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Occupational tuberculosis: a review of the literature and the local situation

職業性結核病：文獻資料及本港情況的檢討

Objective. To review the risks and control of occupation-related tuberculosis.
Data sources. Statutory notification data, local tuberculosis programme data, and census data were reviewed. Literature search of PubMed was performed up to December 2005.
Study selection. Original and major review articles related to tuberculosis among health care workers and guidelines for prevention were reviewed.
Data extraction. Relevant data were extracted from our literature review and local sources.
Data synthesis. Earlier experimental data demonstrated an airborne spread of tuberculosis and a steady state mathematical model for quantification of the transmission risk. In the post-chemotherapy era in developed countries, few studies demonstrated an occupational risk of tuberculin conversion outside of outbreak settings, and few studies were able to conclusively demonstrate an increased risk of active tuberculosis among health care workers. In countries with limited resource, the situation may be different, with a higher tuberculosis incidence among health care workers. Local tuberculosis programme and notification data from the Labour Department did not show an increased risk of active tuberculosis among health care workers. Although administrative control, engineering control, and personal protection are widely accepted control measures, it is difficult to quantify their cost-effectiveness.
Conclusions. Although an increased liability to tuberculosis among health care workers is expected due to the concentration of infectious patients in their environment, prompt diagnosis and initiation of treatment may minimise the risk. A high background rate of disease and possible healthy worker effect may make it difficult to pick up a small risk differential. With the ongoing threat of a nosocomial outbreak, continuing vigilance is called for.

目的：檢討因工感染結核病的風險和控制。
資料來源：回顧法定疾病呈報、本地結核病防治計劃和人口普查的數據；亦從美國國家醫學圖書館「生物醫療相關文獻索引」（PubMed）搜索直至2005年12月的文獻。
研究選取：關於醫護人員感染結核病和預防指引的論著和綜述。
資料選取：從涉獵到的文獻和本地資料中抽取。
資料綜合：早期的實驗數據顯示結核病透過空氣傳播，並可用數學模式把傳播風險量化。在踏進後化療時代的已發展國家，很少研究顯示結核菌素測試轉變會在爆發情況以外的工作環境中出現，亦有很少研究能歸納出醫護人員有較高感染結核病的風險。在資源有限的國家，情況可能有些不同，醫護人員染上結核病的數字較高。來自本地結核病防治計劃和勞工處疾病呈報的數字，並無顯示醫護人員有較高的活躍結核病風險。雖然行政控制、工程控制和個人保護被廣泛採納作為控制結核病的措施，它們的成本效益則難以量化。
結論：雖然醫護人員因工作於患者集中的環境而被認為感染風險較高，盡早診斷和治療有助減低這風險。高背景發病率及「健康工人效應」可能掩蓋細微的風險差異。醫療設施內結核病爆發的威脅仍然存在，必須繼續維持高度警戒。

Key words:
Health personnel;
Hong Kong;
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Introduction

Tuberculosis (TB) is still an important infectious disease today. The recent World Health Organization (WHO) TB Fact Sheet[1] states that it kills approximately 2 million people each year. It is estimated that between the years 2002 and 2020 inclusive, approximately 1000 million people will be newly infected. Over the same period, according to the fact sheet over 150 million people will become sick, and 36 million will die from TB, if control of the disease is not further strengthened.

Hong Kong has been classified as a place with an intermediate TB burden yet good health care infrastructure. Although there is a general downward trend in the TB notification rate over the past 40 to 50 years, the rate of decline has slowed and become rather ‘stagnant’ in the last decade. The notification rate was 89.9 per 100 000 population in 2005.

The relation of TB to occupation can be broadly classified into three categories:

1. Occupations involving workers who are themselves at high risk of TB, like workers with less favourable socio-economic conditions: unskilled labourers and lower-paid workers.
2. Occupations that increase susceptibility to the infecting organisms: workers predisposed due to silicosis (eg mining, quarrying, foundry, and pottery work).
3. Occupations that increase the chance of exposure to infection in environments conducive to transmission: working in hospitals, mycobacteriology laboratories, and autopsy rooms.

In recent years there have been renewed concerns about the last category, largely due to the SARS (severe acute respiratory syndrome) epidemic in 2003, in which many health care workers (HCWs) were affected. Consequently, the risk of exposure to TB for HCWs has also attracted much attention and will be the focus of this article.

Transmission dynamics

In assessing the risk of TB, it is necessary to differentiate between transmission of infection and the subsequent development of disease. The former depends on the dissemination of the infectious agent from the source and its transfer to a receptive site in the host, whilst the latter is a reflection of the complex interaction of the pathogen and its resident host. In general, around 5% of TB infections progress to disease within the first 2 years, and another 5% reactivate and develop active disease later. Thus, most infected individuals have latent infection and are generally free of symptoms and not infectious.

Tuberculosis is transmitted through air as small droplets (1 to 5 μm diameter particles). They can remain suspended in air indefinitely, and have a tendency to be deposited in alveoli when inhaled. Such small particles contain few microbes, and in any they are susceptible to ultraviolet germicidal irradiation (UVGI) in air. Nonetheless, the usual respiratory droplets are much larger (>100 μm in diameter) and normally settle on surfaces within 1 m of the source. They contain many microbes and are UVGI resistant on surfaces. Examples of infections transmitted through large respiratory droplets include staphylococcus, respiratory syncytial virus, and influenza.[2]

In 1962, Riley et al[3,4] conducted the first classical experiment using guinea pigs to demonstrate that TB is transmitted by air. By studying the total number of guinea pigs infected over a 4-year period, and calculating the volume of air they breathed, the volume of air containing one infectious dose (1 quantum) was estimated to be around 11 000 cubic feet. This figure is consistent with the estimated average amount of air breathed by a student nurse working on a TB ward in the pre-chemotherapy era before her tuberculin skin test converted to positive. It can also be derived that on average, a person would have a 50% chance of becoming infected after spending 8 hours per day for 6 months with an infectious patient:

Result from guinea pig studies:
Volume for 1 quantum=11 000 cu ft=a
Let tidal volume of breath (human being)=500 mL=b
breaths per minute (human being)=12/min=c
Volume breathed per unit time=V=bc (mL/min)
Time required to breathe 1 quantum=a/V=865 hours≈22 weeks (assuming 40 working hours in a week) or around 6 months

A steady-state mathematical model has been developed to describe the transmission of airborne infectious diseases, which is well known as the Wells-Riley equation[3]:

No. of newly infected cases=$C=S(1 - e^{-Jqpt/Q})$
where: S=number of susceptible individuals
J=number of infectors
q=quanta of airborne infection produced by an infectious person
p=pulmonary ventilation rate per susceptible
t=duration of exposure to infection
Q=infection free ventilation (outdoor or disinfected air)

From the equation, it can be seen that, however small the risk from brief exposure (casual contact), a few out of a large population may become infected through casual contact. By using this model, the quanta of infection produced by infectious TB patients under different circumstances have been estimated from a number of observed incidents in the literature (Table 1).[4-9] Comparing the dissemination rates in terms of quanta per hour, generally TB appears to be much less infectious than acute infections like measles.

How much is the risk?

Menzies et al[10] reviewed the risks of TB infection and disease among HCWs reported in the medical literature, as

Table 1. Estimated infectiousness of tuberculosis (TB) and measles under different circumstances[4-9]

Setting	Dissemination rate (quanta per hour)	Volume of air containing 1 quantum (cu ft)	Reference
TB wards (long stay)	N/A*	24 000	Riley and O'Grady,[5] 1961
TB ward (newly treated patients)	1.25	11 000-12 500	Riley et al,[4] 1962
Cavitary TB in poorly ventilated building	13	N/A	Nardell et al,[6] 1991
Laryngeal TB	60	200	Riley et al,[4] 1962
Bronchoscopy	250	69	Catanzaro,[7] 1982
Autopsy	N/A	3.5	Templeton et al,[8] 1995
Measles outbreak at school	Index≈5500 Secondary=500	N/A	Riley et al,[9] 1978

* N/A denotes not available

well as risk factors found for single case transmission and prolonged hospital TB outbreaks. A significantly increased risk of TB was found in the pre-chemotherapy era. In the post-chemotherapy era, the risk ratios ranged from 0.6 to 2.0, with the highest risk occurring among those whose occupations involved the preparation of histological specimens and involvement with autopsy procedures. However, there were a number of major limitations to these studies, including lack of age adjustment, healthy worker effect, possible misclassification of occupation, recall bias, and low response rates in some of the questionnaire studies. A Hong Kong study included in the review also did not show any excess risk of TB among HCWs.[11]

Review of TB infection rates in HCWs showed that the annual risk of infection (ARI) during the pre-chemotherapy era was as high as 80%.[10] In the post-chemotherapy era, the ARI in different evaluation studies was to a large extent related to surrogates of TB exposure. Such surrogates include the annual number of patients admitted with TB, the number of HCWs exposed per corresponding admission, and jobs involving relatively high TB exposure in the health care settings.[10] It was estimated that 1 to 10% of HCWs may become infected annually in hospitals with more than 200 TB admissions per year. The major limitations of these studies included: sensitivities and specificities of the tuberculin skin test, low participation rates, and lack of good control groups with comparable non-occupational exposure.

In outbreak reports included in the review,[10] the percentages of exposed HCWs being infected ranged from 14 to 55%, whilst the percentages developing active disease ranged from 2.2 to 8.4%. Factors contributing to such outbreaks included delay in diagnosis, poor ventilation without negative pressure in isolation rooms or not keeping the doors closed, high levels of air recirculation, and precautions not fully taken during high risk procedures like aerosolisation of bacilli through mechanical ventilation, bronchoscopy, dress change, jet irrigation of thigh abscess, and autopsy procedures. Inadequate use of masks by HCWs going into, or by patients coming out of isolation rooms, and difficulties in control of drug-resistant strains were other contributing factors.[10] However, it appeared difficult to assess the precise magnitude of the risk from protected as opposed to unprotected exposures. Several outbreaks of multidrug-resistant TB (MDR-TB) in the US have led to occupational deaths among HCWs, arousing much public concern. Special care needs to be exercised in the treatment of latent TB infections (LTBI), as certain regimens employing rifampicin and pyrazinamide have been associated with fatalities.[12]

A more recent review by Nardell and Sepkowitz[13] summarised debates on the relative contribution of community versus occupational exposure to tuberculin test conversion in HCWs in the US. Before 1985, it was remarked that community-based exposure predominated. This observation was based on findings from studies, which showed that the HCW tuberculin conversion rate was related to socio-economic status or place of residence rather than the job categories. During the period 1985 to 1992, a number of nosocomial TB outbreaks occurred in the US. Analysis revealed that these were associated with concomitant HIV infection or MDR-TB,[14] and that jobs with higher TB exposure risks were associated with tuberculin conversion.[15,16] However, during the same period, few studies demonstrated any occupational risk outside the setting of outbreaks, and tuberculin conversion was mainly associated with place of residence and socio-economic status.[17,18] From these observations, the US Centers for Disease Control and Prevention (CDC) believed strongly that outside outbreak settings, community exposure was the dominant risk factor for tuberculin test conversion in the US health care work force.[13]

Tuberculosis incidence among HCWs in developed countries other than the US is also close to the incidence in the surrounding community.[19,20] Such inferences may not be applicable in resource-limited countries. Transmission to HCWs in a public hospital in Brazil of 4% (suggested by the overall annual tuberculin skin test conversion rate), was approximately four times greater than the rate in the community.[21] In countries like Estonia,[22] Turkey,[23,24] Malawi,[25,26] India,[27] and Thailand,[28] the TB incidences among HCWs were also high, and the quoted risks were 1.5 to 11 fold that in the general population or other comparator groups. The observed differences between developed and resource-limited countries probably reflect the availability

Table 2. Number of tuberculosis cases in health care staff notified to the Hong Kong Labour Department (2001-2005) by age and job title[31]

Age (years)	Medical doctor	Nurse	Other allied health professional	Other supporting staff	Total
20-24	0	15	0	2	17
25-29	9	31	7	0	47
30-34	7	24	3	3	37
35-39	6	13	5	2	26
40-44	2	6	2	6	16
45-49	1	5	1	5	12
50-54	0	1	2	8	11
55-59	1	0	0	3	4
60-64	0	0	0	2	2
65-69	0	0	0	0	0
Total	26	95	20	31	172

of resources and infection control measures in health care settings.

Local situation

In Hong Kong, since 1997 TB in HCWs is notifiable to the Commissioner for Labour under the Occupational Safety and Health Ordinance. It is also a "prescribed" occupational disease under the Employees' Compensation Ordinance, with a prescribed period of 6 months.[29] The objective of "prescribing" an occupational disease in the Employees' Compensation Ordinance is to facilitate the application of the principle of presumption of its occupational origin in compensation claims. Whenever such a disease is diagnosed within the statutory "prescribed period" from the date the worker last stayed in the job, it can be presumed to be of occupational origin. Thus, an employee incapacitated by the specified disease is relieved from the legal complications of having to prove its occupational origin and hence the compensation process is expedited.

From the surveillance data of the Labour Department, 30 to 42 cases of occupation-related TB were notified each year during the period 2001 to 2005.[30] The age profile and nature of occupations are shown in Table 2.[31] They were generally younger, predominantly female, mainly new cases (without past treatment), and more likely to have negative pretreatment sputum smears and cultures, in comparison to all TB patients notified during the same period (Table 3).[31] These observations were in line with what was expected from the very nature of the workforce.

Some idea of the rate of TB among local HCWs may be inferred using the surveillance data from Labour Department (Table 2[31]) as numerator and the relevant manpower statistics in the latest census (2001) as denominator.[32] Excluding 31 cases involving supporting staff, there were 141 cases of occupational TB in a combined period of 5 years, from a denominator of 57 869 doctors, nurses, paramedical/paradental staff in the 2001 census. Thus, the estimated annual incidence of clinical (active) TB among HCWs would be (141/5)/57 869, or 48.7 per 100 000 population. This figure appears comparable to the TB rate in the same working age range of the general population (Fig). However, it has to be noted that the method of estimation is very crude, as both the numerator and denominator could be subject to considerable ascertainment and classification errors.

Table 3. Tuberculosis (TB) patients notified to registries during the inclusive period 2001-2005[31]

	TB in health care workers, n=172	All TB cases, n=32 351
Mean age (years)	35.3	53.7
Female	72.7%	35.4%
Site		
Pulmonary	76.7%	87.7%
Pulmonary and extrapulmonary	1.7%	3.2%
Extrapulmonary	21.6%	9.1%
Smear positive	22.7%	31.2%
Culture positive	54.7%	60.3%
Having previous treatment	5.2%	9.3%

In a review by Seto,[33] the age-adjusted rate of TB in the general population ranged from 87 to 94 per 100 000 from 1994 to 1998. The corresponding rates among HCWs in large, acute-care public hospitals ranged from 38 to 84, and thus were not significantly different from the rate in the corresponding age-group of the Hong Kong general population. Similarly, in an analysis of the occupational data of the 2001 cohort of TB patients as captured by the TB Programme Forms completed by medical practitioners in Hong Kong, a total of 47 TB patients were classified as medical and paramedical staff.[31] Using the 2001 census data again as the denominator, the rate thus calculated is 47/57 869 or 81.2 per 100 000. Despite the possible methodological limitations and considerable variations, the available estimates suggest a rate which is quite comparable to that in the general population.

Although an increased risk was expected because of the concentration of infectious sources, prompt diagnosis and initiation of treatment may minimise such risk. With a relatively high background rate of disease, largely through endogenous reactivation of remote infection[34] and possible

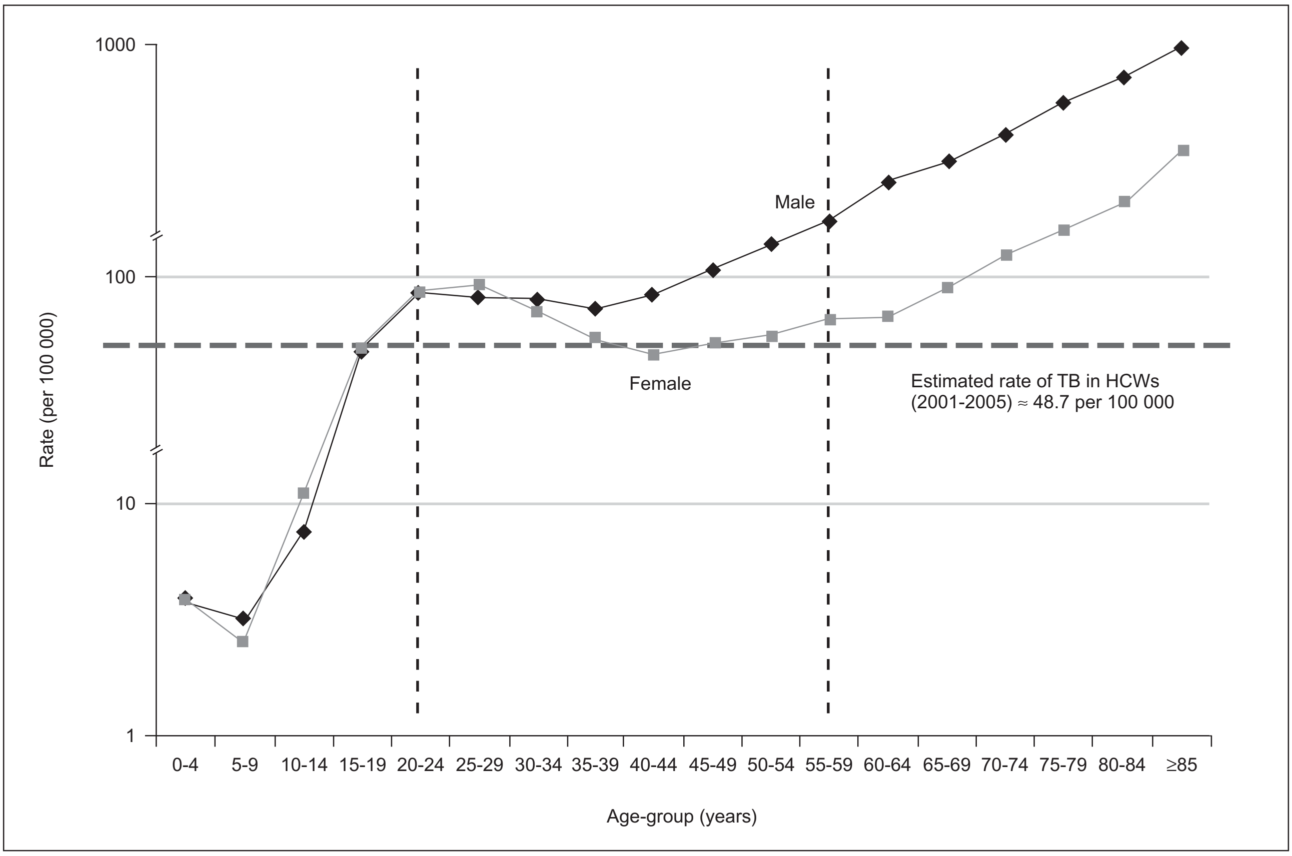

Fig. Mean tuberculosis (TB) notification rate of 2001-2005 and estimated rate among health care workers (HCWs) in 2001-2005

healthy worker effect, it may not be easy to pick up a small risk differential through routine surveillance data. The problem of background noise is best exemplified by the relative contribution of community versus household transmission of infection among household members observed in areas with a very high TB incidence. A study in Cape Town, South Africa found that among 33 households with more than one TB case, 18 had culture isolates with different DNA fingerprints within the same household.[35] Another study also from Cape Town showed that only 81 (19%) of 433 secondary cases arose from sources within the households; the rest being from sources beyond the respective households.[36]

Control of tuberculosis transmission in health care settings

Both US CDC and WHO have issued guidelines on the control of TB transmission in health care settings.[37-39] The 2005 version of the CDC Guidelines is an update of the 1994 version, reflecting the shifts in TB epidemiology, advances in scientific understanding, and changes in health care practice that have occurred. Local guidelines on TB infection control in health care settings have also been published.[40,41] The hierarchy of controls, in order of importance, include (1) administrative controls, (2) engineering controls, and (3) personal controls.

Administrative measures include risk assessment, implementation and evaluation of an infection control plan, training and education of workers, surveillance, patient triage, early identification, diagnosis, isolation and treatment, and patient education. To enhance cost-effectiveness, the 'rule-out ratio'—ie ratio of suspected cases admitted to isolation rooms versus cases truly with infectious risk—should ideally be kept at a lower level to reduce over-isolation.[13] Attention should be paid to the care provided to patients under isolation, as there were unpublished anecdotal reports that these patients may receive inferior medical care.[13] Prompt isolation and treatment appears to rapidly reduce the infectious risk, as evidenced by studies showing a marked fall in the concentration of viable bacilli by 2 logs after 7 days of treatment, and a much larger fall after 14 days.[42] Thus, it is generally recommended that infectious TB patients be kept under isolation for a period of 2 weeks from commencement of therapy.

Engineering controls include ventilation, UVGI, and high efficiency particulate air filtration. Among these, ventilation is the most important. It has been estimated that maintaining ventilation at 6 air changes per hour (ACH) can reduce the concentration of contaminants in 1 hour.[37] This rate is generally the minimum recommended for isolation wards, while a higher ACH rate is desirable for areas with a higher exposure risk such as bronchoscopy rooms or intensive care units. On the other hand, natural ventilation (as in older TB facilities with big windows and open door) has the advantage of being cheap and provides a much higher ACH rate than mechanical means of ventilation.[43] Ultraviolet germicidal irradiation is also cheap, but its limitations include: potential kerato-conjunctivitis, low penetration power, and reduced efficacy with the high humidity (as in the local setting). High efficiency particulate air filters can provide a minimum particulate removal efficiency of 99.97%, but at the same time they increase the resistive load, and the used filters constitute high-grade biohazards that must be properly disposed.

Respirators are the chief means for personal protection. In situations with low exposure risk such as the general TB ward where patients are under effective treatment, personal respirators generally play a smaller role compared to ventilation control. Where the risk of exposure is moderate like isolation wards holding patients with cavitary TB, the maintenance of an effective ACH rate and use of respirators have been described as having a multiplicative effect.[44,45] The use of respirators becomes increasingly more important in situations with high exposure risk, such as in the bronchoscopy or autopsy rooms. The effectiveness of surgical masks versus high-grade disposable particulate respirators in TB infection control programmes has not been rigorously evaluated. However, in some observational studies under non-outbreak situations, there was no evidence to suggest superiority of one over the other.[46,47] The use of periodic fit testing for use of high-grade disposable particulate respirators is another area of controversy.[48-51]

Bacille Calmette-Guérin (BCG) vaccination has been recommended as another means of personal protection for HCWs, although evidence of its efficacy in HCWs is scarce.[52,53] Several studies and decision analysis found more favourable results with BCG vaccination in comparison with periodic tuberculin screening and treatment of LTBI.[54-57] In Hong Kong, with a near 100% coverage of neonatal BCG vaccination, the bulk of the population has received BCG vaccination at some point in time. In health care settings, comprehensive infection control programme must remain a priority and routine revaccination of HCW is not recommended. Nevertheless, for HCWs who have never received BCG, they should be counselled on the risks and benefits. The possible roles of tuberculin surveillance and treatment of LTBI should also be explained. Under special high-risk circumstances, eg exposure to MDR-TB, BCG may be considered for previously unvaccinated and uninfected individuals after documentation with a negative tuberculin test.

As the incidence of TB among local HCWs is not significantly different from that of the general population, contact screening of HCWs for disease is considered unlikely to result in a high yield. However, it may be indicated when the index case is highly infectious, contacts are exceptionally vulnerable, the degree of contact is approaching that of close contact in the household setting, or when there are signs of ongoing transmission like case clustering. Health education on early symptom recognition may be more cost-effective than radiographic screening on a mass scale. The value of using tuberculin test for contact screening and possible treatment of LTBI in the local health care settings remains undefined. The exact circumstances have to be assessed on a case-by-case basis and liaison with the infection control team is desirable.[40] Following lapses in infection control measures or when significant unprotected exposure has occurred, targeted screening for active disease or latent infection may be indicated. Restriction fragment length polymorphism and other new molecular tests may be useful for evaluation of transmission dynamics.[58,59] Newer tests like antigen-specific T cell-based interferon-γ assays may offer better diagnostic specificity for the targeted treatment of LTBI.[60]

Based on the CDC guidelines and particularly in reference to engineering control measures, the cost of preventing one case of occupational TB in a hospital could run into millions of US dollars.[33] The CDC also stated that the information provided in its guidelines was primarily conceptual and intended to educate staff in the health care facilities concerning engineering controls and how they could be used as part of a TB infection control programme.[38] The guidelines should not be used in place of consultation with experts. Engineering control measures must be tailored to each facility based on needs and the feasibility of implementing ventilation and air-cleaning recommendations. As a control measure is only likely to work in circumstances where it is feasible and affordable, a prudent approach is necessary for its actual implementation in any infection control guidelines.

Conclusions

The risk of exposure to infectious TB in health care settings is generally expected to be higher than that in the community. However, based on surveillance data and study findings in different health care settings, this issue remains heated in controversies. Nevertheless, continuing vigilance is called for and effective infection control measures must be maintained to contain the potential risk of nosocomial transmission. These include, in the order of importance, various administrative control, engineering control, and personal protection measures. With the development of better diagnostic tests and drugs, the control of TB infection in health care settings can be enhanced through quicker identification of infectious cases and targeted treatment of the latently infected workers. Transmission dynamics can also be better understood through molecular epidemiological studies and relevant control measures can be refined.

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