

Tuberculosis Infection Control: An Interdisciplinary Perspective

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ABSTRACT

Although tuberculosis rates have declined in the United States over the past 19 years, new cases and cases of drug resistant strains continue to appear. Healthcare workers are at particular risk for contracting tuberculosis as they care for those who are undergoing diagnosis. This article proposes an interdisciplinary tuberculosis management protocol which will reduce the exposure of laboratory and radiography staff to tuberculosis high risk patients during diagnostic testing. Further, we demonstrate the use of interdisciplinary diagnostic management teams to improve communication of tuberculosis exposure risk and reduce the infection of healthcare workers.

ABBREVIATIONS: *Mycobacterium tuberculosis* (TB), Infectious Dose (ID), Centers for Disease Control and Prevention (CDC), Electronic Health Record (EHR), high efficiency particulate air (HEPA), Occupational Safety and Health Administration (OSHA), Personal Protective Equipment (PPE)

INDEX TERMS: *Mycobacterium tuberculosis*, radiography, Latent Tuberculosis, tuberculosis, pulmonary, Infectious Disease Transmission, Patient-to-Professional, multi-drug-resistant-tuberculosis (MDR-TB), extensively drug resistant tuberculosis (XDR-TB)

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INTRODUCTION

Disease caused by *Mycobacterium tuberculosis* is "...characterized pathologically by inflammatory infiltration, formation of tubercles, caseation, necrosis, abscesses, fibrosis, and calcification."¹ While fairly uncommon in the United States, *Mycobacterium tuberculosis* (TB) remains a difficult infection to control in countries with public health management concerns. These areas may harbor multi-drug-resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB), due to inadequate or incomplete antimicrobial treatment.² MDR-TB is defined as tuberculosis that is resistant to either isoniazid or rifampin, while XDR-TB is additionally resistant to fluoroquinolones and to at least one second line injectable aminoglycoside. Individuals in areas with poor sanitation, overcrowding and lack of nutritious diet are at higher risk for acquiring TB. In developed countries such as the United States, routine screening of health personnel and treatment of the general public has greatly curtailed the incidence of active TB.³ Despite these trends, it still remains an issue in low income and urban settings. These individuals may have limited access to health care or do not utilize available services routinely.⁴

Access to medical care does not guarantee patient compliance as the well-reported case of Andrew Speaker illustrates. In 2007, Andrew Speaker, a patient infected with XDR-TB, defied physician orders and boarded

several international flights.^{5,6} This patient risked potential exposure of several passengers to XDR-TB, which was later correctly diagnosed as MDR-TB, a less resistant form.⁷ Concern for public health is an obvious priority for any country trying to prevent the spread of infectious diseases. In many cases, the patient care providers are most at risk for acquiring these infections. Medical tourism, as defined by the medical tourism association, "... is where people who live in one country travel to another country to receive medical, dental and surgical care while at the same time receiving equal to or greater care than they would have in their own country, and are traveling for medical care because of affordability, better access to care or a higher level of quality of care".⁸ This may also include travel for procedures not routinely performed in their native country. As medical tourism becomes more common due to changes in access to medical care, the spread of TB may increase as travelers return to their native countries.

Regardless of patient situations, an interdisciplinary team of healthcare individuals must diagnose and treat patients who carry latent TB, have acute TB, or provide prophylactic treatment to those who have been exposed to carriers. Often the full diagnostic team's role in providing diagnostic information and in infection control is not considered. While medical laboratory scientists and technicians are the focus of concern due to handling and examination of laboratory specimens, other staff may be exposed to TB.

The concept of diagnostic management teams and the use of interdisciplinary teams of healthcare professionals have been discussed as the next important step in patient diagnosis and treatment.⁹ The diagnosis and management of TB is an excellent example of an interdisciplinary healthcare team providing the best possible patient care and infection control. The intent of this work is to provide a protocol to prevent transmission of TB to healthcare workers during the diagnostic process. The bulk of current literature focuses on two main areas: diagnostic testing and treatment and post-exposure treatment of health professionals.^{10,11,12} Literature is not well developed in the area of applied infection control in suspected TB cases, and certainly does not examine an interdisciplinary approach including radiologic technologists and medical laboratory staff.

Despite the general decline in TB rates in the United States over the past 19 years, new cases continue to appear. The incidence of MDR-TB continues to plague both physicians and the public health sector. Healthcare workers are at particular risk for contracting TB as they care for patients with undiagnosed disease, particularly in geographic areas with higher disease prevalence due to immigration such as California, Florida, New York, and Texas.¹³ An interdisciplinary TB management protocol is required to protect healthcare workers.

Transmission of Tuberculosis

Mycobacterium tuberculosis is a causative agent of tuberculosis. However, other species such as *Mycobacterium bovis* and *Mycobacterium africanum* can also cause tuberculosis-like disease. Generally, tuberculosis refers to infections with *Mycobacterium tuberculosis*, but can refer to the set of common tuberculosis causing organisms as *Mycobacterium tuberculosis* complex. Additionally, immunocompromised patients, especially those with human immunodeficiency virus, may develop tuberculosis or disseminated disease from *Mycobacterium avium-intracellulare* complex. For a review on non-*Mycobacterium tuberculosis* and other types of disseminated disease see Tan et al.¹⁴

TB is spread through aerosolized bacteria via sneezing, coughing, or speaking. In medical settings, tuberculosis can also be spread through respiratory secretions from ventilators and other respiratory equipment or through handling of patient respiratory samples. TB bacteria are easily carried in aerosolized respiratory secretions that are spread by inhalation. Overall, TB is not common in most communities in the United States, but healthcare providers are at increased risk of exposure to TB. In particular, emergency care providers, radiologic technologists, and medical laboratory scientists are more likely to be exposed to patients with undiagnosed active TB. Because TB has a low infectious dose (ID) (ID₅₀ is less than 10 bacteria), even isolated contact with patients with active TB can spread the infection. While many patients are pre-screened using the tuberculin skin test, diagnosis involves more testing. The FDA has approved two interferon-gamma release assay (IGRA) tests for TB infection, QuantiFERON®-TB Gold In-Tube test (GFT-GIT) and T-SPOT®TB for the diagnosis of tuberculosis.¹³ The typical specimens or imaging used to detect TB include sputum, blood

samples, and chest radiographs. A patient suffering from a chronic cough, chest pain, and fatigue may not necessarily be identified as “at-risk” for TB. This increases the exposure risk to healthcare personnel interacting with the patient during the initial diagnostic process.

The Role of the Medical Laboratory in Diagnosis of Tuberculosis

Patient respiratory samples are collected and plated on specific media such as American Thoracic Society, Löwenstein-Jensen, or Middlebrook medias. Upon growth of *Mycobacterium tuberculosis* on semisolid media, colonies are small and appear rough and buff colored (Figure 1A). However, colonies may appear smooth or have other colors.^{15,16} Smears made from colonies are weakly gram positive, strongly acid fast, or fluorescent depending on the stain used, and may exhibit cording morphology. (Figure 1B, 1C, and 1D) Sputum samples are generally positive for *M. tuberculosis* during active TB infections that present with cavitory lesions. One drawback is that latent TB is not usually detected in sputum specimens. The immune system creates characteristic granulomas that form calcified deposits in the lung. Due to calcification, the bacteria do not appear in the sputum. Latent TB is more likely to be identified by radiologic imaging, blood testing using interferon gamma release assays or through the tuberculin skin test. In the tuberculin skin test, *M. tuberculosis* antigens are injected under the skin in the epidermis. The presence of cell mediated immunity to TB causes activation of T cells and inflammation causing an induration of the skin. The test is interpreted as positive or negative depending on the presence or absence of induration. Unfortunately, individuals from endemic countries are often vaccinated against TB. These individuals generally show a positive TB skin test in the absence of infection. In these cases, blood testing for latent TB should be utilized. *M. tuberculosis* antigens are added to a patient's blood sample, which cause TB specific T-cells to release interferon gamma as part of the cell-mediated immune response. The amount of interferon gamma released is quantified and interpreted as either positive or negative. Blood tests using this assay can also detect active TB and infections in patients vaccinated with the Bacille Calmette-Guérin vaccine.¹⁷⁻²¹

Although TB patient may be asymptomatic, typical

presenting symptoms include low grade fever, recurrent cough, fatigue and weight loss. In the United States, most cases are diagnosed and treated with an antibiotic regimen after a positive skin test and chest x-rays consistent with TB. The cough is consistently productive and may be accompanied by chest pain.²²

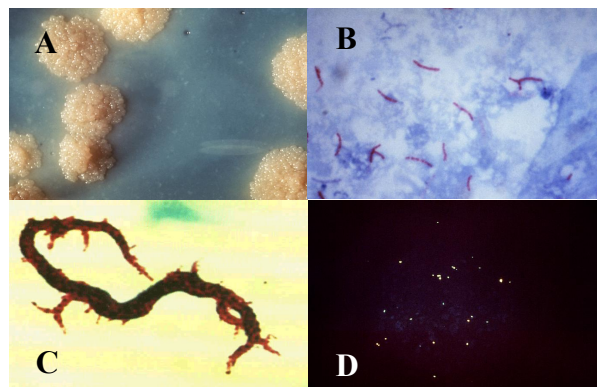


Figure 1. A: Characteristic small, rough, buff colored colonies of *Mycobacterium tuberculosis* acid-fast bacilli in a sputum sample. Public Health Image Library (PHIL) ID# 5789 Center for Disease Control and Prevention. Dr. George P. Kubica. B: This photomicrograph reveals *Mycobacterium tuberculosis* bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000X. C: Kinyoun stained smear from liquid culture showing the serpentine cord formation typical of *M. tuberculosis*. (600X) Dr. Bruce Hanna, New York University Medical Center. D: Public Health Image Library (PHIL) ID# 6469 Center for Disease Control and Prevention. Wilbur D. Jones. This micrograph reveals the presence of *Mycobacterium tuberculosis* stained with Truant's fluorochrome stain; 100x magnification

The Role of Medical Imaging in the Diagnosis of Tuberculosis

When a patient goes to see their primary care manager with a cough or chest congestion, the patient care manager typically orders a chest x-ray. When the patient comes to the imaging department, the radiologic technologist will ask the patient to disrobe from the waist up. A gown will be provided for patient privacy. If the patient is female, it will be determined if pregnancy is a possibility. If so, the technologist must inform the ordering provider who will determine if the benefit outweighs the risks prior to the exam.

Proper positioning of patients is vital to achieving clear diagnostic images.²³⁻²⁵ The radiologic technologist prepares the exam room prior to the patient's arrival. For an optimal image, the patient is in an upright orientation and a 72 inch source image distance is used.

The radiologic technologist selects the appropriate imaging receptor and technical factors. The patient is positioned with shoulders forward and their chest against the chest stand (Figure 2a). The central ray is aligned with the seventh thoracic vertebral body. The patient is given breathing instructions that facilitates adequate inspiration prior to exposure. After the image is obtained, the technologist critiques the image. In a properly exposed and positioned image, ten posterior ribs should be visible (Figure 2b).

When performing imaging procedures, two opposing 90 degree views are typically obtained.²³⁻²⁵ After the posteroanterior projection is completed, a lateral view is acquired. The patient is positioned with their left side against the chest stand with both arms above their shoulders (Figure 2c). Prior to the exposure, the patient is given breathing instructions to insure adequate inspiration. The image is critiqued for quality before submission to a radiologist for interpretation. Figure 2d is an example of an acceptable image. Radiographically, active TB may manifest as patchy infiltrates or abscesses (Figures 2e and 2f). The radiologist's interpretation of the posteroanterior chest radiograph indicates left upper and lower lobe consolidation and pleural effusion.

Imaging staff are often unaware that a patient has TB when they report for imaging. The lack of information regarding relevant patient history and symptoms presents an exposure risk to the radiologic technologist. Imaging staff practice universal precaution when at risk for contact with blood and bodily fluids. However, universal precautions do not specify respiratory protection. Close contact between the patient and the radiologic technologist while they are being positioned increases the risk of airborne transmission. This is especially true as the patient exhales following deep inspiration. Deep inspiration is a recognized trigger for coughing, which generates potentially infectious aerosols particularly in confined spaces.¹¹ If the patient is subsequently diagnosed with active TB, the potential exposure is reported to employee health services. Employees in direct contact with the patient will be evaluated by employee health. The technologist who performed the exam, and any other medical personnel in direct contact with the patient are notified and a TB skin test obtained. In the event of a positive skin test, a chest x-ray is requested. If the chest x-ray is abnormal, the technologist is referred to the local health

department. If a diagnosis of TB is confirmed, the technologist will be prescribed a regimen of isoniazid and rifampicin. These medications are taken for a period of nine months.

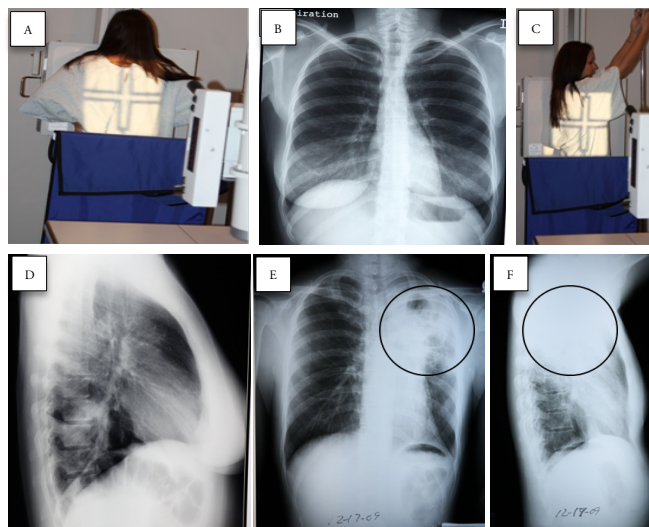


Figure 2. A: Patient in position for a posterioranterior chest exam B: Normal posterioranterior chest image C: Patient in position for a lateral chest exam D: Normal lateral chest image E: Posterioranterior chest image showing TB F: Lateral chest image showing TB

Policy Concerns about TB Exposure Control

Generally policies in hospitals and clinics are used to identify patients with TB after diagnosis and testing is complete. Patients with a positive diagnosis are reported to the state public health authority for contact investigation. Once identified as an active TB patient, precautions such as isolation, masking, and aerosol reduction can be implemented. Unfortunately, use of personal protective equipment (PPE) is left to the discretion of the medical professional caring for at risk patients. It is incumbent on the professional to exercise caution when interacting with patients exhibiting TB – like symptoms yet most medical professionals end up using PPE only after the diagnosis has been made and exposure has occurred. There is a clear need for a TB protocol that assists in identifying potentially positive patients to prevent exposure.

An Interdisciplinary Tuberculosis Management Protocol

The move toward interdisciplinary healthcare teams presents both a unique opportunity and a challenge to reduce the exposure of healthcare workers to TB. The stakeholders in this interdisciplinary process include

professionals from the departments of respiratory and physical therapy, phlebotomy, medical laboratory, radiology, physician services, nursing and other non-medical personnel such as volunteers or administrative assistants. While some of these departments have historically maintained effective respiratory infection control programs, others have no practical safety plan. Since the risk for contracting TB is perceived to be low, effective respiratory infection control is not a priority in medical imaging and outpatient phlebotomy departments. However, a recent study demonstrated that infectious doses of *M. tuberculosis* as low as 5.4 colony forming units are capable of infecting 95% of challenged mice.²⁶ This ultra-low dose model has also been demonstrated in fish and guinea pigs and may be consistent with human infection. In 2005, the Centers for Disease Control and Prevention (CDC) updated their recommended guidelines for preventing the transmission of TB in health-care to include a broader spectrum of settings. These guidelines now apply to the laboratory and ambulatory care facilities such as radiography suites. The list of healthcare workers who should be monitored for TB exposure control has also been expanded to include phlebotomists and radiology staff.¹¹ Therefore, we propose an interdisciplinary TB management protocol for the outpatient phlebotomy and radiography departments. This protocol should be followed whenever healthcare workers in these departments interact with the patients who meet any of the following criteria: persistent cough lasting three weeks or longer, chest pain, bloody sputum, weight loss or loss of appetite, fever, chills, night sweats and malaise.¹³ The World Health Organization further stipulates that tuberculosis infection should be suspected in patients who are at high risk for contracting tuberculosis and those who have been in contact with infected persons.²⁷ These patients should be identified as “TB high risk patients” in the electronic health record (EHR) signaling the need to implement the proposed tuberculosis management protocol. An example of this protocol is shown in Figure 3. The involvement of interdisciplinary teams should facilitate communication and implementation of this policy.

The proposed interdisciplinary tuberculosis management protocol includes the previously discussed method for identifying high-risk TB patients and communication of this risk to all healthcare workers via the EHR. Infection control, airborne precautions, and

post-exposure treatment are the remaining components of the protocol. The airborne precautions policy ensures three levels of protection for healthcare workers. The protective levels are organizational controls, engineering controls, and PPE (Table 1). Administrative controls focus on identifying areas where TB high-risk patients will be treated. Minimally these include the areas identified in CDC document Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005.¹¹ Attempts should be made to minimize areas treating TB high-risk patients. An organizational work-flow chart is helpful in identifying and restricting these areas.

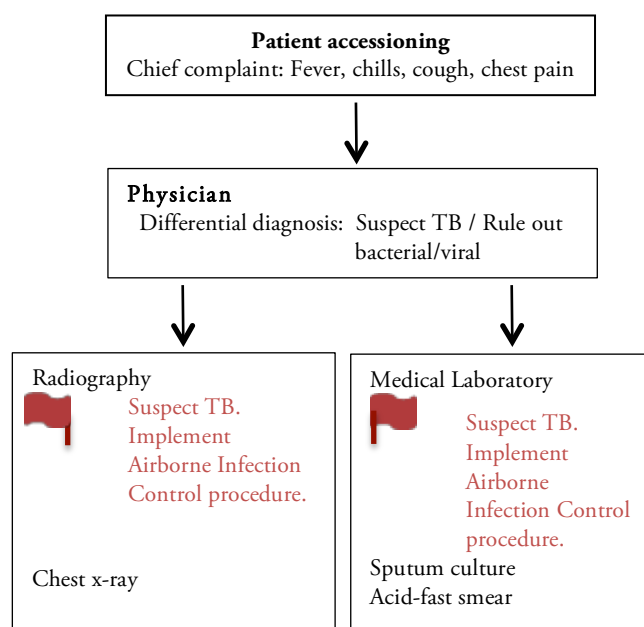


Figure 3. Electronic health record (EHR) flow chart for dissemination of TB risk information to high risk health care workers.

Engineering controls are designed to reduce the concentration of airborne TB bacilli with the intent of reducing the risk of infection to both healthcare workers and visitors. Airborne infection isolation rooms should be used for TB high-risk patients and should maintain continuous negative pressure (0.01 inch or 2.5 Pa) in relation to the air pressure outside of the room.^{11,28,29} While it may not be feasible to have a dedicated airborne infection isolation room available for all patient treatment rooms, every effort should be made to equip at least one room for the purpose of treating patients suspected of active TB infection. This room should be used for cough-inducing procedures, including deep breathing as required for chest x-ray and

sputum collection. High Efficiency Particulate Air

Table 1. Personal protective equipment (PPE) and engineering controls (EC) recommended for healthcare workers at high risk for exposure to TB.

	Radiologic Technologist	Phlebotomist	Medical laboratory professionals	Respiratory therapist
PPE	N95 mask Gloves (when performing surface disinfection)	N95 mask Gloves (as part of Universal Precautions standard)	Gloves (as part of Universal Precautions standard)	N95 mask Gloves (when performing surface disinfection)
EC	Dedicated Airborne Infection Isolation exam room	Dedicated Airborne Infection Isolation room for sputum collection	BSL 2 / BSL 3 for work with MDR-TB cultures All sputum. Sample processing should be performed in a biosafety cabinet	Dedicated Airborne Infection Isolation treatment room

(HEPA) filters should be used to clean air from this room prior to external exhausting, airborne infection isolation re-circulation, or exhausting airborne infection isolation air into the general circulation. Where the potential exists for patients with undiagnosed TB infection to pass through community spaces, ultraviolet germicidal irradiation is an economic alternative to use of HEPA filtering to disinfect air flowing through ductwork. These community spaces include emergency rooms and waiting areas.¹¹

PPE includes National Institute for Occupational Safety and Health Administration (OSHA) approved respiratory protection and tuberculocidal disinfecting agents. Respirator selection guidelines are published by the CDC.²⁹ N95 respirators, both disposable and reusable, are approved for work with *M. tuberculosis* and filter 95% of airborne particles that are 0.3 microns or larger in size. The most important consideration in selecting a respirator is proper fit. OSHA requires a respiratory protection program whenever respirators are

in use. This program ensures that the wearer understands the risks and responsibilities of respirator use, has been properly fit tested for his or her respirator, and has received proper training in the use of the respirator. Fit testing and training should be provided annually. Respirators are required by OSHA for all healthcare workers treating patients suspected of TB infection.³⁰ The proposed interdisciplinary tuberculosis management protocol includes fit testing and use of N95 respirators whenever healthcare workers contact patients suspected of having an active TB infection.

Sterilization is required for all critical medical equipment such as needles that contact bodily fluids. Sterilization is recommended for all semi-critical medical equipment that contact mucous membranes, such as bronchoscopes. Tuberculocidal disinfecting agents should be used to clean those surfaces which do not come into contact with the patient or which contact only intact skin, classified as non-critical medical equipment. Tuberculocidal agents are not required for cleaning environmental surfaces such as floors and tabletops as *M. tuberculosis* is not contracted from environmental sources.^{11, 30}

The final component of the proposed interdisciplinary tuberculosis management protocol mandates post-exposure investigation and treatment. All healthcare worker exposures to patients known to have active TB infections must be investigated. If a healthcare worker displays a positive tuberculin skin test, the employee should be medically evaluated and treated if necessary. When results of the tuberculin skin test are equivocal, chest x-ray or sputum evaluation should be used to definitively rule out latent TB infection or active TB disease. Medical evaluation can be obtained at employee health services, public health departments, or private medical clinics. Latent TB should be treated in most healthcare workers in support of the United States public health goal of eliminating TB. Treatment is contraindicated for patients with liver disease or with a known high level of alcohol consumption. Combined therapy with isoniazid and rifampicin is the recommended treatment regimen.^{31, 32}

Evaluation of the TB management protocol should be done following implementation. Managers in the radiography and outpatient phlebotomy areas should be instructed to track patients treated in their areas which

are identified as high risk for TB and correlate this to the number of patients eventually diagnosed with TB. Managers should also track exposure of their staff to patients unidentified as high risk for TB. Hopefully, after implementation of the suggested protocol, the number of staff exposures should decrease as more patients are correctly identified as high risk for TB. Because this protocol suggests a screening process, it is expected that not all patients initially identified as high risk for TB will have a corresponding diagnosis of TB. This sacrifice of clinical specificity is expected in screening procedures. Further confirmatory testing should improve specificity and provide an accurate final diagnosis as TB positive or negative.

CONCLUSION

Implementation of the proposed interdisciplinary tuberculosis management protocol presented here could prevent accidental exposure to emergency care providers, radiologic technologists, and medical laboratory personnel. Effective communication between members of interdisciplinary diagnostic management teams regarding patients' differential diagnoses and potential risk for exposure to infectious diseases is paramount. Because of the cost and inconvenience associated with some of the TB infection control procedures, healthcare workers' compliance is inconsistent. However, communication of the risk of exposure based on the physician's initial exam and differential diagnosis mandates use of PPE and engineering controls when the risk for exposure to *M. tuberculosis* is high. Simply relying on post-exposure evaluation and treatment does not make the best use of available resources such as dedicated exam and radiography suites and N95 respirators. The cost of treating an infected healthcare worker ranges from approximately \$10,000 for nonresistant strains to over \$700,000 for fatal cases caused by drug resistant TB.^{34,31} Avoidance of exposure potentially represents a significant, avoidable cost to healthcare organizations.

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