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Tuberculosis

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Educational Objectives

Upon completion of this course, the student should be able to:

- Detail the history of Tuberculosis.
- Understand the difference between latent infection and disease.
- Describe the process of Tuberculosis transmission.
- Recognize risk factors associated with Tuberculosis disease.
- Discuss the testing and diagnostic procedures associated with Tuberculosis.
- Understand the management and referral of patients with infectious Tuberculosis.
- Assess the dental practice setting for risk of Tuberculosis transmission.
- List elements of a good dental office Tuberculosis Control Plan.

Introduction

According to the Centers for Disease Control and Prevention, “Although TB case counts and incidence are decreasing in the United States, progress is insufficient to achieve in this century the goal of TB elimination. Measures to diagnose and treat active TB disease must continue, and new strategies aimed at accelerating progress toward TB elimination in the United States, such as targeted testing for and treatment of LTBI, should also be employed. Expanded partnerships with health care providers outside of the public health sector will be important in effectively implementing such a strategy” (Schmit et al, 2020).

TB Infection simply means that the individual has the bacteria present in his or her body and may develop TB in their lifetime. A person who only has TB infection cannot spread TB. A person with TB disease gets sick (has symptoms of the disease) and can spread the disease. An individual is capable of infecting others with *M. tuberculosis* only when the disease is active. Understanding the difference between TB infection and TB disease is fundamental in controlling TB. In the US, 90% of infected individuals will remain free from developing TB disease in their lifetime. Five percent (5%) of recently infected individuals will develop TB disease within 1-2 years after infection. The other 5% will develop TB later in life. Therefore, the greatest risk of developing TB disease is within the first 1-2 years after infection.

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Statistical Timeline

“...it was the fashion to suffer from the lungs; everybody was consumptive, poets especially; it was good form to spit blood after each emotion that was at all sensational, and to die before reaching the age of thirty” (Alexandre Dumas, Author, *The Three Musketeers*, *The Count of Monte-Cristo*)

According to a morbidity and mortality weekly report done March 24th 2017, on the Center for Disease Control and Prevention website, “In 2016, a total of 9,287 new tuberculosis (TB) cases were reported in the United States; this provisional* count represents the lowest number of U.S. TB cases on record and a 2.7% decrease from 2015 (1). The 2016 TB incidence of 2.9 cases per 100,000 persons represents a slight decrease compared with 2015 (-3.4%) (Figure). However, epidemiologic modeling demonstrates that if similar slow rates of decline continue, the goal of U.S. TB elimination will not be reached during this century. Although current programs to identify and treat active TB disease must be maintained and strengthened, increased measures to identify and treat latent TB infection (LTBI) among populations at high risk are also

needed to accelerate progress toward TB elimination” (Schmit et al., 2017).

Today, the recent TB epidemic continues worldwide. In the poorer countries, TB still ravages the population. In the richer countries, a routine decline in the incidence of TB halted in the 1980's. Immigration, HIV infection, and drug resistance are factors within the more developed countries that have caused this turnaround in the occurrence of TB (Sarrel, M, 2006).

As a part of its Stop TB Strategy, the WHO firstly relies on Directly Observed Therapy (DOT). Many patients do not continue to comply with the drug regime as it may be required for up to a full year; therefore, DOT helps to ensure that the drugs are being used as needed (Marais, F, 2019).

Excerpt from online source for the World Health Organization:
<http://www.who.int/mediacentre/factsheets/fs104/en/>

WHO pursues 6 core functions in addressing TB:

1. Providing global leadership on matters critical to TB.
2. Developing evidence-based policies, strategies and standards for TB prevention, care and control, and monitoring their implementation.
3. Providing technical support to Member States, catalyzing change, and building sustainable capacity.
4. Monitoring the global TB situation, and measuring progress in TB care, control, and financing.
5. Shaping the TB research agenda and stimulating the production, translation and dissemination of valuable knowledge.
6. Facilitating and engaging in partnerships for TB action.

The WHO "End TB Strategy", adopted by the World Health Assembly in May 2014, is a blueprint for countries to end the TB epidemic by driving down TB deaths, incidence and eliminating catastrophic costs. It outlines global impact targets to reduce TB deaths by 90%, to cut new cases by 80% between 2015 and 2030, and to ensure that no family is burdened with catastrophic costs due to TB.

Ending the TB epidemic by 2030 is among the health targets of the newly adopted Sustainable Development Goals. WHO has gone one step further and set a 2035 target of 95% reduction in deaths and a 90% decline in TB incidence – similar to current levels in low TB incidence countries today.

The Strategy outlines three strategic pillars that need to be put in place to effectively end the epidemic:

- Pillar 1: integrated patient-centred care and prevention
- Pillar 2: bold policies and supportive systems
- Pillar 3: intensified research and innovation

The success of the Strategy will depend on countries respecting the following 4 key principles as they implement the interventions outlined in each pillar:

- government stewardship and accountability, with monitoring and evaluation
- strong coalition with civil society organizations and communities
- protection and promotion of human rights, ethics and equity
- adaptation of the strategy and targets at country level, with global collaboration.

5000 to 2400 BC	The earliest evidence of tuberculosis (TB) in humans is from a Neolithic grave in Germany, dating back to 5000BC. Egyptian mummies showed evidence of spinal tuberculosis. The Babylonians, Greeks and Hindus also mention a consumptive disease, which caused widespread death. Hippocrates, the Greek physician, documented the early stages of 'phthisis' (meaning, "I waste away") and its inescapable course of destruction (Marais, F 2017) (Sarrel, M. 2017) (Padilla, M. 2006).
1600's	<p>Writings discussed the potential infectious nature of the disease and described pathophysiologic conditions. By the early 1700's, Dr. Benjamin Martin (an English physician) wrote about "amiculae": tiny, minute creatures, which could generate the symptoms of Tuberculosis. In his work, A New Theory of Consumption, Dr. Martin contemplated the contagious nature of the disease. He warned against "...habitual lying in the same bed with a consumptive person...or very frequently conversing so nearly as to draw in part of the breath..." (Sarrel, M. 2017).</p> <p>Cures or effective treatment for consumption (early term for TB) remained elusive. In ancient times, individuals believed disease to be a curse or punishment. People used amulets, charms and ritual chants to dispel "the evil" from one's body.</p> <p>At the height of the epidemic, TB was believed to be an aristocratic disease, infecting primarily artists and scholars (Padilla, M. 2006).</p>
Early to Mid-1800's	As the disease spread, it became clear that consumption was not a disease restricted to the upper class. Nearly all

	Europeans were infected and one in four deaths was due to consumption (TB). In the US, one in five deaths were due to TB. Urbanization, crowded living conditions and malnutrition were all factors in the spread of TB (Sarrel, M. 2017) (Padilla, M. 2006).
In the mid-1800's	Discovery of a specific infectious agent dispelled any previous belief that TB occurs spontaneously. A French surgeon, Jean-Antoine Villemin, was able to "infect" healthy rabbits with the sputum of humans and cows (Padilla, M. 2006).
1881	Robert Koch isolated Mycobacterium tuberculosis (M. tuberculosis, or Mtb) as the cause of "consumption". Institutionalizing individuals with TB in "sanitariums" soon followed, in effect isolating diseased individuals from the general population. Tuberculosis sanitariums provide the consumptive individual with proper nutrition and fresh air. Surgical interventions (collapsing the lung and reducing lung volume) and the use of roentgenograms (x-rays) to monitor patients was instituted as part of patient therapy (Marais, F 2017) (Sarrel, M. 2017) (Padilla, M. 2006).
1921	Bacteriologists Calmette and Guerin attenuated a strain of Mycobacterium bovis (M. bovis) at the Pasteur Institute and administered it as a vaccine (known simply as BCG) destruction (Marais, F 2017) (Sarrel, M. 2017).
1943	Discovery of streptomycin provided the first effective treatment for those afflicted with TB. However, streptomycin-resistant TB appeared almost immediately (Sarrel, M. 2017).
1952, 1963	In 1952 isoniazid was introduced to combat TB. Later, in 1963, rifampicin was produced. These drugs, and others, in a four-drug regime have been of great use in the alleviation of TB (Sarrel, M. 2017).
1993	World Health Organization (WHO) declares rise of TB cases a global health emergency.
2000	WHO launches the Stop TB Strategy (WHO, May 2017).
2009	WHO calls for universal access to tuberculosis culture by 2015.
2012	FDA approves bedaquiline for treating multi-drug-resistant tuberculosis. It is the first new medicine for tuberculosis in more than forty years.
2015	The secretariat is based in Geneva, Switzerland and, since 2015, has been administered by UNOPS. Previously it was hosted by the World Health Organization.
2016-2020	The vision grows in ambition & turns into The Global Plan to End TB, not just to Stop TB. The World Health Assembly passed a resolution in May 2014 approving with full support

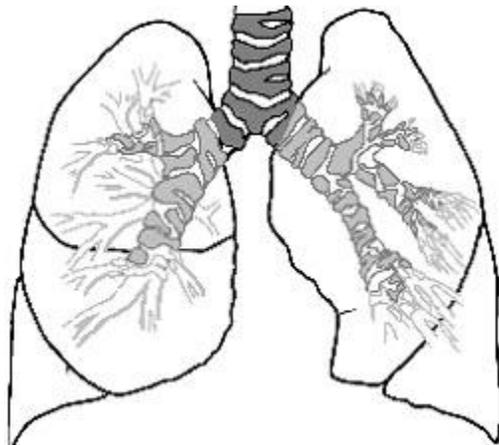
	the new post-2015 End TB Strategy with its ambitious targets.
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Pathogenesis

Definition

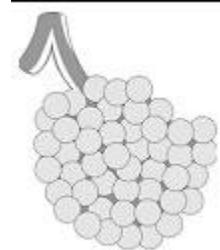
In the US, tuberculosis is primarily caused by *Mycobacterium tuberculosis*. Three other mycobacteria (*M. bovis*, *M. africanum* and *M. microti*) make up the *M. tuberculosis* complex and can cause TB. *M. bovis* and *M. africanum* are very rare in the United States (US) and *M. microti* does not cause TB in humans. Other mycobacteria (e.g., *M. leprae* and *M. avium*) which do not cause TB are called “nontuberculosis mycobacteria”.

Transmission



Inhalation of droplet nuclei from an infectious person is the primary mode of transmission. When an infectious person sneezes, coughs or in any other way expels infected particles into the air, another person can inhale the particles containing *M. tuberculosis*. Droplet nuclei (1-5 microns in diameter) can remain suspended in the air for several hours. Although large droplets can also be inhaled, they become lodged in the nose and throat and are unlikely to cause infection.

Droplet nuclei containing *M. tuberculosis* travel down into the alveoli where infection begins. The bacteria multiply in alveolar macrophages, and spread throughout the body via the lymphatic system and blood stream. TB is usually located within the lungs (pulmonary) or it can be located elsewhere in the body (extrapulmonary). TB disease occurring in multiple locations is Miliary TB.



Within 2-10 weeks, an individual's immune system usually halts the multiplication of the bacteria. Encapsulation of bacteria by granulomatous inflammation is part of the immune process. These encapsulated bacteria (tubercles) calcify and leave permanent scars in the lung. These scars are the hallmark of tuberculosis and are usually visible on a chest radiograph.

The tubercle bacilli may remain inactive for many years (latent infection). Infection progresses to disease when the immune system can no longer keep the tubercle bacilli under control.

Infection Versus Disease

TB Infection simply means that the individual has the bacteria present in his or her body and may develop TB in their lifetime. A person who only has TB infection cannot spread TB.

A person with TB disease gets sick (has symptoms of the disease) and can spread the disease. An individual is capable of infecting others with *M. tuberculosis* only when the disease is active.

Understanding the difference between TB infection and TB disease is fundamental in controlling TB. Please review Table 1 to become familiar with the similarities and differences between infection and disease.

Table 1 Differences Between TB Infection and Disease (CDC, 2020)	
TB Infection	TB Disease (In the lungs)
Tubercle bacilli in the body	
Tuberculin skin test reaction usually positive	
Chest radiograph usually normal	Chest radiograph usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures positive
No symptoms	Symptoms (cough, fever, weight loss, night sweats)
Not Infectious	Often infectious prior to treatment
Not a case of TB	A case of TB

In the US, 90% of infected individuals will remain free from developing TB disease in their lifetime. Five percent (5%) of recently infected individuals will develop TB disease within 1-2 years after infection. The other 5% will develop TB later in life. Therefore, the greatest risk of developing TB disease is within the first 1-2 years after infection (CDC, 2020).

Although any extrapulmonary site where tubercles are located may be the foci for new growth of *M. tuberculosis*, the upper lung is the usual site for re-activation. Conditions that increase risk of progression from infection to disease are listed in Table 2.

Table 2 Conditions That Increase Risk of TB Disease (CDC, 2020)	
AIDS	170 times higher
HIV Infection	≥ 100 times higher
Recent infection with <i>M. tuberculosis</i> (within 1-2 years)	15 times higher
Certain other medical conditions	3-16 times higher

HIV-infection is the strongest known risk factor for progression of TB infection to TB disease. The risk of progression from TB infection to TB disease is 7 to 10% per year in individuals infected with both HIV and *M. tuberculosis*. Other medical conditions that increase the risk of progression from infection to disease include certain types of cancer, immunosuppressive therapy, kidney and intestinal diseases, diabetes mellitus and low body weight (10% to 19% or more below ideal). Injection of illicit drugs also increases the risk. Intravenous drug users are at higher risk due to concomitant factors such as homelessness and exposure to other immuno-compromising agents.

Factors Influencing Transmission

As stated previously, disease transmission normally occurs through inhalation of droplet nuclei (containing *M. tuberculosis*) from an infectious person. If TB infection progresses to TB disease, an individual becomes infectious.

There are three factors influencing whether TB is transmitted:

1. Infectiousness of the person with TB,
2. Environment in which transmission takes place, and
3. Duration of exposure to infectious person.

Let us look at each one of these factors individually.

Infectiousness - The infectiousness of a person with TB depends on:

1. Where the TB disease is located:

Transmission of TB from extrapulmonary locations is unusual. Persons with active pulmonary or laryngeal TB are not infectious if they meet all the following criteria:

- They have received adequate therapy for 2 to 3 weeks,
- They have a favorable clinical response to therapy, and
- They have three consecutive negative sputum smear results from sputum collected on different days.

TB infection caused by inhalation of aerosols produced by tissue irrigation and autopsies have been reported but is highly unusual. Transmission through the skin (abscess containing *M. Tuberculosis*) does take place (Cleveland, Gooch, Bolyard, et al, 1995).

2. Whether or not he or she has started treatment:

The amount of treatment or therapy an individual has received influences their infectiousness. Individuals just beginning treatment for active TB disease are

more likely to spread TB because antibiotic therapy is not complete. Obviously, those individuals who are not yet diagnosed, have active disease and are not isolated, are at greatest risk for spreading TB. An individual with active TB, may not know that his or her behavior is placing others at risk for infection. Once educated, these individuals can take steps to prevent the TB infection in others.

3. His or her age:

The age of a person with TB is a factor. Adults, who can more forcefully cough or expel air, may be at an increased risk of spreading TB infection. Generally, children do not produce sputum when they cough.

Environment - Environment plays a critical role in the transmission of TB. Overcrowded and poorly ventilated areas are conducive to transmission.

Duration - Frequent and prolonged contact with an infectious individual increases the risk of transmission. Close contacts, who spend prolonged time with an infectious individual (e.g., family, friends and coworkers), are more likely to become infected. In the US, infection rates among close contacts to infectious individuals are approximately 30% (CDC, 2020).

Sites of Outbreaks and Transmission

Health care facilities, correctional facilities, and nursing homes are sites of disease transmission. Correctional facilities face high disease potential due to:

- a large percent of population infected with TB,
- an increasing number of HIV-infected individuals, and
- overcrowding and poor ventilation.

Nursing home residents face two times the disease rate of those outside nursing homes (CDC, 2020).

Outbreaks and transmissions are not isolated to the aforementioned settings; transmission can occur anywhere an infectious person is in contact with an uninfected individual. Schools, churches, subways, businesses, home, courtrooms, restaurants, and airplanes have been investigated as transmission settings.

Zoonotic transmission of TB (*M. bovis*) occurs via ingestion of infected dairy products. Pasteurization and TB control methods make this type of transmission rare. Wild and/or exotic domesticated animals are sources of zoonotic *M. bovis* transmission. One outbreak investigation, "...strongly suggests *M. tuberculosis* transmission between humans and elephants, as evidenced by DNA fingerprinting" (Michalak, Austin, Siesel, et al, 1998).

Clinical Manifestations

Symptoms occur when TB infection progresses to TB disease. TB may mimic other conditions (e.g., fungal infections, bronchitis and pneumonia).

Systemic symptoms of TB (pulmonary and extrapulmonary) include:

- Fever
- Malaise
- Night sweats
- Loss of appetite
- Weight loss
- Fatigue

Pulmonary Tuberculosis

85% of all TB cases are pulmonary.

Symptoms of pulmonary TB include:

- Productive cough (lasting more than three weeks)
- Chest pain (dull aching or tightening)
- Hemoptysis (coughing up blood)

Extrapulmonary Tuberculosis

Extrapulmonary TB accounts for 15% of all TB cases. TB can be located just about anywhere in the body.

Common extrapulmonary TB sites include:

- Spine
- Genitourinary
- Lymph Nodes
- Bones
- Meninges
- Peritoneum
- Pericardium

Extrapulmonary TB disease is more common in HIV-infected individuals. Symptoms of extrapulmonary TB depend upon the location of the organ or tissue infected.

Screening and Diagnosis

The purpose of screening individuals for TB is to (1) identify infected individuals who are

at high risk for TB disease, (2) identify persons with TB disease who need treatment, and (3) identify persons with TB disease in places where risk of transmission is high.

There are four components in diagnosing TB disease:

1. Interview, Medical History and Physical Examination
2. Tuberculin Skin Test
3. Chest Radiograph
4. Bacteriologic Examination (of sputum)*

*The definitive test for diagnosing pulmonary TB disease is a positive M. tuberculosis culture.

Interview, Medical History, Physical Examination

Conducting a client interview and obtaining a health history is vital in order to find out whether a person was exposed, has symptoms, had prior TB disease or has risk factors for developing TB.

A physical exam alone cannot confirm TB infection or disease, yet this is a valuable component of the screening process. Most cases of TB disease are diagnosed when patients seek medical care for TB-related symptoms or other medical conditions.(5) Physical examination and interviews allow the practitioner to become familiar with the individual's general health and other information that may be useful in the diagnosis and treatment of TB.

Mantoux Skin Test

The Mantoux skin test (Tuberculin Skin Test, PPD Test) is the standard test used to evaluate individuals for TB infection. This test detects an immune response to tuberculin, not the presence of tuberculin bacilli.

An injection of purified protein derivative (PPD) tuberculin is delivered intradermally to the inner surface of the forearm. This technique produces a wheal (pale elevation of skin) 6-10 mm in diameter. Between 48 and 72 hours later, a trained health care worker evaluates the reaction. A positive reaction to the Mantoux skin test results in a palpable swelling, or induration. The induration is measured in millimeters. Redness, discoloration and/or bruising **is not** measured, **nor** is it indicative of a positive reaction. It generally takes 2-10 weeks after TB infection for an immune response to take place.

Generally, a reading of ≥ 15 mm is positive in individuals with no risk factors. Please review Appendix A for an in-depth look at the classification of positive Mantoux test results.

Interpreting a positive result depends on individual risk factors for TB and the size of the

induration. **False-positive** and **false-negative** results occur. (See Table 3). Most people who have had a positive skin test reaction will always have a positive reaction if tested in the future. This is true whether they receive treatment or not.

Table 3 Reasons for False-Positive and False-Negative Skin Test Results	
False-positive	False-negative
Infection by nontuberculosis mycobacteria Vaccination with BCG Skin test is given/or read incorrectly	Anergy Recent Infection (< 10 weeks) Young age (< 6 months of age) Skin test is given/or read incorrectly
Note: Any individual with symptoms of TB should be evaluated for disease regardless of their skin test reaction.	

False-Positive Reactions

The two primary causes of a false-positive reaction are infection with another mycobacterium other than *M. tuberculosis* and previous vaccination with BCG.

False-Negative Reactions

Anergy (lack of response) is possible in individuals with HIV infection or other severe viral infections, Hodgkin’s disease, and other immunosuppressive conditions. PPD tests used before the body is able to launch an immune response will give a false negative result. Individuals who are close contacts of someone with infectious TB should be re-tested 10 weeks after their last contact with the infectious individual. Very young individuals (< 6 months of age) do not have fully developed immune systems and therefore may have a false-negative reaction.

Chest Radiograph

A chest radiograph is recommended:

- after positive skin test
- if TB symptoms are present
- when skin test results may be unreliable
- when diagnostic delays may result in large-scale exposure, or
- if prevalence of TB disease is high.

A chest radiograph does not definitively diagnosis TB disease. A radiograph rules out active pulmonary TB or uncovers abnormalities suggestive of previous TB disease or silicosis. Infiltrates (collection of fluid and cells in the tissues of the lungs) or cavities (hollow spaces within the lung that may contain tubercle bacilli) can appear on a chest radiograph. However, a person with TB disease can have a “normal” chest radiograph.

Bacteriological Examination: Sputum Smear and Culture

Sputum is material brought up from the respiratory tract (lungs). Saliva, or mucus from the nose and throat are not considered good specimens. Extrapulmonary TB may be identified using urine, spinal fluid, etc. The first step in this process is a smear examination. The detection of acid-fast bacilli (AFB) provides the first clue that mycobacteria are present. The definitive test for diagnosing pulmonary TB disease is a positive *M. tuberculosis* culture. Because many individuals with TB disease have negative AFB smears, cultures are done on all specimens. Results are available within ten days to two weeks.

Drug susceptibility testing determines what anti-tuberculosis agents will be effective in treatment.

Counseling and HIV testing is available to anyone suspected or confirmed with TB disease.

Reporting

Every state in the US, the District of Columbia, New York City, U.S. dependencies and possessions and independent nations in free association with the US require reporting of TB cases and suspects, by law. Refer to Appendix B for TB Control Office telephone numbers.

Verification of TB cases requires:

- Positive culture for *M. tuberculosis*, or
- Positive smear for AFB, but a culture has not or cannot be done, or
- Positive tuberculin skin test reaction, signs and symptoms of disease,
- treatment with two or more TB drugs and a complete diagnostic
- evaluation.

Early reporting of cases, suspects and drug susceptibility is vital in controlling TB. Drug susceptibility information is valuable in tracking drug-resistant *M. tuberculosis*.

After a case (or suspected case) of TB disease has been reported, a case worker is assigned and begins patient education, contact identification, medical referrals and development of an initial treatment and monitoring plan.

Prevention and Treatment of Tuberculosis

Levels of Prevention

Primary prevention efforts aim at reducing an individual's susceptibility to disease, illness or injury. Education, changes in lifestyle, and behavior modification are components of primary prevention. Secondary prevention is accomplished via screening and diagnostic procedures, which identify disease-producing states in a particular population. After a disease, illness or injury is diagnosed; Tertiary prevention strategies limit disability, slow progression and reduce the need for excessive care (Timmreck, 1994) (Copstead, 1995).

Primary Prevention of Tuberculosis

Identification and treatment of individuals with Tuberculosis disease is the first strategy in controlling Tuberculosis.

Primary prevention efforts include educating the public, health care workers and most importantly, groups at high risk. The education should include the nature of TB transmission, infection and disease. Your local health department (See Appendix B) can provide you with educational materials and more information about TB.

Attempts made to reduce TB transmission and progression to disease include economic support, nutritional support and HIV counseling. Targeting legislative, political, and cultural factors reduces the incidence of TB disease. Pressuring lawmakers to fund educational programs and improve living conditions of high-risk populations will help prevent the spread of TB. Once health care providers become aware of cultural influences that hinder participation in TB prevention and treatment programs, modifications can be made to make treatment acceptable.

Vaccine

The Bacillus Calmette Guerin (BCG) is a vaccine used in many countries to prevent TB disease.

BCG has not been adopted for widespread use in the US due to:

- the low risk of *M. tuberculosis* infection,
- its ability to cause a positive skin reaction (which complicates interpretation of tuberculin skin test result), and
- its questionable effectiveness in preventing *M. tuberculosis* infection (CDC,1996).

Secondary Prevention of Tuberculosis

Preventive Therapy

Screening tests (See Section “Screening and Diagnosis”), and preventative therapy accomplish secondary prevention efforts. Implementation of preventative therapy (treatment with anti-tuberculosis drugs) reduces the risk that TB infection will progress to TB disease. A description of these drugs is provided at the end of this section. Generally, persons under the age of 35, with no known risk factors for TB, are evaluated for preventative therapy if his or her PPD reaction is ≥ 15 mm.

Children under six months of age are at high risk for developing TB disease, if infected, and may have a false negative skin test reaction. If a child under the age of six months is exposed to infectious TB, the pediatrician is likely to begin preventive therapy, regardless of his or her lack of skin test reaction. (See Appendix C for details regarding selection of candidates for therapy.)

Before starting preventive therapy, a physician must rule out current or previous TB disease and contraindications to isoniazid (an anti-tuberculosis drug). Isoniazid (INH) is considered the primary anti-tuberculosis drug. The standard regimen for preventive therapy is daily isoniazid INH (INH) for a minimum of six continuous months for adults or six to nine months for children and adolescents. It is likely that INH therapy will continue for 12 months in individuals who are HIV-infected or immunosuppressed.

Individuals who may not adhere to the regimen undergo **directly observed prevention therapy (DOPT)**. This means a health care worker watches the patient swallow the medication. If an individual is resistant or intolerant to INH, rifampin (RIF) is used. The health provider monitors individual adherence to the prescribed regimen and possible side effects related to therapy.

Tertiary Prevention of Tuberculosis

Medical Treatment

Current treatment regimens can successfully treat individuals with active TB disease. The success of treatment depends on:

- Behaviors of patients and health care providers,
- Personal and social characteristics of patients and health care providers,
- Health care infrastructure,
- Extent of patient’s knowledge about TB,
- Quality of training health care providers have received, and
- Economic, political, legislative and cultural influences.

An individual with active TB is infectious. Special precautions or isolation may be necessary to keep the individual from transmitting TB to others. Once the individual begins treatment and continues to follow the prescribed regimen, the individual is usually noninfectious within days or weeks.

Four anti-tuberculosis drugs: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (SM) are used as initial treatment for most patients. The drug regimen is adjusted if side effects occur or after drug susceptibility tests are available.

First-line Drugs

Isoniazid (eye-soe-NYE-a-zid) is commonly abbreviated INH. It is used alone for preventive therapy or in combination with other antituberculosis drugs for treatment of active disease. INH is considered the primary preventive TB drug. Up to 20% of individuals taking INH will develop liver abnormalities.(23) The risk of developing liver problems while taking this drug increases with alcohol use, chronic liver disease and use of injected drugs. It is bactericidal, very active against *M. tuberculosis*, penetrates all body fluids, and inexpensive.

Rifampin (rif-AM-pin) is commonly abbreviated RIF. It is considered nontoxic and is bactericidal for *M. tuberculosis*. It may accelerate clearance of drugs metabolized in the liver.

Pyrazinamide (peer-a-ZIN-a-mide) is commonly abbreviated PZA. This tuberculocidal drug works on mycobacteria within the macrophages.

Ethambutol (e-THAM-byoo-tole) is commonly abbreviated EMB. This drug is considered bacteriostatic on *M. tuberculosis*.

Streptomycin, commonly abbreviated SM, is an Aminoglycoside (a-mee-noe-GLYE-koe-side). Aminoglycosides treat a variety of severe bacterial infections. Injection of this drug is necessary because it is not absorbed from the gut.

Second-line Drugs

- Para-aminosalicylic acid
- Ethionamide
- Cycloserine
- Capreomycin
- Kanamycin

Surgical Intervention

The use of corticosteroids and surgery is more common in cases of extrapulmonary TB.

Surgery enables access to diseased sites to obtain specimens of infected fluids.

Complications in Treating TB

Nonadherence to Therapy

Nonadherence to prescribed treatment regimen complicates recovery. 25% of individuals receiving treatment for TB disease do not complete the program within 12 months.(7) Inadequate treatment leads to relapse, continued transmission and the development of drug resistance. If an individual refuses treatment for TB (and it is determined that he or she presents a threat of infecting others) legal intervention can be used to assure compliance.

Use of DOT for all patients is ideal. When a health care worker watches the patient take his or her medication, the incidence of disease relapse and drug resistance is significantly reduced. The health provider prescribes fixed-dose combinations when therapy is self-administered.

The length of treatment depends on the type of drugs used, drug susceptibility and the patient response. Most adults complete therapy in 6 to 9 months. HIV-infected individuals receive the same therapy but as mentioned earlier, may need to remain in treatment longer if response is slow. Extrapulmonary TB, with few exceptions, requires the same regimen as pulmonary TB.

Drug-resistant TB

Resistance to drugs used to treat TB **usually** stems from inadequate prior treatment. Strains of drug-resistant TB exacerbate successful treatment of active disease. Resistance to antibiotics began with the streptomycin, the first antibiotic used to treat TB. Multidrug-resistant tuberculosis (MDR-TB) is TB that is resistant to at least INH and RIF. Drug susceptibility tests guide decision making regarding drug regimen and DOT monitoring. Drugs used to treat MDR-TB are generally less effective and cause significant side effects. These factors extend the time needed to treat individuals, which increases the likelihood of nonadherence.

Groups at risk for drug-resistant TB include (Simone and Dooley, 1994):

- Individuals who have been previously treated with antituberculosis drugs,
- Contact of individuals who have drug resistant tuberculosis,
- Foreign born individuals from a country with a high prevalence of drug resistant tuberculosis, and
- Individuals whose smear or culture remain positive after having been treated for three consecutive months with antituberculosis drugs.

Individuals with drug-resistant TB will be infectious for a longer period of time. Isolation of individuals with MDR-TB is likely, due to increased incidence of treatment relapse or failure.

HIV and AIDS-Related TB

This risk of TB infection is no greater in HIV-infected individuals. However, HIV-infected individuals are at a much higher risk (up to 100%) of developing TB disease than those infected with *M. tuberculosis* alone (CDC, 2020). Progression from TB infection to disease occurs more rapidly and diagnosis may be complicated by unusual chest radiographs and coinfection with other pulmonary pathogens. HIV-related MDR-TB outbreaks have occurred with very high mortality rates (Simone and Dooley, 1994).

Epidemiology of Tuberculosis

TB in the US

The national TB statistics reported by the Centers for Disease Control and Prevention, show that in 2014 a total of 9,421 new TB cases were reported in the United States. This was a decline of 1.5% from 2013. The reported case rate was 3.0 cases per 100,000 population, which is 2.2% lower than the rate in 2013. These are the lowest rates recorded since national reporting began in 1953, although the declines are small.

It is believed that less than 230 of these cases of TB were bovine TB caused by *Mycobacterium bovis*.

Foreign born people continued to be disproportionately affected. In 2014, 66% of TB cases occurred in foreign born people. The top five countries of origin of foreign born persons with TB were Mexico, the Philippines, India, Vietnam and China.

It is likely that TB infection in these individuals occurs before immigration into the US. Racial and ethnic minorities 75% of the reported TB cases in the US (CDC, 2017).

Increased rates in these groups may be due to other risk factors such as:

- low socioeconomic status,
- higher rates of HIV infection,
- immigration from a country with a high prevalence of TB, and
- exposure to TB in congregate settings.

Groups with a high prevalence of TB Infection include:

- Residents of long term care facilities,
- Persons who inject drugs,
- Locally identified high risk groups (migrant workers, homeless persons), and

- Persons who may have occupational exposure to TB.

TB in the World

Although TB is declining in the US, it is worsening in southeast Asia, eastern Europe and sub-Saharan Africa. “It is estimated that between 2000 and 2020, nearly one billion people will be newly infected, 200 million people will get sick, and 35 million will die from TB - if control is not further strengthened” (WHO, 2017).

- Someone in the world is newly infected with TB every second (WHO, 2017).
- Infection with the TB bacillus occurs in 1/3 of the world’s population (WHO, 2017).

Dental Implications

Now that you have a better understanding of the epidemiology and pathophysiology of TB infection and disease, you probably want to know how you can apply this knowledge to the dental setting.

Transmission of TB in Dental Settings

Routine observance of universal precautions is a familiar feature of any infection control plan. Infection control begins with a thorough knowledge of disease transmission and the design of a systematic method for preventing infection and disease transmission in the dental setting. Obtaining a thorough health history, clinical assessment, use of protective attire and barrier techniques, hand washing, and continuous training are the mainstays of an effective infection control protocol.

There is documentation of transmission of *M. tuberculosis* in the dental setting. One outbreak in England (1979-1980) resulted in 10 cases of TB (Smith, Mason, Davies, and Onions, 1982). Each of these ten individuals had teeth extracted by a dentist with active pulmonary TB. The site of the lesions included the palate, cervical lymph nodes, tooth socket and lungs. Transmission of MDR-TB between two dental workers may have occurred in an HIV dental clinic (Cleveland, Kent, et al, 1995). It is believed that one dental worker infected the other or that both workers were in contact with the same highly infectious patient. No positive skin test results were found in any other dental staff member.

These incidents are troubling. However, risk of transmission in dental settings is very low (CDC, 2003). Recommendations to prevent transmission begin with assessing the risk of *M. tuberculosis* transmission in your facility.

Assessing Risk of Transmission in the Dental Setting

The Centers for Disease Control and Prevention (CDC) provides guidelines for preventing transmission of TB in health care settings (CDC, 2005). This updated guideline stresses the importance of a conducting a risk assessment, a written TB infection control plan, training/education, screening of health care workers, and evaluation of control measures.

Risk assessment is the foundation of TB control policies. In most private practice settings the dentist or appointed infection control personnel will provide the risk assessment and design TB control procedures. Larger facilities (public health settings, hospitals, prisons, etc.) will probably follow protocol designed by an epidemiologist or occupational health specialist (CDC, 2005). The health department, local university or hospital may be able to assist you by providing training information or specific guidance.

Table 4 Dental Setting Risk Categories

Factor	Risk Category
<ul style="list-style-type: none"> • Does not treat patients with active TB. • No TB cases reported within the community in the past 12 months. 	Minimal Risk
<ul style="list-style-type: none"> • Does not treat patients with active TB. • TB cases reported in the community. • Screens patients for active TB and refers suspect cases to collaborating facility for evaluation and management. 	Very Low Risk
<ul style="list-style-type: none"> • Provides treatment to fewer than six patients with active TB per year. • No evidence of <i>M. tuberculosis</i> transmission in the facility.♣ 	Low Risk
<ul style="list-style-type: none"> • Provides treatment to six or more patients with active <i>M. tuberculosis</i> per year. • There is no evidence of TB transmission in the facility. 	Intermediate Risk
<ul style="list-style-type: none"> • Evidence of transmission of <i>M. tuberculosis</i> in the facility. 	High Risk
♣ As evidenced by PPD skin test conversions among dental workers or patients.	
Cleveland, J.L., Gooch, B., Bolyard, E.A., Simone, P.M., Mullan, R. J., and Marianos, D.W. (1995). TB infection control recommendations from the CDC, 1994: Considerations for dentistry. Journal of the American Dental Association, 126, 593-600. used by permission © ADA Publishing	

Most dental settings will probably fall in the minimal to very low risk categories.

The risk assessment is based upon the following three questions:

1. What is the prevalence of active TB in the community?
2. How many patients with active TB were treated in the practice setting within the previous year? (This does not include patients who were identified as suspects and then referred for evaluation prior to any dental treatment taking place.)
3. Was transmission of TB confirmed by a PPD skin test conversion among dental workers or between patients within the practice setting?

The local public health department has information about the incidence and prevalence of TB within the community, and should be able to provide it over the telephone. See Appendix B for more information about contacting the health department.

Writing a TB Control Program

After you have completed a risk assessment for your practice setting, it is necessary to develop a written TB control program. See Table 5 for the elements of a TB Infection Control Program.

Table 5 Elements of a TB Infection Control Plan (CDC, 2005) (Cleveland, Gooch, Bolyard, et al, 1995)					
Element*	Risk Level Category				
	Minimal	Very Low	Low\oplus	+Inter-mediate	+High
Assigning responsibility for conducting a TB risk assessment	R	R	R	R	R
Baseline risk assessment	R	R	R	R	R
Community TB profile	R	R	R	Y	Y
Written TB infection control plan	R	R	R	R	R
Reassessment of risk	Y	Y	Y	Every 6-12 mos.	Every 3 mos.
Protocol for identifying and referring patients who may have active TB	R	R	R \times	R	R
Protocol for managing patients with active TB relative to providing urgent dental care	R \approx	R \approx	R	R	R
Engineering controls	N/A*	O**	R	R	R
Respiratory protection program	N/A*	N/A*	R	R	R
Educating and training dental	R	R	R	R	R

workers regarding TB					
Counseling dental workers regarding TB	R	R	R	R	R
Baseline PPD testing of dental workers	O	R	R	R	R
Periodic/Routine testing of dental workers	N/A	N/A*	Y	Every 6-12 mos.	Every 3 mos.
Protocol for identifying and referring dental workers who may have active TB and/or positive PPD test results	R	R	R	R	R
Protocol for investigating unprotected occupational exposures to TB	R	R	R	R	R
<p>R=Recommended; Y=Yearly; N/A=Not Applicable; O=Optimal ⊕Intermediate and high-risk dental settings may need to perform some elements more frequently. ≈Minimal and very-low risk dental settings should identify appropriate dental facilities for referral of patients in need of evaluation, management or urgent dental treatment. ‡Low, intermediate or high-risk dental facilities providing dental treatment to patients who have, or are strongly suspected of having, infectious TB should provide TB isolation. +Intermediate and High Risk categories were adapted from the CDC's Guidelines for preventing the transmission of Mycobacterium tuberculosis in health care facilities. **Some very low risk dental settings providing treatment to patients at high risk for active TB may elect to use engineering control for general use areas (for example, waiting rooms). These controls may include general ventilation, high-efficiency particulate air filtration (HEPA) filters or ultraviolet germicidal irradiation.</p>					
<p>Adapted from: Cleveland, J.L., Gooch, B., Bolyard, E.A., Simone, P.M., Mullan, R. J., and Marianos, D.W. (1995). TB infection control recommendations from the CDC, 1994: Considerations for dentistry. Journal of the American Dental Association, 126, 593-600. used by permission © ADA Publishing. Centers for Disease Control and Prevention. 1994. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care facilities. MMWR, 43 (No. RR-13): 113-120.</p>					

Health History

The dental health history form should contain questions pertaining to the symptoms of TB disease and any current TB treatment if applicable. You must ensure patient confidentiality.

Questions that might be included on a health history form include:

Are you experiencing any of the following?

- Persistent cough (lasting more than three weeks)

- Coughing up blood
- Night sweats
- Weight loss
- Fever
- Loss of Appetite

A positive response to any of these may not necessarily indicate TB disease. Ask follow-up questions to clarify the patient's current health status. A direct question, "Have you been diagnosed with Tuberculosis?" should also be part of the health questionnaire.

A health history form may include a "yes or no" question regarding PPD status.

For example:

- Are you a PPD converter?
- Are you PPD positive?

If the answer is yes, you may want to inquire as to when the individual was skin tested and whether or not the individual is currently receiving preventive therapy.

If at any time during the dental visit you have a high level of suspicion a person may have active TB (Cleveland, Gooch, Bolyard, et al, 1995):

- Isolate the patient from other patients and dental personnel,
- ask them to wear a surgical mask to help reduce infectious aerosols,
- and
- refer the patient for medical evaluation.

Treatment and Contraindications to Treatment

Obviously, any elective dental treatment should be deferred until a patient is confirmed as either not having active TB or until they are no longer infectious. A primary care provider or health department worker provides clearance for dental treatment.

Facilities (Low, Intermediate, or High Risk) that provide emergency treatment to patients with active TB disease should have an isolation room and respiratory protection that meets CDC guidelines for safety (CDC, 2005).

Minimal and very low risk facilities should obtain the name of a collaborating facility where patients with suspected or active TB can go for urgent dental treatment. Designate a collaborating facility in advance to ensure prompt and safe referrals (CDC, 2005).

For individuals undergoing preventive therapy, dental treatment is not contraindicated. Remember that these individuals are not infectious.

Drug Interactions and Contraindications

Dental patients who are undergoing preventive therapy or treatment for TB disease take anti-tuberculosis drugs that may cause side effects. Drug induced hepatitis is the major side effect of antituberculosis drugs (CDC, 2020). Alteration in vision, hepatic and renal function, and other changes may indicate adverse antituberculosis drug reaction. Monthly or weekly monitoring of individuals for adverse effects is the responsibility of his or her TB care provider. However, you should not hesitate to question patients undergoing preventive therapy or treatment for TB about possible adverse drug reactions.

If you encounter patients undergoing preventive therapy or treatment for TB disease you should:

- ask about symptoms due to adverse reactions to medication,
- note symptoms in the patient's record, and
- refer them immediately for follow up care with their TB care provider.

Caused by	Adverse Reaction	Signs and Symptoms
Any drug	Allergic reactions	Skin rash
Ethambutol	Eye damage	Blurred or changed vision, Changed color vision
Isoniazid Pyrazinamide Rifampin	Hepatitis	Abdominal pain Abnormal liver function test results Dark urine Fatigue Fever for 3 or more days Flu-like symptoms Lack of appetite Nausea Vomiting Yellowish skin or eyes
Isoniazid	Nervous system damage	Dizziness Tingling or numbness around the mouth
Pyrazinamide	Stomach upset	Stomach upset, vomiting, lack of appetite
	Increased uric acid	Abnormal uric acid level Joint aches Gout (rare)
Rifampin	Bleeding problems	Easy bruising Slow blood clotting Bleeding gums

	Discoloration of body fluids	Orange to red-colored urine, sweat, saliva or tears. Permanently stains soft contact lenses
Streptomycin	Ear damage	Balance problems Hearing loss Ringing in the ears
	Kidney damage	Abnormal kidney function test results

These side effects (See Table 6) do not usually interfere with routine dental treatment.

Aside from hepatitis, INH may produce peripheral neuropathy. Often, pyridoxine (Vitamin B6) is included as part of drug therapy to ameliorate this reaction (CDC, 2020).

Rifampin induces hepatic enzyme release, which may decrease activity of drugs metabolized in the liver (e.g., narcotics and analgesics). Rifampin decreases the effectiveness of fluconazole. Ketaconazole may reduce both drug levels (ketaconazole and rifampin). Topical antifungals can be used to treat mild to moderate oropharyngeal candidiasis without interaction (Reznik, 1998) (CDC, 2020). Rifampin and INH may temporarily lower the number of white blood cells and platelets. Minimal gingival bleeding, bruising, and delayed wound healing may be experienced (CDC, 2005) (CDC, 2017). Ethambutol creates infrequent adverse reactions. The most common reactions are blurred vision and red-green color blindness (CDC, 2020).

The primary adverse reaction to Streptomycin is ototoxicity. This can result in vertigo and potentially some hearing loss. Streptomycin should not be given to pregnant women (CDC, 2017).

Respiratory Protection and Environmental Control

Dental facilities that treat patients within a high TB prevalence population should have specially equipped waiting areas. Ventilation and high efficiency particulate air filtration (HEPA) filters are recommended.

Personal respiratory protection should be used by dental workers treating patients with (or suspected of having) infectious TB. These respirators should meet Occupational Safety and Health Administration (OSHA) guidelines.

Education and Training

All dental workers, regardless of practice location, should receive education and training about TB. Training should be tailored to job category and risk level of the individual receiving training (Cleveland, Gooch, Bolyard, et al, 1995).

Screening of Dental Workers for TB

Frequency of skin tests for TB is determined after the risk assessment is complete. As you can see in Table 5, recommendations exist for baseline testing of all dental workers except those employed in minimal risk settings. Furthermore, repeated testing at regular intervals is recommended for dental workers employed in low, intermediate and high-risk settings (Cleveland, Gooch, Bolyard, et al, 1995).

The CDC recommends testing dental workers who have not used appropriate precautions while treating or exposed to patients with infectious TB. If the PPD test is positive, further evaluation by a physician is necessary to confirm the presence of TB disease. Complete medical evaluation of dental workers exhibiting signs or symptoms of TB disease can help to ensure workplace safety. If diagnosed with active TB, the dental worker should not return to the dental setting until cleared by a physician (Cleveland, Gooch, Bolyard, et al, 1995).

A PPD skin test converter is an individual who has a change in skin test reaction from negative to positive. Infection takes place between the initial skin test and a subsequent skin test. Dental workers who convert should seek TB experts for consultation regarding appropriate action (Cleveland, Gooch, Bolyard, et al, 1995).

Conclusion

TB is an old nemesis of the human race. The end of suffering seems within reach, yet this infectious disease has managed to elude eradication for centuries. TB is familiar to every world culture and thrives on ignorance. The incidence of TB is declining in parts of the world, yet it flourishes in many countries. Immunosuppressive diseases like HIV, multi-drug resistance, and poor adherence to treatment protocol has threatened the decline of TB. Successful drug regimens are available, and vaccine research is ongoing. International organizations are active in assisting governments and public health agencies in developing strategies and implementing programs that reduce the incidence of TB infection and progression to disease.

Now that you have a better understanding of the nature and progression of this disease, you can actively pursue TB control and elimination in your community.

- When given the opportunity, share what you know about TB with other dental professionals.
- Have educational information about TB available in your office.
- Conduct a TB education and training course for your coworkers.
- Contact your health department for information regarding the incidence and prevalence of TB in your community.
- Conduct a Risk Assessment for transmission of TB in your practice setting.

- Construct a TB Control Plan for your practice setting.
- Encourage your patients to complete preventive therapy and/or treatment for TB.

Appendices

Source: Centers for Disease Control. (2000). Core curriculum on tuberculosis: What the clinician should know. 4th Edition.

Appendix A Classification of the Tuberculin Reaction

A tuberculin reaction of ≥ 5 mm of induration is classified as positive in the following groups:

- Persons known to have or suspected of having HIV infection
- Recent contacts (family, friends, coworkers, etc.) of a person with infectious TB persons with fibrotic changes on chest radiograph consistent with old healed TB
- Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of ≥ 15 mg/day of prednisone for ≥ 1 month)

A tuberculin reaction ≥ 10 mm of induration is classified as positive in persons who do not meet the preceding criteria but who have other risk factors for TB:

- Recent arrivals (< 5 years) from high-prevalence countries
- Injection drug users residents and employees of high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health-care facilities, residential facilities for AIDS patients, and homeless shelters
- Mycobacteriology laboratory personnel with clinical conditions that place them at high risk
- Children < 4 years of age, or children and adolescents exposed to adults in high-risk categories.

A tuberculin reaction of ≥ 15 mm is positive:

- classified as positive in persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.

Remember: A health care provider or individual who may have occupational exposure to TB may have a different cut-off for a positive reaction. Individual risk factors and the prevalence of TB in the facility or place of employment are considered.

Appendix B Health Department

The health department's role includes:

- Identification and treatment of all persons with TB disease, and to ensure all patients complete appropriate therapy.
- Identify and evaluate contacts to persons with infectious TB; offer therapy as appropriate
- Screen high-risk groups for TB infection; offer therapy as appropriate

Other care providers provide TB tests, care and treatment. However, the ultimate responsibility of TB control rests with the local and state health department. A patient's ability to pay is not a factor in receiving TB-related services from the health department.

The health department and many voluntary organizations can provide training and education at no cost (or minimal cost). Consultation services, printed information, videotapes, and other materials are available. Contact your health department for more information.

Many health departments do not provide TB skin tests for employment purposes. TB skin tests are usually available at minimal cost through a primary care provider or local hospital. Your employer may be required to provide initial and periodic TB skin tests depending on practice location and risk assessment outcome. Contact your local dental association or employee manual for more information.

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NEW YORK New York State Department of Health Empire State Plaza Corning Tower, Room 840 Albany, NY 12237-0669 Tel: 518-474-7000 Fax: 518-473-6164	NORTH CAROLINA North Carolina Department of Health & Human Services 1200 Front Street, Suite 101 Raleigh, NC 27609 Tel: 919-733-7286 Fax: 919-733-0084
NORTH DAKOTA North Dakota Department of Health State Capitol 600 East Boulevard, Dept. 301 Bismarck, ND 58505-0200 Tel: 701-328-2377 Fax: 701-328-2499	OHIO Ohio Department of Health Bureau of Infectious Disease and Control 35 E. Chestnut St., 7th floor Columbus, OH 43215 Tel: 614-466-2381 Fax: 614-387-2132
OKLAHOMA Oklahoma State Department of Health	OREGON Oregon Public Health Division

1000 NE 10th Street, Room 608 Oklahoma City, OK 73117-1299 Tel: 405-271-4060 Fax: 405-271-6680	800 NE Oregon, Suite 1105 Portland, OR 97232 Tel: 971-673-0174 Fax: 971-673-0178
PENNSYLVANIA Pennsylvania Department of Health TB Control Program Health and Welfare Building, Room 1013 625 and Forester Street Harrisburg, PA 17120 Tel: 717-787-6267 Fax: 717-772-4309	RHODE ISLAND Rhode Island Department of Health 3 Capitol Hill, Room 106 Providence, RI 02908 Tel: 401-222-2577 Fax: 401-222-2488
SOUTH CAROLINA South Carolina Department of Health and Environmental Control Mills/Jarrett Complex, Box 101106 1751 Calhoun Street Columbia, SC 29201 Tel: 803-898-0558 Fax: 803-898-0685	SOUTH DAKOTA South Dakota Department of Health 615 East 4th Street Pierre, SD 57501 Tel: 605-773-4784 Fax: 605-773-5509
TENNESSEE Tennessee Department of Health Cordell Hull Building, 1st Floor 425 5th Avenue North Nashville, TN 37243-0001 Tel: 615-741-7247 Fax: 615-253-1370	TEXAS Texas Department of State Health Services 1100 West 49th Street Austin, TX 78756 Tel: 512-533-3000 Fax: 512-533-3179
UTAH Utah Department of Health, TB Control and Bureau of Epidemiology Box 142105 Salt Lake City, UT 84114-2105 Tel: 801-538-6191 Fax: 801-538-9913	VERMONT Vermont Department of Health PO Box 70 Drawer 41 108 Cherry Street Burlington, VT 05401 Tel: 802-863-7245 Fax: 802-863-9962
VIRGINIA Virginia Department of Health 109 Governor Street, 3rd floor Richmond, VA 23219 Tel: 804-864-7906 Fax: 804-371-0248	WASHINGTON Washington State Department of Health 111 Israel Rd, S.E. PO Box 47837 Olympia, WA 98504-7837 Tel: 360-236-3443 Fax: 360-236-3405
WEST VIRGINIA West Virginia Department of Health & Human Resources TB Control Program, Room 125 350 Capitol Street Charleston, WV 25301-1417 Tel: 304-558-3669 Fax: 304-558-1825	WISCONSIN Wisconsin Department of Health & Family Services 1 West Wilson Street, Room 318 Madison, WI 53702 Tel: 608-261-6319 Fax: 608-266-0049

<p>WYOMING Wyoming Department of Health Qwest Building, Suite 510 6101 Yellowstone Road Cheyenne, WY 82002 Tel: 307-777-6563 or 3562 Fax: 307-777-5402 or 777-5573</p>	
TERRITORIES	
<p>AMERICAN SAMOA Department of Health American Samoa Government Department of Health LBJ Tropical Medical Center P.O. Box F Pago Pago, AS 96799 Tel: 011-684-633-4690 Fax: 011-684-633-5692</p>	<p>FEDERATED STATES OF MICRONESIA Department of Health, Education & Social Affairs Federated States of Micronesia P.O. Box PS-70 Kolonias, Pohnpei, FM 96941 Tel: 011-691-320-2619 Fax: 011-691-320-8382</p>
<p>GUAM Department of Public Health & Social Services National TB Control Program 123 Chalan Kareta, Route 10 Manqilao, GU 96910-2816 Tel: 011-671-735-7145, 7157, or 7131 Fax: 011-671-735-7318</p>	<p>NORTHERN MARIANA ISLANDS CNMI TB Control Program Department of Public Health & Commonwealth Health Center P.O. Box 500409 CK Saipan, MP 96950-0409 Tel: 011-670-236-8376 or 8377 Fax: 011-670-236-8736</p>
<p>PUERTO RICO Puerto Rico Department of Health P.O. Box 70184 San Juan, PR 00936 Tel: 765-2929 ext. 3861 Fax: 787-274-5559</p>	<p>REPUBLIC OF MARSHALL ISLANDS National TB Control Program Ministry of Health P.O. Box 16 Majuro Hospital Majuro, MH 96960-0016 Tel: 011-692-625-0074 or 7321 Fax: 011-692-625-4372 or 4543</p>
<p>REPUBLIC OF PALAU Palau Ministry of Health Republic of Palau P.O. Box 6027 Koror, Republic of Palau 96940-0845 Tel: 011-680-488-2925 or 1360 Fax: 011-680-488-4800</p>	<p>VIRGIN ISLANDS Virgin Islands Department of Health Old Municipal Hospital, Bldg. 1 Knud Hansen Complex St. Thomas, VI 00802 Tel: 340-774-9000 Fax: 340-776-5466</p>

(CDC. Updated May 2017)

Appendix C Preventive Therapy

Preventive therapy reduces the risk that TB infection will progress to TB disease. Certain groups are at high risk for developing disease after they become infected.

High Priority Candidates

People who have a positive IGRA result or a TST reaction of 5 or more millimeters

- HIV-infected persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Organ transplant recipients
- Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF- α antagonists)

People who have a positive IGRA result or a TST reaction of 10 or more millimeters

- Recent immigrants (< 5 years) from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
- Mycobacteriology laboratory personnel
- Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories

Online Source: <https://www.cdc.gov/tb/> Centers for Disease Control and Prevention. (2020). *Treatment of Latent Tuberculosis Infection*.

Appendix D Number of Reported Tuberculosis Cases by State (2020)

State	No. Of Cases	State	No. Of Cases
Alabama	133	Montana	6
Alaska	62	Nebraska	38
Arizona	193	Nevada	74
Arkansas	93	New Hampshire	11
California	2,145	New Jersey	308
Colorado	64	New Mexico	50
Connecticut	60	New York	787
Delaware	22	North Carolina	195
District of Columbia	32	North Dakota	15
Florida	595	Ohio	156
Georgia	335	Oklahoma	59
Hawaii	136	Oregon	77
Idaho	11	Pennsylvania	209
Illinois	320	Rhode Island	21
Indiana	108	South Carolina	79
Iowa	54	South Dakota	8
Kansas	40	Tennessee	151
Kentucky	80	Texas	1,269
Louisiana	121	Utah	31
Maine	14	Vermont	2
Maryland	198	Virginia	198
Massachusetts	199	Washington	195
Michigan	145	West Virginia	13
Minnesota	147	Wisconsin	47
Mississippi	74	Wyoming	2
Missouri	79		

Online Source: <https://www.cdc.gov/tb/statistics/indicators/2018/StateCity-TBReport.htm>
 Accessed May 2020

Appendix E Sample Risk Assessment and TB Control Form

Your Practice Name & Location			
Date of TB Risk Assessment			
Name of Dental Office TB Control Coordinator:			
Health Department Phone Number:			
Health Department Contact Person:			
Incidence of TB disease in your community:			
Number of Patients with Active TB Treated in Your Facility within the Past 12 months:			
Evidence of <i>M. tuberculosis</i> Transmission Within Your Facility?	Yes	No	
Risk Category: (Refer to Table 4 for risk assessment categories, and circle appropriate risk category)	Minimal Very Low	Intermediate High	Low
Collaborating Agency to Whom You Refer Active or Suspected TB Cases:			
Controls	Necessary Or Recommended	Not Necessary	Date Completed
Policies & protocols for early identification of patients with active TB	Y	Y	
Protocol for prompt isolation of patients with active TB	Y	Y	
Skin test surveillance of dental workers	Y	Y	
Record skin test results in confidential personnel file	Y	Y	
Training and Education of dental workers	Y	Y	
General ventilation	Y	Y	
Local exhaust ventilation	Y	Y	
UV germicidal irradiation	Y	Y	
HEPA filtration	Y	Y	
Personal Respiratory Protection	Y	Y	
Respiratory Protection Program	Y	Y	

Appendix F Glossary

Aerosol: The droplet nuclei that are expelled by an infectious person (e.g., by coughing or sneezing); these droplet nuclei can remain suspended in the air and can transmit *M. tuberculosis* to other persons.

Alveoli: The small air sacs in the lungs that lie at the end of the bronchial tree; the site where carbon dioxide in the blood is replaced by oxygen from the lungs and where TB infection usually begins.

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

Bacillus of Calmette and Guérin (BCG) vaccine: A TB vaccine used in many parts of the world.

Booster phenomenon: A phenomenon in which some persons (especially older adults) who are skin tested many years after infection with *M. tuberculosis* have a negative reaction to an initial skin test, followed by a positive reaction to a sub-sequent skin test. The second (i.e., positive) reaction is caused by a boosted immune response.

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

Cluster: Two or more PPD skin-test conversions occurring within a 3-month period among HCWs in a specific area or occupational group, and epidemiologic evidence suggests occupational (nosocomial) transmission.

Contact: A person who has shared the same air with a person who has infectious TB for a sufficient amount of time to allow possible transmission of *M. tuberculosis*.

Conversion, PPD: See PPD test conversion.

Culture: The process of growing bacteria in the laboratory so that organisms can be identified.

Directly observed therapy (DOT): An adherence-enhancing strategy in which an HCW or other designated person watches the patient swallow each dose of medication.

Droplet nuclei: Microscopic particles (i.e., 1–5 μm in diameter) produced when a person coughs, sneezes, shouts, or sings. The droplets produced by an infectious TB patient can carry tubercle bacilli, can remain suspended in the air for prolonged periods, and are carried on normal air currents in the room.

Drug resistance, acquired: A resistance to one or more anti-TB drugs that develops while a patient is receiving therapy and which usually results from the patient's nonadherence to therapy or the prescription of an inadequate regimen by a health-care provider.

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

Drug-susceptibility tests: Laboratory tests that determine whether the tubercle bacilli cultured from a patient are susceptible or resistant to various anti-TB drugs.

Ethambutol: A first-line, oral anti-TB drug sometimes used concomitantly with INH, rifampin, and pyrazinamide.

Exposure: The condition of being subjected to something (e.g., infectious agents) that could have a harmful effect. A person exposed to *M. tuberculosis* does not necessarily become infected (see Transmission).

False-negative: A negative reaction in a person who is infected with TB.

False-positive: A positive reaction in a person who is not infected with TB.

First-line drugs: The most often used anti-TB drugs (i.e., INH, rifampin, pyrazinamide, ethambutol, and streptomycin).

Fluconazole*: Trade name Diflucan. Anti-fungal drug used to treat candidiasis.

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

Immunosuppressed: A condition in which the immune system is not functioning normally (e.g., severe cellular immunosuppression resulting from HIV infection or immunosuppressive therapy). Immunosuppressed persons are at greatly increased risk for developing active TB after they have been infected with *M. tuberculosis*. No data are available regarding whether these persons are also at increased risk for infection with *M. tuberculosis* after they have been exposed to the organism.

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

Infection: The condition in which organisms capable of causing disease (e.g., *M. tuberculosis*) enter the body and elicit a response from the host's immune defenses. TB infection may or may not lead to clinical disease.

Infectious: Capable of transmitting infection. When persons who have clinically active pulmonary or laryngeal TB disease cough or sneeze, they can expel droplets containing *M. Tuberculosis* into the air. Persons whose sputum smears are positive for AFB are probably infectious.

Intradermal: Within the layers of the skin.

Isoniazid (INH): A first-line, oral drug used either alone as preventive therapy or in combination with several other drugs to treat TB disease.

Ketaconazole* – Trade name Nizoral. Anti-fungal drug used to treat candidiasis.

Latent TB infection: Infection with *M. tuberculosis*, usually detected by a positive PPD skin- test result, in a person who has no symptoms of active TB and who is not infectious.

Mantoux test: A method of skin testing that is performed by injecting 0.1 mL of PPD-tuberculin containing 5 tuberculin units into the dermis (i.e., the second layer of skin) of the forearm with a needle and syringe. This test is the most reliable and standardized technique for tuberculin testing (see Tuberculin skin test and Purified protein derivative [PPD]- tuberculin test).

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

***M. tuberculosis* complex:** A group of closely related mycobacterial species that can cause active TB (e.g., *M. tuberculosis*, *M. bovis*, and *M. africanum*); most TB in the United States is caused by *M. tuberculosis*.

Nosocomial: An occurrence, usually an infection that is acquired in a hospital or as a result of medical care.

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

Preventive therapy: Treatment of latent TB infection used to prevent the progression of latent infection to clinically active disease.

Purified protein derivative (PPD)-tuberculin test: A method used to evaluate the likelihood that a person is infected with *M. tuberculosis*. A small dose of tuberculin (PPD) is injected just beneath the surface of the skin, and the area is examined 48–72

hours after the injection. A reaction is measured according to the size of the induration. The classification of a reaction as positive or negative depends on the patient's medical history and various risk factors (see Mantoux test).

Purified protein derivative (PPD)-tuberculin test conversion: A change in PPD test results from negative to positive. A conversion within a 2-year period is usually interpreted as new *M. tuberculosis* infection, which carries an increased risk for progression to active disease. A booster reaction may be misinterpreted as a new infection (see Booster phenomenon and Two-step testing).

Pyrazinamide: A first-line, oral anti-TB drug used in treatment regimens.

Radiography: A method of viewing the respiratory system by using radiation to transmit an image of the respiratory system to film. A chest radiograph is taken to view the respiratory system of a person who is being evaluated for pulmonary TB. Abnormalities (e.g., lesions or cavities in the lungs and enlarged lymph nodes) may indicate the presence of TB.

Rifampin: A first-line, oral anti-TB drug that, when used concomitantly with INH and pyrazinamide, provides the basis for short-course therapy.

Second-line drugs: Anti-TB drugs used when the first-line drugs cannot be used (e.g., for drug-resistant TB or because of adverse reactions to the first-line drugs). Examples are cycloserine, ethionamide, and capreomycin.

Smear (AFB smear): A laboratory technique for visualizing mycobacteria. The specimen is smeared onto a slide and stained, then examined using a microscope. Smear results should be available within 24 hours. In TB, a large number of mycobacteria seen on an AFB smear usually indicate infectiousness. However, a positive result is not diagnostic of TB because organisms other than *M. tuberculosis* may be seen on an AFB smear (e.g., nontuberculous mycobacteria).

Source case: A case of TB in an infectious person who has transmitted *M. tuberculosis* to another person or persons.

Sputum: Phlegm coughed up from deep within the lungs. If a patient has pulmonary disease, an examination of the sputum by smear and culture can be helpful in evaluating the organism responsible for the infection. Sputum should not be confused with saliva or nasal secretions.

Streptomycin: A first-line, injectable anti-TB drug.

TB case: A particular episode of clinically active TB. This term should be used only to refer to the disease itself, not the patient with the disease. By law, cases of TB must be

reported to the local health department.

TB infection: A condition in which living tubercle bacilli are present in the body but the disease is not clinically active. Infected persons usually have positive tuberculin reactions, but they have no symptoms related to the infection and are not infectious. However, infected persons remain at lifelong risk for developing disease unless preventive therapy is given.

TB suspect: An individual likely to have clinically active tuberculosis.

Transmission: The spread of an infectious agent from one person to another. The likelihood of transmission is directly related to the duration and intensity of exposure to *M. tuberculosis* (see Exposure).

Tuberculosis (TB): A clinically active, symptomatic disease caused by an organism in the *M. tuberculosis* complex (usually *M. tuberculosis* or, rarely, *M. bovis* or *M. africanum*).

Zoonotic: Transmitted by animals or animal products

Sources: Unless otherwise noted, all information provided in this glossary was obtained from The Centers for Disease Control and Prevention. (2005). Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities. December 30, 2005 /54(RR17);1-141.

*The Bantam Medical Dictionary, 5th Edition. 2004. Market House Books. Ltd. New York.

Appendix G TB-Related Resources (Internet)

American Lung Association

This site provides an overview of TB geared toward the public.

1-800-LUNG-USA

<http://www.lungusa.org/>

Core Curriculum on Tuberculosis

A comprehensive course for use in training and education of health care workers.

Includes a test. Can be viewed/printed online. Centers for Disease Control and Prevention Division of Tuberculosis Elimination NCHSTP, CDC

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

Division of Tuberculosis Elimination

Homepage of the DTBE. Links to publications, research information, FAQ's and other TB Elimination organizations. <http://www.cdc.gov/nchstp/TB/>

HIVDENT

This site provides useful information about TB-HIV/AIDS. It is geared primarily toward dental practitioners. It is updated frequently and is an excellent dental resource.

<http://hivdent.org/> TB drug interactions <http://www.hivdent.org/drugs/drugsoutheas.htm>

National Institute for Occupational Safety and Health (NIOSH)

Protect Yourself Against Tuberculosis; A Respiratory Protection Guide for Health Care Workers DHHS (NIOSH) Publication No. 96-102 <http://www.cdc.gov/niosh/tb.html>

Guide to the Selection and Use of Particulate Respirators DHHS (NIOSH) Publication No. 96-101 <http://www.cdc.gov/niosh/userguid.html> 1-800-356-4674

World Health Organization Global Tuberculosis Programme

This site has detailed information regarding TB elimination and control worldwide. It features current global statistics and developments in TB control and elimination.

<http://www.who.int/gtb/>

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Course Exam: Tuberculosis

1. Robert Koch is responsible for:
 - a) Discovering streptomycin
 - b) Isolating *M. tuberculosis*
 - c) Demonstrating TB is an infectious disease
 - d) Attenuating *M. bovis* for the BCG vaccine

2. The primary mode of *M. tuberculosis* transmission is:
 - a) Inhalation of infected droplet nuclei
 - b) Drinking of non-pasteurized dairy products
 - c) Aerosol-producing procedures in an unventilated room
 - d) Contact with contaminated surfaces or objects

3. An infected individual is at greatest risk of developing TB disease:
 - a) Within the first 2-10 weeks after infection
 - b) In the first 1-2 years after infection
 - c) Between 20 and 25 years after infection
 - d) Risk is the same throughout a person's lifetime
4. The greatest risk factor in the progression of TB infection to TB disease is:
 - a) HIV infection
 - b) Diabetes Mellitus
 - c) Repeated contact with contaminated objects
 - d) Immunosuppressive therapy
5. Which of the following statements is true regarding TB infection and TB disease:
 - a) Infection always leads to disease at some point
 - b) Individuals who are infected develop blotchy skin, and suffer night blindness
 - c) If infected, sputum cultures are positive for TB
 - d) Infected individuals have the bacteria present in his or her body and may develop TB in their lifetime
6. Mantoux skin tests are read by:
 - a) Measuring redness at injection site
 - b) Measuring induration at injection site
 - c) Measuring skin discoloration of any kind
 - d) By individuals at home using a ruler
7. After a person has become infected with TB disease, how long before a Mantoux skin test can detect an immune response
 - a) 1-2 years
 - b) Immediately
 - c) 2 weeks to 10 weeks
 - d) Not until a positive chest radiograph or sputum culture
8. The definitive procedure used for diagnosing pulmonary TB disease is:
 - a) Mantoux skin test
 - b) Lung volume test
 - c) Blood test
 - d) Sputum culture

9. The primary preventive anti-tuberculosis drug is:
- a) Streptomycin
 - b) Isoniazid (INH)
 - c) Rifampin
 - d) Penicillin
10. Nonadherence to TB treatment leads to:
- a) Relapse, continued transmission and development of drug resistance
 - b) HIV infection
 - c) Insomnia and blotchy skin
 - d) Outbursts of violent behavior
11. Drug resistance usually results from:
- a) Excessive liver damage
 - b) Successful completion of TB therapy
 - c) Pregnancy
 - d) Inadequate prior treatment of TB
12. The risk of TB infection is the same for HIV-infected individuals as non HIV-infected individuals.
- a) true
 - b) false
13. A factor related to the increase in TB cases between 1984-1993 is:
- a) Emergence of managed care
 - b) HIV/AIDS epidemic
 - c) Less restrictive isolation policies
 - d) Decreased availability of anti-tuberculosis drugs
14. In the US, approximately how many individuals were reported, in 2014, as newly infected with TB?
- a) Only foreign born individuals
 - b) Less than 10 thousand
 - c) 250 million
 - d) 10 to 15 million

15. The risk of transmission in dental settings is considered to be:
- a) Minimal
 - b) Very low
 - c) Low
 - d) Intermediate
16. The foundation of a TB control policy in the dental office is:
- a) Treating many individuals with TB Disease
 - b) Taking a TB Control course annually
 - c) Refusing dental treatment
 - d) Conducting a TB Risk Assessment
17. The CDC recommends yearly skin testing of dental workers in dental settings with designation:
- a) Low risk
 - b) Minimal risk
 - c) Very low risk
 - d) None of the above
18. Which of the following patients has a positive skin test reaction (Refer to Appendix A):
- a) Ms. Gonzales, 25 years old, native of Mexico, 7 mm of induration
 - b) Mr. Jones, 20 years old, no risk factors, 14 mm of induration
 - c) Ms. Smith, 37 years old, HIV-infected, 8 mm of induration
 - d) All of the above
19. Mr. Wu emigrated from Mainland China. He is given a TB skin test and the result is 17 mm of induration. He says he was vaccinated against TB as a child. He also says his wife was treated for pulmonary TB disease last year. From this scenario you surmise:
- a) His wife is likely to die of the disease
 - b) He's not telling the truth, because there is no vaccine for TB
 - c) This could be a false-positive reaction due to the vaccination
 - d) He is HIV positive

20. If a patient states he or she is PPD positive you should:
- a) Isolate the patient because they are infectious
 - b) Ask them to wear a surgical mask, gloves and gown
 - c) Ask when they were tested and if they are receiving preventive treatment for TB
 - d) None of the above
21. A major side effect of anti-tuberculosis drugs is hepatitis.
- a) True
 - b) False
22. Topical antifungals negatively interact with Rifampin.
- a) True
 - b) False
23. You call the health department and find out there were six cases of TB in your community last year. You do not treat active TB cases in your practice setting and have referred anyone suspected of having active TB to a collaborating facility. Your dental setting risk category is considered to be:
- a) Low
 - b) Very low
 - c) High
 - d) Intermediate
24. The anti-tuberculosis drug that causes some body fluids (urine, sweat, saliva or tears) to become orange-red in color is:
- a) INH
 - b) Rifampin
 - c) Ethambutol
 - d) Pyrazinamide
25. Dr. Gordon had a Mantoux skin test her senior year in dental school and the result was negative. She was recently tested again and the result (based on her risk factors) was deemed positive. She is considered to be:
- a) HIV Positive
 - b) A TB case
 - c) A PPD converter
 - d) Allergic to INH