infections with MBT can be divided into treatment of LTBI and treatment of TB disease. Guidelines with detailed management recommendations are published and updated regularly.<sup>1,51</sup>

#### **Treatment of Latent TB infection**

The risk for progression from LTBI to TB disease is highest during the first two years after infection and is often predicated on concomitant medical conditions that alter the ability of the immune system to maintain the isolation of MBT (Table 2).<sup>52-53</sup> HIV infection is the most important risk factor.<sup>55-59</sup> It has been estimated persons infected with MBT and co-infected with HIV have a 6-10% risk per year of developing TB disease, while an immunocompetent person infected with MBT has a 10% life-time risk for TB disease.<sup>60</sup> Isoniazid, given for nine months in a single daily dose, is the drug of choice for the treatment of LTBI.<sup>6</sup> Patients who become TST positive following exposure to patients with MBT resistant to isoniazid and those patients with intolerance to isoniazid may be treated with rifampin for four months.<sup>61</sup> For patients with known exposure to MDR TB disease, a regimen with two drugs to which MBT is susceptible is recommended for nine to 12 months.<sup>62,63</sup>

#### **The Treatment of LTBI in Pregnant Patients**

A TST or BAMT should be administered to all women who are at risk for MBT infection, and those who have LTBI should be treated to prevent maternal and congenital TB disease.<sup>6,64</sup> It is postulated an MBT infection in utero is either the

result of (1) hematogenous infection through the umbilical vein or (2) prenatal aspiration of infected amniotic fluid.<sup>65,66</sup> Congenital TB is rare but fatal if untreated and it is difficult to diagnose in time to treat successfully without knowledge of a maternal history of TB.<sup>66,67</sup> Isoniazid is considered safe for the treatment of LTBI in pregnancy.<sup>68</sup>

### **Treatment of TB Disease**

#### **Treatment of Susceptible TB Disease**

All isolates of MBT are tested for antimycobacterial susceptibility, but results generally do not become available for at least two weeks. Until susceptibility results are available, the empirical initial phase of treatment consists of isoniazid, rifampin, pyrazinamide, and ethambutol.<sup>1,51</sup> When the infection proves to be caused by fully susceptible strains of MBT, the initial phase of treatment continues for two months with isoniazid, rifampin, and pyrazinamide. The continuation phase of treatment, predicated on the results of sputum cultures at two months, may last for an additional four to seven months (Table 5).<sup>1,51</sup>



Disseminated TB disease, tuberculous meningitis, and infections in children are usually treated for nine to 12 months. Osteomyelitis is usually treated for six to nine months. For patients who cannot tolerate rifampin, an alternative nine to 12 months regimen includes isoniazid, ethambutol, and pyrazinamide, with or without a fluoroquinolone.

#### **Treatment of Resistant TB Disease**

Resistance to isoniazid is the most common pattern to mycobacterial drug resistance. These infections are treated with rifampin, pyrazinamide, and ethambutol for six to nine months.<sup>51</sup> Streptomycin is an alternative to ethambutol, and a fluoroquinolone is often added to the regimen if there is extensive disease. MDR TB disease is treated with  $\geq 4$  drugs to which the organisms are susceptible. Three drugs are usually given by mouth and the fourth by injection. AFB smears and cultures are performed monthly and treatment is continued for 18 to 24 months or 12 to 18 months after the microbiological studies become

**Table 5. Duration of standard continuation therapy for susceptible MBT.<sup>1,51</sup>**

Initial Chest Radiography	Microbiology at 2 Months		Drug Regimens	Duration in Months
	AFB smear	AFB culture		
-	-	-	isoniazid/rifampin	4
			isoniazid/rifapentin	4
-	-	+	isoniazid/rifampin	4
			isoniazid/rifapentin	7
-	+	+	isoniazid/rifampin	4
+	+	-	isoniazid/rifampin	4
+	+	+	isoniazid/rifampin	7

negative. The parenteral drug is continued for six months after culture conversion.

#### **Treatment of TB Disease in Patients with HIV Infection**

The treatment of TB disease is complicated by co-infection with HIV.<sup>1,51</sup> CD4 cell counts <100 cells/ml have been associated with rifamycin resistance. Furthermore, rifamycins induce hepatic CYP3A4 enzymes and can accelerate the metabolism of protease inhibitors and some non-nucleoside reverse transcriptase inhibitors, decreasing their bioavailability to sub-therapeutic levels.

#### **Treatment of TB disease in the Pregnant Patient**

Untreated LTBI can lead to maternal and congenital TB disease. Hematogenous infection of the fetus through the umbilical vein leads to primary lesions in the liver, and prenatal aspiration of infected amniotic fluid leads to primary gastrointestinal and pulmonary disease.<sup>65,66</sup> When there is moderate to high suspicion of TB disease during pregnancy, treatment is initiated because the risk of TB disease to the fetus is greater than the risk of adverse drug effects. The initial regimen includes isoniazid, rifampin, and ethambutol. Each of these drugs crosses the placenta but none is

teratogenic. Pyrazinamide is probably safe and may be substituted for ethambutol, depending on susceptibility testing.<sup>68</sup>

#### **TB Infection-Control Strategies in Oral Healthcare Settings**

There is a paucity of data linking dental instrumentation to the generation of droplet nuclei containing MBT (Figure 4).<sup>69,70</sup>

Similarly, the reported incidence of TST conversion among oral healthcare workers (OHCWs) is low.<sup>71-73</sup> However, it can be anticipated that OHCWs and patients with infectious TB disease will generate droplet nuclei by coughing, sneezing, laughing, and talking; therapeutic intervention could further stimulate coughing and promote the generation of infectious particles. Since patients and OHCWs share the same air space, the potential for the transmission of MBT cannot be discounted.<sup>74</sup> The probable transmission of MDR TB disease from patients to two OHCWs has been documented, and there is evidence of TB disease transmission from an oral surgeon to 15 patients following extractions.<sup>75,76</sup>

The 2005 CDC guidelines for preventing the transmission of MBT in healthcare facilities explicitly identify oral healthcare settings as outpatient settings in which patients with



**Figure 4.** While high-speed and ultrasonic dental instrumentation clearly generate droplet nuclei, there is a paucity of data linking dental instrumentation to the generation of droplet nuclei containing MBT.

suspected or confirmed infectious TB disease are expected to be encountered.<sup>1</sup> This inclusion is based on the assumption patients with infectious TB disease may present in the dental setting for urgent or routine dental care and OHCWs might share air space with persons with infectious TB disease or might come in contact with clinical specimens that contain MBT. Consequently, every oral healthcare facility should have a TB infection-control plan that is part of its written infection control/exposure control protocol.

Standard precautions provide a hierarchy of preventive strategies to prevent or reduce the risk of occupational exposure to blood and other potentially infectious material (OPIM). However, standard precautions are inadequate to prevent

the spread of organisms through droplet nuclei 1-5  $\mu\text{m}$  in diameter, and additional measures (e.g., transmission-based precautions) are necessary to prevent the spread of MBT. The TB infection-control component of an overall infection control/exposure control program should be appropriate for the level of risk in the specific healthcare setting and should be based on a three-level hierarchy of administrative, environmental, and respiratory-protection controls.<sup>1,77-79</sup> The CDC recognizes the specific details of a TB infection-control program will differ from setting to setting according to the prevalence of TB in the community, the patient population served in the setting, and the type of oral healthcare services provided in the setting.

### **Administrative Controls**

In the three-level hierarchy of TB infection-control program, the first and most important level is the implementation of administrative controls (Table 6).<sup>1</sup>

Administrative controls are intended to reduce the risk of exposure to persons who might have infectious TB disease, and they are essential prerequisites for the effectiveness of environmental controls and respiratory-protection controls in all settings where patients with suspected or confirmed TB disease are expected to be encountered.<sup>1</sup>

### ***TB Risk Assessment for the Oral Healthcare Setting***

As mentioned previously, the overall risk of OHCWs for exposure to a patient with infectious TB disease is probably low. Nevertheless, every oral healthcare setting should conduct initial and ongoing (annual) evaluations of TB risk for the setting.<sup>1</sup> Determine the demographics of the patient population served in the setting (see Table 1 and Table 2). The TB risk assessment for the community will determine the types of

**Table 6. Administrative control.**<sup>1</sup>

1. Conduct a TB risk assessment for the oral healthcare setting
2. Develop, implement, and enforce a written TB infection-control plan to ensure prompt detection, airborne infection isolation, and treatment of persons with suspected or confirmed TB disease
3. Implement an ongoing training and education program
4. Screen and evaluate OHCWs who are at risk for TB disease or who might be exposed to MBT



administrative, environmental, and respiratory-protection controls that are needed for the particular setting. Consult with the local or state health department.

### ***TB Infection-control Program the Oral Healthcare Setting***

The primary risk of exposure to MBT in the oral healthcare setting is contact with patients with undiagnosed or unsuspected infectious TB disease.<sup>1</sup> A high index of suspicion and rapid implementation of precautions are essential to prevent and interrupt the transmission of MBT. Specific precautions will vary depending on the setting, i.e., prevalence of TB in the community, patient population served (Table 1), and the type of services provided in a particular setting. Minimum requirements in a community-based oral healthcare setting is implementation and enforcement of a TB infection-control protocol that provides for the following:

1. Prompt identification of patients with suspected or confirmed infectious TB disease.
2. Separation of patients with suspected and confirmed TB disease from other OHCWs and patients.
3. Referral of patients with suspected and confirmed TB disease for a medical evaluation and/or required oral healthcare procedures to a facility with appropriate environmental controls and respiratory-protection controls.<sup>1</sup>

### ***Identification of Patients with Suspected or Confirmed TB Disease***

When reviewing medical histories (initial and periodic update), including a review of organ

systems, all patients should be routinely asked about the following:

1. Their history of exposure to TB, LTBI, and any history of TB disease.
2. Any medical conditions that increase the risk of TB disease (Table 2).
3. Any signs and symptoms of TB disease (see Clinical Manifestations).<sup>1</sup>

Patients with a history of LTBI and confirmed TB disease should be questioned about the status of their antimycobacterial treatment. Ideally, the medical history should be elicited from patients in their primary language with the assistance of an interpreter if necessary. A provisional diagnosis of respiratory TB disease should be considered for any patient with signs and symptoms of infection in the lungs or airways, coughing for >3 weeks, loss of appetite, unexplained weight loss, night sweats, bloody sputum or hemoptysis, hoarseness, fever, fatigue, and chest pain.<sup>1</sup>

### ***Isolation of Patients with Suspected or Confirmed TB Disease from Other Patients and OHCWs***

Patients suspected of having TB disease and patients with documented infectious TB disease who have not completed antimycobacterial treatment should not be kept in the community-based oral healthcare setting any longer than required. While in the oral healthcare setting, these patients should be promptly isolated from other patients and OHCWs and instructed to observe strict respiratory hygiene and cough etiquette procedures.<sup>1</sup> They should wear a surgical mask (if possible). When coughing or sneezing, they should turn their heads away from other persons and cover their mouth and nose with their hands or preferably a disposable facial tissue.

### ***Referral of Patients with Suspected or Confirmed TB Disease for a Medical Evaluation and/or Required Urgent Dental Care***

Routine dental care should be postponed until a physician confirms the patient does not have infectious TB disease or until confirmation the patient is no longer infectious.<sup>1</sup> Oral healthcare settings in which patients with suspected or confirmed TB disease are rarely seen and in which such patients are not treated are not

**Table 7. Suggested components of a TB education and training program for OHCWs.<sup>1</sup>**

- Epidemiology of TB in the local community, the U.S., and worldwide
- Basic concepts of MBT transmission, pathogenesis, clinical signs and symptoms, diagnosis of LTBI and TB disease, and treatment of LTBI and TB disease
  - TB and impaired immunity
- Potential for occupational exposure to infectious TB disease in the oral healthcare setting
  - TB infection-control surveillance
- The hierarchy of TB infection control measures in the oral healthcare setting
  - Administrative controls
  - Environmental controls
  - Respiratory-protection controls

required to develop and implement environmental controls and respiratory-protection controls. Consequently, patients with suspected or confirmed TB disease requiring urgent dental care must be promptly referred to an oral healthcare facility that meets the requirements for an airborne infection isolation (AII) room (see Environmental Controls); while performing procedures on such patients, OHCWs should use at least an N95 disposable respirator (see Respiratory-Protection Controls).

#### ***TB Education and Training Program for OHCWs***

Education and training of OHCWs is an essential part of administrative controls in a TB infection-control program. OHCWs include all paid and unpaid persons working in the oral healthcare setting who have the potential for exposure to MBT through air space shared with persons with suspected or confirmed infectious TB disease.<sup>1</sup> By definition, this includes all full-time, part-time, temporary and contract personnel, as well as students (dental, dental hygiene, and dental assistant). Table 7 reflects suggested elements of a TB education and training program for OHCWs.<sup>1</sup> The level of training will vary according to the risk classification of the setting. The training may be combined with other required infection-control-related education and training programs and should be documented.

#### ***Screening for LTBI and TB Disease in OHCWs***

The CDC recommends the TB risk classification for the setting be used to determine the need for and the frequency of TB screening of HCWs.<sup>1</sup>

The classification of low risk is applied to settings in which persons with infectious TB disease are not expected to be encountered. This classification also applies to HCWs who will never be exposed to persons with infectious TB disease or to clinical specimens that might contain MBT. The CDC also states if uncertainty exists regarding whether to classify a setting as low risk or medium risk, the setting typically should be classified as medium risk. The CDC guidelines explicitly identify oral healthcare facilities as settings in which patients with suspected or confirmed TB disease are expected to be encountered. Consequently, oral healthcare facilities are considered medium risk settings. All paid and unpaid OHCWs who have the potential for exposure to MBT through air space shared with persons with suspected or confirmed infectious TB disease or to clinical specimens that might contain MBT shall be included in the TB screening program. The administration, reading, and interpretation of TST or other tests are to be performed by trained personnel as follows:

- **Baseline TB Screening.** All OHCWs should receive baseline TB screening at the time of hire, using the two-step TST or a single BAMT such as the QFT-G.<sup>1</sup>
- **Follow-up TB Screening.** After baseline testing, follow-up TB screening should be performed annually.<sup>1</sup> All OHCWs should be symptom screened, and those with baseline-negative results should to be retested (TST or BAMT).<sup>1</sup>

### ***Management of Baseline-positive or Newly-positive OHCWs***

OHCWs with positive test results should be evaluated promptly for TB disease.<sup>1</sup> A thorough history of the exposure to MBT should be obtained to determine whether the infection is occupational or community acquired. Baseline-positive and newly-positive OHCWs and those with documented treatment for LTBI or TB disease should receive one chest radiograph as part of the evaluation to rule out TB disease. If the result of the initial radiographic examination is negative, no further radiographs are necessary unless symptoms suggestive of TB disease develop. Periodically, OHCWs with positive test results should be reminded about the signs and symptoms of TB disease and the need for prompt evaluation of any pulmonary symptoms. Routine chest radiographs are not required on TST- or BAMT-negative personnel.

## **TB Infection-Control Strategies in Oral Healthcare Settings**

### **Administrative Controls**

#### ***Preventive Therapy***

Preventive therapy (see Treatment of LTBI) should be offered to all personnel with baseline-positive TST or BAMT results if they are younger than 35 years. It should further be offered to the all personnel, regardless of age, who have conversion of their TST or BAMT results. Preventive therapy may be provided through the local or state health department or by other healthcare providers, as appropriate.<sup>1,6</sup>



#### ***Post-exposure Management of OHCWs***

As soon as possible after an exposure to MBT (i.e., exposure to a person with pulmonary or

laryngeal TB for whom proper isolation precautions have not been implemented), TST or BAMT testing should be done on personnel known to have had negative results on previous testing.<sup>1</sup> If the initial post-exposure test is negative, repeat the test 12 weeks after exposure. Do not perform TST or BAMT testing or chest radiographs on personnel with previous positive test results, unless they have symptoms suggestive of TB disease.

#### ***Workplace Restrictions for OHCWs***

Personnel with TB disease (pulmonary or laryngeal) should be excluded from the workplace until documentation is provided from their healthcare provider that (1) they are receiving adequate therapy, (2) their cough has resolved, and (3) they have had three consecutive sputum smears collected on different days with negative results for AFB.<sup>1</sup> After personnel return to work, obtain periodic documentation from their healthcare provider that effective drug therapy has been maintained for the recommended period of time and that sputum smears remain negative for AFB.

Personnel with TB disease who discontinue treatment before cured should be promptly evaluated for their infectious status. Exclude from duty those who are found to remain infectious until (1) treatment is resumed, (2) an adequate response to therapy is documented, and (3) sputum smear results are negative for AFB.<sup>1</sup> Consider direct observed therapy for personnel with TB disease who have not been compliant with drug regimens. Do not exclude personnel from the workplace who have TB only at sites other than the lung or larynx. Do not restrict personnel from their usual duties if they are receiving preventive therapy because of positive TST results, even if they are unable or unwilling to accept or complete a full course of preventive therapy. Instruct them to seek prompt evaluation if symptoms suggestive of TB disease develop.

#### ***Immunocompromised OHCWs***

OHCWs who are known to be immunocompromised should be referred to their personal health professionals who can individually counsel them regarding their risk of TB.<sup>1</sup> At the request of immunocompromised personnel, offer accommodations for work settings in which they would have the lowest possible risk for occupational exposure to MBT. Consider the provisions of the

Americans With Disabilities Act of 1990 and other federal, state, and local regulations in evaluating such situations.

### Environmental Controls

The second level of hierarchy is the use of environmental controls. Environmental controls are physical or mechanical measures (as opposed to administrative measures) intended to prevent the spread and reduce the concentration of infectious droplet nuclei 1-5  $\mu\text{m}$  in diameter in ambient air. Patients with suspected or confirmed TB disease requiring urgent dental care must be treated in a room meeting requirements for airborne infection isolation (an "All room").<sup>1</sup> All rooms provide negative pressure in the room so air flows under the door gap into the room. They have an air exchange rate of 6-12 ACH (air exchange rate as the number of air exchange units per hour), and a direct exhaust of air from the room to the outside of the building, or provide for a recirculation of air through a high efficiency particulate air (HEPA) filter.

### Respiratory Protection Controls

The first two control levels minimize the number of areas in which exposure to MBT might occur, thus, minimizing the number of persons exposed.

However, these controls do not eliminate the risk of exposure in limited areas. The third level of the hierarchy is the use of respiratory equipment in situations that pose a high risk for exposure. OHCWs performing urgent dental care on a patient with suspected or confirmed TB disease must wear at least an N95 disposable respirator.<sup>1</sup> N95 disposable respirators are nonpowered, air-purifying, particulate-filter respirators. The N (not resistant to oil)-series respirators are available with filtration efficiencies of 95% (N95), 99% (N99), and 99.7% (N100) when challenged with 0.3  $\mu\text{m}$  particles.

### Summary

The risk of MBT transmission in the oral healthcare setting is probably low, but the consequences of exposure can be substantial. Consequently, OHCWs must be knowledgeable about the potential risks of occupational exposure, the importance of TB infection-control surveillance, and the importance of post-exposure management strategies for those potentially exposed to MBT. A clear, written TB infection-control protocol should promote the importance of surveillance in the setting and provide for timely clinical care for patients with suspected or confirmed TB disease.

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