



Preventing the Transmission of Tuberculosis in Health Care Settings: Administrative Control

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It is well established that health care workers (HCWs) have a considerably higher risk of occupationally acquired tuberculosis (TB). To reduce the transmission of TB to HCWs and patients, TB infection control programs should be implemented in health care settings. The first and most important level of all protection and control programs is administrative control. Its goals are to prevent HCWs, other staff, and patients from being exposed to TB, and to reduce the transmission of infection by ensuring rapid diagnosis and treatment of affected individuals. Administrative control measures recommended by the United States Centers for Disease Control and Prevention and the World Health Organization include prompt identification of people with TB symptoms, isolation of infectious patients, control of the spread of the pathogen, and minimization of time spent in health care facilities. Another key component of measures undertaken is the baseline and serial screening for latent TB infection in HCWs who are at risk of exposure to TB. Although the interferon-gamma release assay has some advantages over the tuberculin skin test, the former has serious limitations, mostly due to its high conversion rate.

Keywords: Tuberculosis; Health Personnel; Tuberculin Test; Interferon-Gamma Release Tests

Introduction

Tuberculosis (TB) infection control is a combination of measures aimed at minimizing the risk of transmission within a population. The fundamental aspects of this control include early and rapid diagnosis and proper management of TB patients. Various guidelines¹⁻⁴ have recommended a combi-

nation of control measures to reduce the transmission of the disease in health care settings to health care workers (HCWs) and patients, many of whom may be immunocompromised. Reports of improved implementation of the recommended controls and fewer outbreaks of TB disease in health care settings suggest that these controls are effective in reducing and preventing health care-associated transmission of *Mycobacterium tuberculosis*⁵.

The World Health Organization (WHO) policy on TB infection control recommends four levels of protection: an overarching managerial level, administrative control, environmental control, and personal respiratory protection³. Similarly, because of the well-known occupational risk to HCWs from TB, the U.S. Centers for Disease Control and Prevention (CDC) have recommended in their guidelines that all health care settings should have a TB infection control program. This should be designed to ensure prompt detection, airborne precautions, and treatment of individuals who have suspected or confirmed TB disease¹ and should be based on a three-level hierarchy of controls, including administrative, environmental, and respiratory protection^{1,2}.

The first and most important level of this hierarchy is administrative control. Its goals are to prevent HCWs, other staff,

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and patients from being exposed to TB and reduce the transmission of infection by ensuring rapid diagnosis and treatment of patients and staff with TB⁵. Another important aspect is to provide a package of prevention and care interventions for HCWs⁶. This article discusses the details of administrative control recommended by the CDC and WHO, after first examining the risk of TB for HCWs. We also review recent reports and disputes concerning the screening of HCWs for TB infection.

Risk of TB among HCWs

1. Risk of active TB

The rate of diagnosis of active TB in HCWs has consistently been reported to be higher than that for the general population in a number of studies conducted in countries with low and high TB prevalence. For example, in England and Wales, HCWs are 2.4 times more likely to contract active TB than other people, after taking into account socioeconomic status, ethnic group, age, and sex⁷. Recently, Chu et al.⁸ conducted a nationwide, population-based cohort study based on the Taiwan National Health Insurance Database for the years 2000–2010. They found that the incidence of active TB was higher for HCWs than for matched subjects, particularly for pulmonary TB compared with extrapulmonary TB. A study in South Korea investigated the prevalence of TB among HCWs employed at a university hospital and found that the prevalence ratio for nurses working in a TB-related department (medical intensive care unit, pulmonary medicine ward, or emergency department) was higher than for the general population, suggesting that some of the HCWs developed active TB disease via a hospital infection⁹.

2. Risk of TB infection

In addition to active TB, it is also well known that HCWs have a substantially increased risk of occupationally acquired TB infection. Menzies et al.¹⁰ showed that the median prevalence of latent TB infection (LTBI) in HCWs was 63% in low- and middle-income countries and 24% in high-income countries, suggesting the risk of LTBI is high for HCWs worldwide. Recently, Casas et al.¹¹ reported that the cumulative incidence of tuberculin skin test (TST) conversion was higher in HCWs who worked in high-risk areas in a tertiary referral hospital in Spain. In South Korea, a prospective study evaluated the annual incidence of LTBI among newly employed nurses at a tertiary care university hospital, and concluded that the annual risk of LTBI for these nurses was at least 3%¹².

Administrative Control

1. Administrative control in the CDC guidelines

According to the CDC guidelines^{1,2}, a TB infection control program should be based on the following three levels of hierarchy: (1) administrative control, which reduces the risk of exposure; (2) environmental control, which prevents the spread of the disease and reduces the concentration of droplet nuclei; and (3) respiratory protection control, which further reduces the risk of exposure in specific areas and circumstances. Of these, the first and most important level is the use of administrative measures to reduce the risk of exposure to people who might have TB disease. According to the CDC guidelines, this level comprises the implementation of a range of activities^{1,2}; these are summarized in Table 1.

Table 1. The activities of administrative control recommended by the U.S. Centers for Disease Control and Prevention

1. Assigning someone the responsibility and authority for TB infection control in the health-care setting
2. Conducting a TB infection control risk assessment of the setting
3. Developing and instituting a written TB infection control plan to ensure prompt detection, separation from others, and treatment of persons who have suspected or confirmed TB disease
4. Ensuring the availability of recommended laboratory processing, testing, and reporting of results
5. Implementing effective work practices for managing those who may have TB disease
6. Ensuring proper cleaning, sterilization, or disinfection of equipment that might be contaminated (e.g., endoscopes)
7. Testing and evaluating workers who are at risk for exposures to TB disease
8. Applying epidemiology-based prevention principles, including the use of setting-related TB infection control data
9. Using posters and signs to remind patients and staff of proper cough etiquette and respiratory hygiene
10. Coordinating efforts between the local health department and high-risk health-care and congregate settings

Modified from the U.S. Centers for Disease Control and Prevention core curriculum on tuberculosis².
TB: tuberculosis.

2. Administrative control in the WHO policy

The administrative control measures according to the WHO policy³, which covers TB infection control in congregate settings (i.e., institutions or environments where people live in close proximity to each other) and households as well as health care facilities, are rather different from those recommended by the CDC. Along with environmental control and personal protective equipment, the WHO's policy for administrative control in health care facilities includes the following³.

1) Prompt identification of people with TB symptoms (triage)

Prompt identification of people with symptoms suggestive of TB is crucial. Generally, people suspected of having TB should be separated from other patients and placed in adequately ventilated areas, and should be diagnosed as a matter of priority.

2) Separation of infectious patients

Separation of infectious patients after triage is important. In particular, immunocompromised patients should be separated from those with suspected or confirmed infectious TB. In addition, people with confirmed or suspected drug-resistant TB—especially TB that is multidrug or extensively drug resistant—should be separated or isolated from other patients, including those with drug-susceptible TB.

3) Control of the spread of the pathogen (cough etiquette and respiratory hygiene)

To minimize the spread of droplet nuclei, any coughing patient with a respiratory infection—particularly, those with or suspected of having TB—should be educated in cough etiquette and respiratory hygiene, that is, the need to cover their nose and mouth when sneezing and/or coughing with a physical barrier, such as a piece of cloth, tissue, or surgical mask. It

is also important that such items are properly disposed of. If such physical barriers are not available, the best practice is for the mouth and nose to be covered with the bend of the elbow or the hands, which must then be cleaned immediately.

4) Minimizing the time spent in health care facilities

Patients should spend as little time as possible in health care facilities, including clinics, to avoid the nosocomial transmission of TB. Except in cases with complicated or concomitant medical conditions that require hospitalization, hospital stay is generally not recommended for the evaluation of people suspected of having TB or the management of patients with drug-susceptible TB. HCWs should ensure they minimize the time spent with such patients in areas that are overcrowded or poorly ventilated.

Serial Testing to Diagnose LTBI in HCWs

1. Serial testing with the TST

Screening of HCWs for LTBI is another key component of the administrative control of hospital TB infection control programs. According to the facility risk classification recommended by the CDC (Table 2), the majority of general hospitals and university hospitals in South Korea correspond to the medium risk level for TB. According to the CDC guidelines¹, in a setting classified as medium risk, all HCWs should receive a baseline TB screening test when they first start employment with the institution using a two-step TST to test for infection with *M. tuberculosis*. After this baseline testing, HCWs should receive annual TB screening using a TST (serial TST) (Table 2). Any HCWs with a baseline positive or newly positive TST result, or with the documentation of previous treatment for an LTBI or TB disease, should undergo chest radiography once to exclude active TB disease.

Table 2. Risk classification for various health care settings and recommended frequency of screening for *Mycobacterium tuberculosis* infection among health care workers

	Risk classification		
	Low risk	Medium risk	Potential ongoing transmission
Setting			
Inpatient <200 beds	<3 TB patients/yr	≥3 TB patients/yr	Evidence of ongoing TB transmission, regardless of setting
Inpatient ≥200 beds	<6 TB patients/yr	≥6 TB patients/yr	
Recommendations for screening frequency			
Baseline two-step TST	Yes, for all HCWs	Yes, for all HCWs	Yes, for all HCWs
Serial TST	No	At least every 12 mo	As needed

Modified from U.S. Centers for Disease Control and Prevention 2005 guidelines¹.
TB: tuberculosis; TST: tuberculin skin test; HCW: health-care workers.

A TST conversion is defined as a TST induration that has increased in size by ≥ 6 mm and has a total size ≥ 10 mm. If such a TST conversion is observed in a HCW with a documented negative (< 10 -mm) baseline two-step TST result, this indicates a recent TB infection. Recent TST converters have a higher risk of TB development (by as much as 15-fold) than subjects with no risk factors, and approximately 5% of people newly infected with *M. tuberculosis* will develop the disease in the 1–2 years after infection^{13,14}. Therefore, among people infected with *M. tuberculosis*, a TST converter is generally classified as high risk for the development of active TB¹⁵. Accordingly, the Korean TB guidelines revised in 2014 have classified anyone with a TST conversion within the previous 2 years as a high-risk group¹⁶. HCWs whose TST result has recently converted to positive should therefore be regarded as candidates for preventive chemotherapy.

When a TST is used for baseline testing, two-step testing is recommended for HCWs whose initial TST results are negative when a booster effect is considered^{17,18}. The concept and the interpretation of the two-step TST are as follows. (1) If the first-step TST result is negative, the second-step TST should be administered 1–3 weeks after the first TST was read. (2) If either the baseline first-step TST result is positive, or the first-step result is negative but the second step is positive, the HCW can be diagnosed as having a LTBI after active TB has been excluded. (3) If the first and second-step TST results are

both negative, the person is classified as not infected with *M. tuberculosis*¹. A positive result of the second step of a baseline two-step TST is thought to be due to a boosting effect that may result from a remote infection of *M. tuberculosis*. The CDC guidelines recommend that all HCWs receive a baseline two-step TST when first employed (Figure 1)¹. In South Korea, most centers have not adopted this approach because of executive difficulties. However, according to one report, the proportion of HCWs who convert to positive in the second step of the two-step TST is not rare in South Korea; among 556 newly employed HCWs at a university hospital, 14.2% experienced a boosted reaction on the second TST¹⁹.

Although there is considerable experience of using the TST over several decades, this test has a number of drawbacks. In particular, the TST requires two or more patient visits to conduct the test because the results are only available 48 to 72 hours later. In addition, a bacillus Calmette–Guerin (BCG) vaccination can cause a false-positive result. Third, although rare, the injections may result in an adverse skin reaction. Finally, the TST result needs to be interpreted by a well-trained person.

2. Serial testing with interferon-gamma release assay

Compared to the TST, the interferon-gamma release assay (IGRA), including the QuantiFERON-TB Gold In-Tube

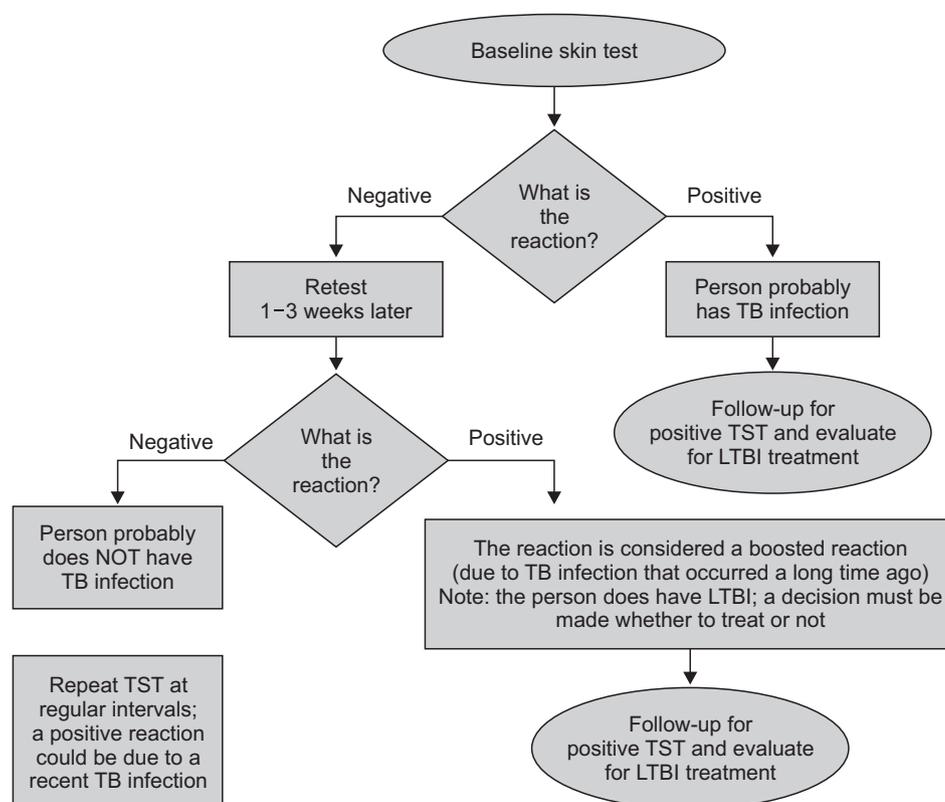


Figure 1. Two-step TST testing (from the U.S. Centers for Disease Control and Prevention core curriculum on tuberculosis²). TB: tuberculosis; TST: tuberculin skin test; LTBI: latent tuberculosis infection.

assay (QFT-GIT) and T-SPOT.TB test, has several distinct advantages. It requires only one patient visit, and the results are unaffected by HCW perception or bias and are available in 24 hours. In addition, a BCG vaccination will not cause a false-positive result. In this context, serial testing with IGRA is attractive because the approach avoids subjective measurement, which can be repeated without sensitization and boosting in subsequent tests, and eliminates the need for multiple visits for the interpretation of the results of the two-step test²⁰.

Since the CDC published guidelines in 2005 indicating that the IGRA may be used in all circumstances in which a TST is recommended, including for the serial screening of HCWs¹, there have been several reports of its use. Slater et al.²¹ reported data regarding the reproducibility of serial QFT-GIT in a large cohort of HCWs in a single North American health care institution. Among 9,153 HCWs who underwent two or more QFT-GIT tests, 8,227 showed an initially negative result, of whom 361 (4.4%) showed a second QFT-GIT result conversion over 2 years. A total of 261 of these HCWs (72.3%) with conversions underwent repeat short-term testing after the first positive result, with 169 (64.8%) reverting. Interestingly, these authors found that the QFT-GIT cut-off would need to be increased by more than 10-fold to yield an equivalent historical TST conversion rate. These results suggest that the manufacturer's definition of QFT-GIT conversion results is an inflated conversion rate, incompatible with the low-risk setting in North America.

Another important study involving HCWs at four health care institutions in the United States also indicated that IGRA is associated with a significantly higher conversion rate than the TST, and that many IGRA conversions appear to be false-positives²². In South Korea, Park et al.²³ evaluated the conversion and reversion rates of IGRA in prospectively enrolled HCWs who were in contact with patients with active pulmonary TB. Of the 48 HCWs who received monthly QFT-GIT, 25 (52%) showed inconsistent results in the serial testing, confirming that fluctuations in QFT-GIT results were also common in HCWs in South Korea. The poor reproducibility and high conversion rate of QFT-GIT appear to stem from variability inherent within the test itself rather than being due to host or pathogen factors²⁴. This finding has particular relevance for HCWs who make up the majority of those tested repeatedly. In this context, it is notable that Canadian guidelines published in 2013 discourage the use of serial IGRA tests for HCWs for this reason⁴. Further studies are required concerning the availability and the optimal cut-off level for QFT-GIT as a serial test for detecting LTBI in HCWs in South Korea.

In contrast to the conclusions of these reports, a recent study has suggested that T-SPOT.TB tests that adopt a borderline zone are reliable for HCW serial screening without the possibility of poor reproducibility or an inflated conversion rate²⁵. However, given the limited number of studies of T-SPOT.TB tests with such a borderline zone for the evaluation of LTBI

in HCWs, further studies will be needed to confirm this finding.

Conclusion

To reduce the transmission of TB to HCWs and patients, TB infection control programs should be implemented in health care settings. Such programs should have a three-level hierarchy, of which administrative control is the first and most important level. The goals of administrative control are to prevent HCWs, other staff, and patients from being exposed to TB and reduce the transmission of infection by ensuring the rapid diagnosis and treatment of patients and staff with TB. According to the CDC and WHO guidelines, administrative control should involve the implementation of a variety of activities, with a key component being baseline and serial screening for LTBI of HCWs at risk for exposure to TB. Although the IGRA has some advantages over the TST, it has serious limitations, mostly due to its high conversion rate. Because the guidelines for TB infection control for HCWs are limited in South Korea, further studies regarding serial LTBI tests for HCWs are needed.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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