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Occupation-Related Respiratory Infections Revisited

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KEYWORDS

• Tuberculosis • Nosocomial transmission • Infection control
• Occupational health

Tuberculosis (TB) is the best known, and most studied, occupational respiratory infectious disease. The wealth of published information regarding nosocomial transmission of TB can provide insight into the risks, mechanisms, and potential preventive measures for the nosocomial transmission of other airborne infections including severe acute respiratory syndrome (SARS), influenza, measles, varicella, and anthrax. The study of occupational TB is particularly informative because transmission can be monitored in 2 ways. The cumulative or periodic incidence of latent infection can be estimated using tests of immune reactions to TB antigens, such as the tuberculin skin test (TST).[1] Transmission that results in disease can be measured with a high degree of specificity using molecular epidemiologic tools such as restriction fragment length polymorphism (RFLP) analysis.[2]

Much of the information regarding risk, risk factors, and prevention of nosocomial transmission is derived from studies conducted in high-income countries.[3] There was considerable interest in this topic in the preantibiotic era, but this waned with the introduction of effective antibiotics.[4] However, the coincident advent of human immunodeficiency virus (HIV) infection and multidrug-resistant (MDR) TB resulted in several major outbreaks in high-income countries, particularly the United States. In a few of these outbreaks more than half of exposed patients became infected, developed disease, and died.[5] In the same hospitals a large number of health care workers were infected, although few developed disease and even fewer died.[5] These outbreaks led to renewed interest in the prevention of transmission of airborne respiratory infections. In the past decade attention has shifted to workers in low- and middle-income countries (LMIC), where risk of disease may be high.[3,6]

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Infect Dis Clin N Am 24 (2010) 655–680
doi:10.1016/j.idc.2010.04.013
id.theclinics.com
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RISK AND RISK FACTORS FOR TB INFECTION AND DISEASE

Several narrative and systematic reviews have been published on the risk of TB infection and disease among health care workers in high-income[4,5] and LMIC.[3,6] Nosocomial TB transmission has also been reviewed in guidelines issued by authoritative agencies including the US Centers for Disease Control[7] and most recently the World Health Organization.[8]

Until recently prevalence and incidence of latent TB infection (LTBI) could be measured only with the TST. In the past decade interferon γ release assays (IGRA) have been increasingly used to measure LTBI prevalence.[9,10] However, few studies have measured incidence of TB infection through serial performance of IGRA. Although IGRA have significantly better specificity in bacille Calmette-Guérin (BCG)-vaccinated populations,[9,10] their ability to predict who will develop active TB is unclear. In addition, studies of serial IGRA testing have reported substantial rates of conversion and spontaneous reversion.[11,12] Until these issues are clarified the usefulness of IGRA for estimation of nosocomial transmission remains questionable, although this is an area of active research. Hence this review focuses on studies using TST to detect prevalent and incident LTBI.

As summarized in **Table 1** a large number of studies have estimated risk of TB infection or disease. Although the estimates are variable, there is consistent evidence that the prevalence and incidence of LTBI in health care workers is substantially higher than the general population, in all settings. In high-income countries the pooled risk of TB disease among workers is only twice that of the general population, whereas the risk of infection is 10 times higher. In low-income countries disease and infection are about 5-fold higher than the general population. The reason for the difference in relative risk between infection and disease in high-income countries may reflect the healthy worker effect[53] or may reflect overestimation of LTBI because of the nonspecificity of tuberculin skin testing in BCG-vaccinated populations.

Risk factors associated with TB infection and disease in all countries are summarized in **Table 2**. Despite the differences in levels of exposure, risk factors are similar. Most of these risk factors can be interpreted to indicate simply that infection and disease are proportionate to likelihood of exposure to patients with TB. It is self-evident that more years of work, in jobs that involve direct patient care, and in hospitals or units caring for more patients with TB, are more likely to result in TB infection and disease. One useful indicator is the number of patients with TB per worker,[3,5] because the same number of patients with TB inevitably creates greater probability of exposure if cared for by a small group of workers, than the per-worker exposure

Table 1
Summary of risk of TB in health care workers relative to general populations

	Studies (N)	Relative Risk	References
LTBI			
High-income countries	27	10.1	13–38
LMIC	9	5.8	39–47
Active TB disease			
High-income countries	12	2.0	48–57
LMIC	20 (222)	5.7	58–79

Data from World Health Organization, Stop TB Department. WHO policy on TB infection control in health-care facilities, congregate settings and households. Geneva (Switzerland): World Health Organization; 2009.

Table 2
Occupational risk factors for TB

General	Specific	LMIC References	High-income References
LTBI			
Exposure	Years of work	44,45,47,58,80–82	37
	TB admissions	—	37
	Known TB contact	43,58	18,37,83
Type of work	Health care/patient care	45,84	83,85
	Physicians	80,86	37,87
	Nurses	45,80,86	21,37,85,88
	Respiratory therapists	58	85
	Trainees	—	18
Location of work	Medical ward	58,81,89	21,88
	HIV ward/care	—	21
	Emergency	86	16
	Laboratory/pathology	86	88,90
	TB ward/clinic	—	18
TB disease			
Exposure	—	—	—
Type of work	Health care/patient care	—	49,50,53,56
	Physicians	63,68,72,73	51,53,55
	Nurses	61,63,67,68,70–73	52,53,55
	Respiratory therapists	—	52
	Trainees	—	54
Location of work	Medical ward	58,70,72,91	—
	TB ward/clinic	58,59,62,66,70,72	—
	HIV ward/clinic	—	—
	Emergency	58,70	—
	Laboratory/pathology	58,63	—

risk in a larger hospital. Other risk factors relate to increased chance of exposure to undiagnosed patients; these include work in emergency departments, or HIV services (the latter because of the atypical clinical manifestations of TB in HIV-coinfected patients). The third category of risk factor relates to specific activities that increase patients' contagiousness. For example, respiratory therapists,[52,92] and pathology workers[2,90,93] have been consistently identified as high-risk workers, because certain of their tasks can result in aerosolization of TB bacilli (eg, intubation,[94,95] sputum induction,[96,97] bronchoscopy,[98] or autopsy[99,100]).

These epidemiologic observations have improved our understanding of nosocomial transmission, and guided the development of infection control recommendations. The consistent observation that risk is proportional to the number of patients with TB per worker has resulted in risk-stratified recommendations: large hospitals with few patients with TB are required to implement fewer measures to prevent nosocomial TB transmission than hospitals with more TB cases. The knowledge that workers in high-incidence countries have 5 times greater risk of infection and disease than the general population has led to the realization that TB is the most common and serious occupational illness in these countries. This finding has stimulated concerted efforts to raise awareness, not least among the workers themselves, many of whom have a stoic and fatalistic approach to occupational TB. This finding also resulted in development of guidelines for TB control in resource poor settings,[101] which have been updated recently.[8]

The identification of high-risk professionals such as respiratory therapists or pathology workers led to the realization that certain tasks were high-risk activities, such as bronchoscopy or autopsy. This finding in turn led to specific infection-control measures for these activities. The identification of increased risk associated with work in emergency departments resulted in administrative measures in these departments to improve triage and separation of patients suspected of TB.

INTERVENTIONS TO PREVENT NOSOCOMIAL TB TRANSMISSION

Interventions to prevent nosocomial TB transmission are generally divided into 3 broad categories: administrative, personal, and engineering.[7] These categories are often referred to as a hierarchy of control measures. Administrative controls are institutional policies that have the general aim of reducing the time between arrival of a patient at a health care facility and their placement in respiratory isolation, definitive diagnosis, and initiation of effective treatment. These controls include rapid triage of patients suspected of active TB, rapid performance of chest radiographs or other screening tests, expeditious processing of sputum samples for acid-fast bacillus (AFB) smear and culture, and more rapid separation of patients with TB (usually in isolation rooms). Personal controls are measures directed at individual workers. These measures include use of personal respirators (masks) and screening for, and treatment of, latent or active TB. Engineering controls are environmental measures that act to reduce the likelihood of workers' exposure to viable airborne TB bacilli. These controls include ventilation to remove and/or dilute airborne bacilli, and to ensure correct direction of flow of contaminated air, and ultraviolet germicidal irradiation (UVGI), which kills airborne bacilli.

As shown in **Table 3**, several studies have examined the effect on indicators of nosocomial transmission when multiple interventions were applied simultaneously. Harries and colleagues[65] implemented a program in 40 facilities in Malawi to train workers to triage, and separate patients with TB, and to enhance natural ventilation. These efforts resulted in a modest decline in overall TB incidence, which was not statistically significant. However, compliance with these measures was suboptimal. In Thailand, 1202 health care workers had serial tuberculin testing before and after administrative, personal, and engineering measures were instituted in one provincial referral hospital. Incidence of LTBI declined substantially but incidence of disease increased.[47] However, the increase in disease may have been a result of a concomitant increase in HIV prevalence, and because the number of patients with TB almost doubled at the same time. In 2 Brazilian hospitals incidence of TST conversion was 8 per 1000 person-months following implementation of the full hierarchy of administrative, personal, and engineering controls, compared with 16 per 1000 person-months in 2 other hospitals without any TB infection-control measures.[45]

Delays in institution of adequate isolation, or diagnosis and institution of effective therapy, have been consistently identified as important factors in almost all reports of nosocomial TB outbreaks.[5] The importance of administrative measures has been identified in a modeling study,[107] but the epidemiologic evidence of the effectiveness of these measures is limited, because, as shown in **Table 4**, few studies have implemented these measures alone. In one Italian hospital, the occurrence of new MDR disease among patients was eliminated after implementation of administrative measures alone.[108] In a US hospital TST conversion was reduced 80% by administrative measures alone.[109] In the Malawi study most of the changes were administrative; these had minimal effect, but as noted earlier, compliance with the measures was poor.[65] In 2 US hospitals administrative measures were introduced first, and interim tuberculin testing was performed before implementation of the rest of the infection control measures. In both hospitals incidence of TST conversion decreased significantly after the implementation of the administrative measures.[110,111] Administrative controls are the cheapest and simplest measures to implement, and all evidence suggests that they are effective and important. Hence, implementation of administrative control measures should be the first priority in all health care facilities.

Personal respirators or masks were the subject of considerable confusion in the early 1990s. Infection control and occupational health practitioners, regulatory agencies, and researchers struggled with conflicting recommendations and confusing terminology regarding personal respirators. In 1994 a single standard was recommended: that personal respirators (masks) should filter at least 95% of particles of 1 μm or larger, with less than 10% face seal air leak.[112] Respirators meeting these standards are referred to as N-95. Given that TB bacilli are 3 to 5 μm in length, these masks should filter at least 95% of TB bacilli out of the air inhaled by health care workers. Modeling studies have concluded that personal respirators should work well.[113] On the other hand, there is no epidemiologic evidence of their effectiveness. No studies have been published in which only personal respirators were implemented. Some modeling studies have found that the effect of personal respirators is modest if they are used in a setting with proper engineering control measures.[114] Fit testing of personal respirators is particularly controversial because studies have shown that the results of fit testing are not reliable or reproducible.[115,116] Nevertheless, most regulatory authorities and most health care institutions insist on fit testing because in theory a better-fitting personal respirator should provide more protection than one that allows some leakage.

Virtually all TB transmission occurs indoors. The risk of TB transmission outdoors is considered virtually nil, because of the bactericidal effect of sunlight as well as the rapid dispersion and dilution of airborne bacilli.[117] Ventilation can reduce the risk of indoor transmission by removal and dilution of airborne TB bacilli.[118] As shown in **Fig. 1**, the concentration of any airborne particles, including TB bacilli, can be reduced effectively with greater air exchange rates. However, the incremental gains diminish as air exchange rates are progressively increased, and the energy costs and construction/capital costs to achieve these higher air exchange rates increase considerably.[119] Natural ventilation, through open windows and doors, can achieve high air exchange rates,[120] but the direction of airflow within the building is unpredictable, as it is largely determined by outdoor temperature and wind direction.[85,121] This situation means that contaminated air from a TB patient's room can move to other occupied areas including staff rooms and other patient rooms. Natural ventilation also has limitations when outdoor temperatures are very high or very low.

When properly designed and installed, mechanical ventilation can control direction of airflow and achieve adequate outdoor air exchange rates. However, the initial capital costs for mechanical ventilation systems are high, as are the operating costs. The latter reflect the need for trained personnel to operate mechanical ventilation systems constantly, and to inspect and maintain them regularly. Energy costs of mechanical ventilation can be substantial in very cold or very hot climates,[119] particularly if high outdoor air exchange rates are mandated.

The effect of ventilation alone has been examined in only 3 studies, summarized in **Table 5**. In a Canadian study of 1274 workers in 17 hospitals, nurses and respiratory therapists who worked on units with ventilation of less than 2 air changes per hour in general patient rooms and wards (ie, nonisolation rooms) had a 3.8 times higher risk of tuberculin conversion than those who worked on units with better ventilation in general wards.[92] Air exchange rates in respiratory isolation rooms were not associated with

Table 3
Effect of administrative, personal, and engineering control measures applied concurrently on nosocomial transmission of TB

LMIC

Author, Year Country Facilities Year of intervention	Preventive Strategy Used			Epidemiologic Measure in Absence of Preventive Measure	Epidemiologic Measure in Presence of Preventive Measure	Effect
	Administrative	Personal	Engineering			
Harries 2002,[65] Malawi 40 TB care facilities (1998)	(1) Priority to patients with chronic cough in OPD (2) Rapid sputum collection, transport and reporting (3) Visitors kept to a minimum (4) CXR at quiet times of the day (5) Patients with TB spend more day time outdoors when possible	(1) Proper cough hygiene (2) Mask worn by patients with TB when undergoing surgical procedures	(1) Increased natural ventilation (2) Windows left open most of the time	Incidence of TB disease before prevention (1996) Clin officer 7407 Pt attd 5014 Wd attd 3543 TB officer 3030 Nurses 2835 Overall 3707	Incidence of TB disease after prevention (1999) Clin officer 3603 Pt attd 4348 Wd attd 3954 TB officer 1785 Nurses 2060 Overall 3222	Incidence of TB disease declined after preventive measures used. Statistically NS
Yanai 2003,[47] Thailand Provincial referral hospital (1997–98)	(1) Early suspicion of TB (2) Early sputum collection and reporting (3) Early initiation of TB treatment (4) Isolation of patients with TB (5) One-stop OPD TB service	(1) N95 mask use by HCWs (2) HEPA filter in laboratory areas	(1) TB isolation room in wards (2) Maximizing ventilation in wards (3) Class II safety cabinets in laboratory (4) UVGI system in laboratory	Incidence of TB disease control measures (1995–1997) All HCWs 179.21 Annual incidence of LTBI before control measures (1995–97) 9.3% (3.3%–15.3%)	Incidence of TB disease after control measures (1999) All HCWs 252.68 Annual incidence of LTBI after control measures (1999) 2.2% (0%–5.1%)	Increase in TB disease Statistically NS Decrease in LTBI rates Statistically significant
Roth 2005,[45] Brazil. 2 hospitals with, and 2 without control measures (1998)	(1) Rapid diagnosis and treatment of Patients with TB (2) Isolation of patients with TB in private rooms	(1) N95 mask use by HCWs (2) HEPA filter in laboratory areas	(1) Negative pressure rooms[a] (one hospital) (2) Class II biosafety cabinets in laboratory areas	Incidence of LTBI in 2 hospitals without control measures (1998–99) 16 per 1000 person-months	Incidence of LTBI in 2 hospitals with control measures (1998–99) 8 per 1000 person-months	Difference in LTBI rates Statistically significant

High-Income Countries

Author, Year Country	Workers Facilities Year of Intervention	TST Baseline Conversion Definition	Infection Control Strategy Used: Administrative	Personal	Engineering	Outcomes: Measure	Before	After
Wenger 1990[102] United States	All HCW 1 hospital 1991	1-Step $T_1<10$, $T_2 \geq 10$ mm TST ≥ 10 mm and ↑ 6+ mm	↑ Isolation ↑ Speed for AFB Sputum induction in respiratory isolation rooms	TST every 4 mo Sub-µm masks Dust-mist masks	Auto door closers Negative pressure isolation rooms	Conv/tested ARI	7/25 28%	3/17 18%
Maloney 1991[103] United States	All HCW 1 hospital 1991	1-Step $T_1<10$, $T_2 \geq 10$ mm	↑ Isolation ↑ Treatment ↑ Speed for AFB	Molded surgical masks	Window exhaust fans	Conv/tested ARI	26/840 3.1%	22/727 3.0%
Fella 1991[104] United States	All HCW 1 hospital 1991–1993	1-Step $T_1<10$, $T_2 \geq 10$ mm	↑ Isolation	Better mask (dust-mist)	Window exhaust fans Upper air UV light	Conv/tested ARI	30/145 21%	51/1007 5.1%
Bangsberg 1992[105] United States	Residents 1 hospital 1992	1-Step $T_1<10$, $T_2 \geq 10$ mm and ↑ 6+ mm	↑ Isolation	Respiratory masks	Negative pressure rooms in ER+OPD Upper-air UV lights	Conv/tested ARI	11/90 5.4%	1/90 0.7%
Blumberg 1992[106] United States	All HCW 1 hospital 1991–1992	1-Step $T_1<10$, $T_2 \geq 10$ mm	↑ Respiratory isolation	TST every 6 months Sub-µm masks	Window exhaust fans	Conv/tested ARI	118/3579 3.3%	185/17618 1.1%
Boudreau 1997[18] United States	All HCW 1 hospital 1989–1992	1-Step $T_1<10$, $T_2 \geq 10$ mm	Drug therapy improved ↑ Isolation procedures Worker education	Better masks	Sputum induction booth UV lights	ARI in HCW	6.9%	1.9%
Blumberg 1998[17] United States	Residents 1 hospital 1992–1997	1-Step $T_1<10$, $T_2 \geq 10$ mm	Isolation procedures TB infection control nurse	Better masks TST of HCWs	50 respiratory isolation rooms	ARI in HCW	6%	1.1%
Louther 1997[26] United States	All HCW 1 hospital 1991–1994	1-Step $T_1<10$, $T_2 \geq 10$ mm and ↑ 10+ mm	↑ Isolation	Better masks	↑ Ventilation	ARI in HCW	7.2%	4.8%

Abbreviations: ARI, annual risk of infection; Clin officer, clinical officer; Conv, conversions; CXR, chest radiograph; ER, emergency room; HCW, health care worker; HEPA, high-efficiency particulate air; NS, nonsignificant; OPD, outpatient department; Pt attd, patient attendant; Wd attd, ward attendant.

[a] Single rooms, R6 air changes per hour, negative pressure or inward airflow, automatic door closing.

Table 4
Effect of administrative measures (triage and separation of patients with TB) (studies in which effect of administrative measures only were studied)

Author (References)	Country	Year of Intervention	Effect Measured in	Outcome Measure	Before	After
Moro[108]	Italy	1993	Patients	New MDR disease	26/90	0/44
Jarvis[109]	United States	1995	HCWs	TST conversion	14.6%	2.9%

Abbreviation: HCW, health care worker.

workers' tuberculin conversion rates.[92] In the same study laboratory workers had greater rates of tuberculin conversions if they worked in laboratories or autopsy suites with lower ventilation levels.[90] A single study has reported on TST conversion rates before and after improvements in ventilation only.[16] In the emergency department of a US hospital, 4 respiratory isolation rooms were created, recirculation of air was eliminated, and laminar airflow introduced. Following these measures tuberculin conversion declined substantially among staff in the emergency department and in other departments (possibly because of reduced recirculation of air from the emergency departments to these other departments).[16]

UVGI is an older technology that was evaluated extensively in the preantibiotic era. With the advent of effective antibiotic therapy, UVGI fell into disuse (along with most aspects of TB infection control). UVGI also fell into disrepute because of concerns regarding skin cancer. These concerns were completely unfounded because the type of ultraviolet irradiation generated by the lamps (UV-C) does not penetrate the skin and so cannot cause mutagenesis in the skin.[117,122] Direct exposure to UVGI can cause skin rash (similar to sunburn) and keratoconjunctivitis (similar to snow blindness). Outbreaks of both conditions have been reported, and all have been mild and self-limited.[122] In every instance these outbreaks were caused by errors in the installation, or operation of the lamps.[122]

Modern lamps are designed to minimize risk of direct exposure. Usually these are installed above eye level in rooms with reflectors so that only the upper air in the

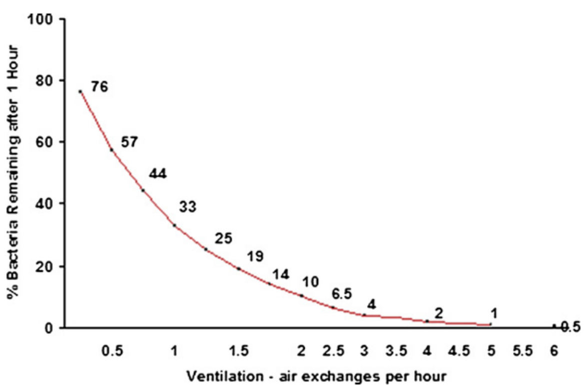

Fig. 1. Percent of airborne bacteria remaining after 1 hour of ventilation at different exchange rates.

Table 5
Effect of ventilation on nosocomial TB transmission (studies in which effect of ventilation alone was studied)

					Effect Measured in		Outcomes	
Author (References)	Country	Year of Intervention	Ventilation	tcome Measure	Type	N	Lower Ventilation	Higher Ventilation
Menzies[90,92]	Canada	1996–98	Mechanical	Relative risk of cumulative TST conversion	Nurses, respiratory therapists	1270	3.8	1.0
					Laboratory workers	120	1.3	1.0
Behrman[16]	United States	1993–96	4 respiratory isolation rooms	TST conversion per 6 months	Emergency department staff	88	10.5%	0
			Nonrecirculating air laminar airflow		Other departments	3000	5.0%	1.2%

room is irradiated. Occasionally such lamps have caused eye irritation as a result of reflected UV light from glossy ceilings.[122] This reflection can be eliminated by use of low-gloss ceiling paint or louvered lamps so that the UV light is emitted only in a narrow beam in the upper air. Effectiveness of UVGI is summarized in **Table 6**. Effect of UVGI installation on TST conversion among hospital workers has been reported in 4 studies. In all 4, the incidence of tuberculin conversion declined substantially, but this may have been a result of other interventions, because UVGI was one of several interventions introduced at the same time. Two studies have irradiated upper air in rooms of patients with TB with UVGI; the air exhausted from these rooms was fed through an animal enclosure. In both studies, animals exposed to air from rooms with UV irradiation had substantially reduced incidence of TB infection and disease.[123,124,128] In vitro studies have also shown the high potency of UVGI in reducing the number of viable airborne BCG,[129] or viable mycobacterial cultures in solid media. Despite solid animal evidence of efficacy and clear evidence that it is safe for humans, authoritative agencies remain reluctant to endorse use of UVGI. As summarized in **Table 7**, UVGI has many advantages compared with mechanical ventilation in terms of proven effectiveness, low initial and recurrent costs, as well as proven safety, yet authoritative agencies continue to recommend it only as an adjunct measure.

SARS

The SARS epidemic from November 2002 until July 2003 provided many important observations regarding determinants and prevention of nosocomial transmission. Interest in infection control with SARS was high because no effective vaccine or treatment was available at the time of the epidemic, and a high proportion of all SARS cases occurred as a result of nosocomial transmission. Ultimately the epidemic subsided following strict enforcement of control measures within health care facilities and in the community. Hence, this epidemic provides many important lessons that are applicable for prevention of nosocomial transmission of TB and influenza.

Several features of SARS were unusual. First, the incubation period was longer than typical for influenza or other respiratory tract viral infections (4–6 days instead of 1–2 days; see **Table 8**) and the course of the illness was slower.[147] Of particular relevance for nosocomial transmission, in most patients the viral load and viral shedding increased to a peak about 10 to 12 days after the onset of symptoms, following which there was a slow decline.[146,147] Because patients typically sought medical care and were hospitalized after a few days of symptoms they became progressively more contagious after their arrival in health care facilities. This situation may have accounted for the disproportionate share of transmission that occurred within health care facilities; it was estimated that 78% of all cases in Singapore, among patients and health care workers, resulted from nosocomial transmission.[150] Overall, health care workers accounted for 21% of all cases,[132] although in most countries they account for only 2% to 3% of the adult population. A rough estimate is that the risk of disease in health care workers was approximately 10-fold higher than the general population. A similar estimate can be derived from Hong Kong, where there was more extensive community transmission, yet the rates in health care workers were more than 10 times higher than the community rates in the worst affected areas.[141]

This situation is similar to TB in high-income countries; community transmission is rare, and patients are often hospitalized when they present with symptoms. After admission, contagiousness and transmission often increase, because the diagnosis is missed or delayed by days to weeks.[156]

Table 6
Effect of improved UVGI only on nosocomial TB transmission

Author (References)	Country	Year of Intervention	Intervention Measured in: Type	N	Outcomes	Before UVGI	After UVGI	Reduction (%)
Studies of HCWs[a]								
Bourdeau[18]	United States	1989–91	All HCWs		TST conv/y	21%	5.1%	76
Fella[104]	United States	1991	All HCWs	1000	TST conv/y	6.9%	1.9%	72
Bangsberg[105]	United States	1991–92	Trainees (residents)	90	TST conv/y	5.4%	0.7%	87
Yanai[b],[47]	Thailand	1997–98	All HCWs	1202	TST conv/y	9.3%	2.2%	76
Studies of laboratory animals								
Riley[123]	United States	1957	Guinea pigs	ns	BCG infection	100%	0	100
Escombe[124]	Peru	2008	Guinea pigs	150	MTB infection	106	29	72
					MTB disease	26	11	60
Studies of microbes								
Ray[125]	United States	1957	Culture plates		Viable MTB	150-350	15–30	90
Riley[126]	United States	1976	Airborne BCG		BCG killing	9	1	90
Xu[127]	United States	2003	Airborne BCG		Viable airborne BCG	5.7×10^4	3.2×10^3	96

Abbreviations: conv, conversions; HCW, health care worker; MTB, *Mycobacterium tuberculosis*.

[a] All 4 studies in health care workers involved multiple interventions applied concurrently. Hence, the reduction seen may have been caused by other interventions (partially or entirely).

[b] UVGI applied in laboratory areas only. In this study there was no reduction in incidence of disease.

Table 7
Comparison of engineering control measures: ventilation versus UVGI (a gap between evidence and recommendations?)

Parameters	Mechanical Ventilation	UVGI
Maximum air exchange rate[a]	12–15	20–25
Effectiveness		
Proved	—	—
In workers	Partially	Partially
In animals	No	Yes
In vitro	No	Yes
Safety		
In theory	Yes	Yes
Shown in workers	No	Yes
Costs		
Initial capital costs	Very high	Moderate
Recurrent costs	—	—
Maintenance	High	Low
Energy	Moderate-High	Low
Personnel (operation)	Moderate	None
Personnel (inspection)	Low	Low
Recommendations (reference)		
United States[7]	Primary mode	Adjunct measure
Canada[130]	Primary mode	Use when recommended ventilation cannot be achieved
WHO[8]	Primary mode	Use when recommended ventilation cannot be achieved

[a] Maximum outdoor air exchange rate that can reasonably be achieved in occupied spaces, yet maintain noise, draft, and temperature within human comfort range. For UVGI this refers to the removal of viable airborne organisms that would be achieved with equivalent levels of ventilation.

Another feature of the SARS epidemic was that a few patients were identified as more contagious than others, so-called superspreaders of the epidemic (SSEs).[137,152,157] One of these persons transmitted SARS to several others on the same floor in a hotel,[141] and another to more than 50 others living in the same apartment complex but different buildings.[137] Neither patient had any direct contact with these secondary cases, supporting the possibility of airborne spread. Reasons for this contagiousness were not identified, but again there is a close parallel with TB. In several studies, the contagiousness of patients with TB has varied widely.[123,158,159] Although contagiousness is generally correlated with extent of pulmonary disease, it is substantially increased if there is laryngeal involvement.[123,159] One can only speculate why the phenomenon of SARS superspreaders occurred, but it seems these few patients were efficient generators of infectious aerosols.

Delayed diagnosis was common to all outbreaks of SARS, as with TB. Triage and separation of patients proved important in containing SARS epidemic, as shown in **Table 9**, another parallel with TB. Other administrative measures, particularly

Table 8
Key epidemiologic and clinical features of influenza A (including H_1N_1) and SARS

	Influenza A	SARS
Features	**Values (References)**	**Values (References)**
Incubation	1.4 days[131]	4.6–6.4 days[132,133]
Transmission		
Mode	Primary droplet[134] Possible contact Possible airborne[134,136] —	Primary droplet[132] Fecal-oral[135] Possible contact[135] Possible airborne[137,138]
Asymptomatic	Minimal[139]	None[140,141]
Increased by	Intubation —	Intubation[142–144] NIPPV[a], [144,145]
Infectiousness (new infections per case)	1.8–20.0	2.4–2.7[146,147]
Duration of contagiousness	3 days[b], [131]	10–20 days[146,147]
Nosocomial transmission		
Outbreaks shown	Yes[139,148,149]	All reports
% Nosocomial	Unknown–low[148,149]	78% in Singapore[150]
Transmission to HCWs		
Estimated risk of infection	No estimates	1%–3% per h[143,151]
HCW as % of all cases	No estimates	21%[132]
Incidence		
Total global cases	401, 276 (H_1N_1 as of September 25, 2009)[c]	8098 (as of July 2003)[132]
Severity (% admitted to ICU)	3.8% (Quebec)	19%–34%[132,141,152]
Mortality (overall)	1.1%[153]	9.6%[132]
age <60 y	—	2.9%–7.0%[141,143]
age >60 y	—	53%–55%[141,143]
HCWs (all ages)	—	2%[141]

Abbreviations: HCW, health care worker; ICU, intensive care unit; NIPPV, nasal intermittent positive pressure ventilation.

[a] Noninvasive positive pressure ventilation such as continuous positive airway pressure or bilevel positive airway pressure.

[b] Contagiousness estimate for nonimmunocompromised adult. Duration is longer if immunocompromised,[154] severely ill[155] or young infant.[154]

[c] US estimates were that more than 1 million cases had occurred in the United States alone by September 12, 2009.[153]

isolation of symptomatic health care workers, limited the health care workers as a source of nosocomial transmission, an important message for influenza control (see later discussion). Personal protective measures seemed the most important in containing the spread of SARS. In almost all situations in which full protective measures were implemented, there was no further nosocomial transmission.[135,145] In an analysis of workers who became infected with SARS despite using full personal protective equipment, lapses or breaches in infection-control procedures were found that could explain every apparent failure.[142] In one ward in a Hong Kong hospital, more than 20 patients were placed on noninvasive positive ventilation, a significant

Table 9
Evidence of importance and effectiveness of infection control measures for influenza and SARS

Influence Control Measures	Influenza: Studies Showing Benefit, N (References)	SARS: Studies Showing Benefit, N (References)
Administrative		
Triage/separation of patients	2[154,160]	2[135,150]
Reduce crowding	1[136]	1[144]
Screen/furlough sick workers	2[154,161]	2[144,150]
Personal		
Vaccination of health care worker	3[162–164]	No vaccine available
Knowledge/training in infection control	—	1[165]
Hand washing	—	2[144,166]
Masks: surgical or N-95	1[167,a]	2[151,166,b,c]
Compliance with all measures	—	3[142,165,166]
Engineering		
UVGI	1[168]	—
Ventilation (risk factor, not intervention)	2[136,169]	1 (Ha 2004)
Full hierarchy of measures	1[160]	2[143,150]
Most important measure	Vaccination	Infection control

[a] Loeb 2009[167]: Randomized controlled trial of surgical versus N-95 masks: no difference in sero-conversion of workers.
[b] Seto 2003[166]: paper masks were not effective; surgical and N-95 were not different.
[c] Loeb 2004[151]: N-95 masks were better than surgical masks, which were better than no masks.

risk factor for aerosolization of infectious particles.[144,145] All workers on this ward were required to be meticulous in their infection-control procedures and use of personal protective equipment; despite the intense exposure, none became infected with SARS.

One controversial issue with regard to personal protective measures remains the type of respiratory protection, or masks. In one survey, nonuse of masks was clearly associated with increased risk of SARS,[165] whereas in another use of either surgical or N-95 masks was protective, although use of paper masks was not.[166] In a Toronto study, use of N-95 masks was associated with greater protection than use of surgical masks, and both type of masks were associated with greater protection than no mask use.[151] Need for N-95 masks depends on the mode of transmission. If transmission is solely by droplet, then face shields, eye protection, and surgical masks are adequate. However, if transmission is airborne, than N-95 masks should be used. As reviewed earlier, there is evidence that airborne transmission of SARS occurred, at least from the superspreaders[137,152] or during aerosol-generating activities such as intubation or suctioning.[142–144,151] Given that superspreaders are identified only in retrospect, it may be more prudent for workers to wear N-95 masks at all times.

Ventilation of occupied indoor spaces is important for diluting and removing airborne contaminants. This practice can help prevent nosocomial transmission of airborne pathogens. As reviewed earlier there is some evidence that SARS could be transmitted by the airborne route; this was the most plausible explanation for the community outbreak.[138] The ward in which nasal intermittent positive pressure ventilation was used achieved high air exchange rates with exhaust fans, which may have helped prevent nosocomial transmission. The efficacy of UVGI was not studied with SARS.

INFLUENZA

There is less information regarding the determinants, and effective prevention, of nosocomial transmission. This situation reflects the availability, for more than 20 years, of an effective vaccine. Also, influenza is typically less severe, with lower case fatality rates than SARS. Influenza also has a shorter incubation period, so that patients are more quickly contagious during the symptomatic phase than with SARS. Hence, there is greater community transmission, making it difficult to identify and study nosocomial influenza transmission. The new pandemic of H_1N_1, which spread rapidly through air travel,[170] and caused millions of cases,[153] before a vaccine became available, underscores the importance of understanding the determinants of nosocomial transmission of influenza, to implement effective infection control.

The effect of nosocomial transmission of influenza is difficult to estimate but there have been well-documented outbreaks in nursing homes, intensive care units, and general medical facilities.[149] Attack rates in these outbreaks ranged from 11% to 59% overall, and from 8% to 63% in exposed health care workers.[149] Mortality among patients ranged from 0% to 66%, with highest mortality among elderly nursing home residents[149,171] and very young infants.[149] Individuals with other immunocompromising conditions are also highly susceptible. An additional problem created by nosocomial influenza transmission is the large number of health care workers who may become ill and unable to work.[163] Their absenteeism may create significant problems in delivery of care, at a time when they are needed most.

As with SARS and TB, delayed diagnosis of cases is a common feature of nosocomial influenza outbreaks.[149] In these outbreaks, health care workers were the most commonly identified source cases,[149] as well as frequently playing a major role in spreading the infection from patient to patient.[148,171] Two studies have reported that screening workers to identify those with influenza and send them home was an effective measure to prevent nosocomial outbreaks.[154]

Little attention has been given to the importance of personal protective equipment such as gowns, gloves, and masks in practice and in guidelines for prevention and management of influenza.[172,173] This situation is because vaccination of health care workers has been shown to reduce or prevent nosocomial transmission.[148,155,163] In one randomized trial, vaccinating health care workers reduced mortality among elderly people in nursing homes.[162] Treatment of influenza with antivirals is effective for individual benefit, but the effect of antiviral therapy on community or nosocomial transmission has not been studied.

The role of airborne transmission of influenza in nosocomial outbreaks is controversial, because the evidence is limited. As reviewed elsewhere,[134,148] there is convincing animal and in vitro evidence that airborne transmission of influenza can occur. There is also evidence from a limited number of outbreaks that supports the role of airborne transmission.[136] As with SARS and TB, a few individuals may be extremely contagious and contribute to airborne transmission, or particularly contagious during aerosol-generating procedures such as intubation or noninvasive ventilation. Given this uncertainty, it seems prudent for nonvaccinated workers to use N-95 masks, particularly during high-risk procedures or with very ill patients.

There is limited evidence, from an older study, that upper-air UVGI is effective in reducing influenza transmission rates.[168] Upper-air UVGI was also shown to be effective in reducing measles transmission among schoolchildren.[174]

SUMMARY

1. The risk of TB infection in health care workers is 5 to 10 times greater than that in the general population, and risk of disease is 2 to 5 times higher. Risk factors for TB infection and disease are mostly associated with greater risk of exposure to patients with TB, particularly undiagnosed patients. Some risk factors relate to specific work activities that can cause aerosolization of TB bacilli.
2. The simplest, cheapest, and quickest interventions to implement, with proven effectiveness, are the administrative measures of triage and separation of patients. These measures should be a part of all TB infection-control programs in all health care facilities.
3. There is little direct evidence for the effectiveness of N-95 personal respirators for protection against occupational TB. Nevertheless, on theoretic grounds alone, their use is supported.
4. There are sound theoretic reasons why air exchange (ventilation) should help reduce nosocomial TB transmission. There is evidence from several observational studies and one interventional study that higher levels of ventilation reduce risk of TB transmission. Natural ventilation can achieve high air exchange rates and should be effective as well as feasible in health facilities in LMIC. However, resultant airflow patterns within buildings are unpredictable, so natural ventilation may result in inadvertent exposure of workers or other patients.
5. UVGI is grossly underused. This is a low-cost, simple, and safe technology. All available evidence suggests that it should be safe and highly effective in reducing nosocomial TB transmission.
6. There are few epidemiologic studies on the effectiveness of infection control measures, alone or in combination, and their effect on reducing nosocomial TB transmission.
7. For the prevention of nosocomial transmission of influenza, the most important action is vaccination of health care workers. However, if an effective vaccine is not available, then other infection-control measures become of paramount importance. For TB, SARS, and influenza, delayed diagnosis (or delayed institution of an effective treatment, if available) is the most common and important factor in nosocomial transmission. Hence, the most important measures are to promptly identify patients with these illnesses and separate them from other patients and from susceptible health care workers.
8. Personal protective equipment including gowns, masks, and gloves is important to prevent transmission by droplet. This is a major mechanism of transmission for SARS and influenza, so should be the major method of protection for health care workers and prevention of spread by health care workers from one patient to another.
9. However, there is clear evidence that airborne transmission of influenza and SARS can occur. Transmission is most likely during performance of procedures that

cause aerosolization of infectious droplets, or with severely ill patients. Therefore, N-95 personal respirators, which should be more effective in preventing acquisition of airborne infections, should be used by workers caring for severely ill patients, or workers performing aerosol-generating procedures. In addition, these patients should be cared for, and procedures performed, in rooms with adequate ventilation and/or upper-air UVGI, as these environmental measures can further reduce the risk of airborne transmission.

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