Occupational respiratory infections

Anete Trajman[a] and Dick Menzies[b]

[a]Pró-reitoria de Saúde, Gama Filho University, Rio de Janeiro, Brazil and [b]Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, McGill University, Montreal, Canada

Correspondence to Dr Dick Menzies, Professor, McGill University, Respiratory Epidemiology Unit, Montreal Chest Institute, 3650 St. Urbain, Room #K1.24, Montreal, QC H2X 2P4, Canada
Tel: +1 514 934 1934x32129; fax: +1 514 843 2083; e-mail: dick.menzies@mcgill.ca

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Purpose of review
In the last decade, descriptions of outbreaks of extensively drug-resistant strains of tuberculosis (TB) have increased concern about the nosocomial transmission of TB – a potentially life-threatening occupational respiratory infection. In addition, outbreaks of avian influenza caused by an H5N1 virus, severe acute respiratory syndrome caused by a coronavirus A and the recent pandemic caused by an H1N1 influenza virus have heightened concern about occupational infectious illnesses among workers in healthcare and agriculture.

Recent findings
The last decade has witnessed extensive research into the modes, patterns, determinants and extent of transmission of these illnesses. The most important findings regarding risk, determinants and preventive measures of these occupational infections and recent guidelines are reviewed in this article.

Summary
Administrative, personal and engineering measures to control respiratory infection are effective and should be implemented in healthcare facilities. The use of N95 personal respirators by healthcare workers who are caring for pulmonary TB and viral respiratory infections patients is strongly recommended. Vaccination against influenza (including H1N1) is effective and strongly recommended for healthcare workers. Ultraviolet germicidal irradiation is underused at present, despite good evidence of safety and efficacy in elimination of airborne respiratory infectious agents including TB.

Keywords
avian influenza, H1N1, infection control, influenza, nosocomial transmission, occupational health, severe acute respiratory syndrome, swine origin influenza, tuberculosis

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Introduction

Although occupational respiratory diseases caused by exposure to gases or dusts at work have been recognized for many decades, most occupational respiratory infections have been recognized more recently. Any infectious agent that is transmitted by airborne aerosol or by droplets can be acquired in the workplace [1]. These include illnesses caused by viral (varicella, measles, rubella, mumps, pertussis, parvovirus B19, respiratory syncytial virus, adenovirus and influenza virus), mycoplasma, bacterial [tuberculosis (TB), psittacosis and anthrax] and fungal (sporotricosis and histoplasmosis) agents.

In the last decade, descriptions of outbreaks of extensively drug-resistant (XDR) strains of TB have increased concern about TB – a potentially life-threatening occupational respiratory infection. In addition, outbreaks of avian influenza caused by an H5N1 virus, severe acute respiratory syndrome (SARS) caused by a coronavirus A and the recent swine flu pandemic caused by an H1N1 influenza virus have heightened concern about occupational viral illnesses among healthcare workers (HCWs), as well as farmers and others working with animals or birds.

The last decade has witnessed extensive research into the modes, patterns, determinants and extent of transmission of TB and these three viral illnesses. The most important findings regarding risk, determinants and preventive measures of these illnesses, particularly features that are common to all of these occupational illnesses, will be reviewed.

Tuberculosis

TB is the best known and most studied occupational respiratory infectious disease. The study of occupational TB is particularly informative because transmission can be monitored in two ways. The cumulative or periodic incidence of latent TB infection (LTBI) can be estimated using tests of immune reactions to TB antigens such as the tuberculin skin test (TST) [2]. Transmission that results in disease can be measured with a high degree of specificity using molecular epidemiologic tools such as restriction fragment length polymorphisms analysis [3]. Much of the information regarding risk, risk factors and prevention of nosocomial transmission is derived from studies [4,5] conducted in high-income countries. The coincident advent of HIV infection and multidrug resistant-TB resulted in several major outbreaks in high-income countries in which more than half of exposed patients became infected, developed disease and died [4], and a large number of HCWs were infected [4]. In the past 5 years, outbreaks of XDR-TB have shifted attention to HCWs in low and middle-income countries (LMICs), where risk of disease may be very high [6,7].

A large number of studies have estimated risk of TB infection or disease, and have been summarized recently [8] (Table 1) [9–48]. Although the estimates are variable, there is consistent evidence that the prevalence and incidence of LTBI in HCWs is substantially higher than the general population, in all settings. In high-income countries, the pooled risk of TB disease among workers is twice that of the general population, whereas the risk of infection is 10 times higher [8]. In LMICs, both disease and infection in HCWs are five-fold higher than the general population [8].

Risk factors associated with occupational TB infection and disease are similar in all settings. Many of the identified risk factors are simply indicators of likelihood of exposure to TB patients, more years of work, in jobs that involve direct patient care, and in hospitals or units caring for more TB patients. Other risk factors relate to increased chance of exposure to undiagnosed patients – these include work in emergency departments or HIV services. The third category of risk factor relates to specific activities that increase patients' contagiousness. For example, respiratory therapists [43,49] and disease workers [28,50,51] have been consistently identified as high-risk occupations. This is because certain of their tasks can result in aerosolization of TB bacilli, for example, intubation [52,53], sputum induction [54,55], bronchoscopy [56] or autopsy [57,58].

These epidemiologic observations have guided infection control recommendations. As risk is proportional to the number of TB patients per worker, recommendations are now risk stratified. The demonstration that workers in LMICs have five times greater risk of infection and disease than the general population, who already have high rates of disease, has led to the realization that TB is the most common and potentially lethal occupational illness in these countries. This has stimulated efforts to raise awareness – not least among the workers themselves – and to develop guidelines for TB control in these countries [59], which have been updated very recently [8].

Interventions to prevent nosocomial tuberculosis transmission

Interventions to prevent nosocomial TB transmission are generally divided into three broad categories: administrative, personal and engineering controls [60]. These are

Table 1 Risk factors for occupational tuberculosis in low–middle and high-income countries

General category	Specific factor	Low–middle income countries (references)	High-income countries (references)
Latent TB infection			
Indicators of exposure	Years of work	[9–15]	[16]
	TB admissions	–	[16]
	Known TB contact	[13,17]	[16,18,19]
Type of work	Direct patient care	[15,20]	[19,21]
	Physicians	[10,22]	[16,23]
	Nurses	[10,15,22]	[16,21,24,25]
	Respiratory therapists	[13]	[21]
	Trainees	–	[18]
Location of work	Medical ward	[11,13,26]	[24,25]
	HIV ward/care	–	[25]
	Emergency	[22]	[27]
	Laboratory/pathology	[22]	[24,28]
	TB ward/clinic	–	[18]
TB disease			
Indicators of exposure			
Type of work	Direct patient care	–	[29–32]
	Physicians	[33–36]	[32,37,38]
	Nurses	[33–36,39–42]	[32,38,43]
	Respiratory therapists	–	[43]
	Trainees	–	[44]
Location of work	Medical ward	[36,41,45,46]	–
	TB ward/clinic	[36,41,45,47–49]	–
	HIV ward/clinic	–	–
	Emergency	[41,45]	–
	Laboratory/pathology	[34,45]	–

TB, tuberculosis.

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 patients at a healthcare facility and their diagnosis, treatment and placement in respiratory isolation. Personal controls are measures directed at individual workers such as use of personal respirators (masks) 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 and include ventilation and ultraviolet germicidal irradiation (UVGI).

Delays in institution of adequate isolation, effective therapy or both have been the most consistently identified factors in nosocomial TB outbreaks [4]. The benefits of administrative measures such as triage and separation of patients suspected of active TB, rapid performance of diagnostic tests or both have been demonstrated in one modeling study [61] and in four epidemiologic studies [62]. Administrative controls are the cheapest and simplest measures to implement, and all evidence suggests that they are effective and important [63]. Hence, implementation of administrative control measures should be the first priority in all healthcare facilities.

Personal respirators (masks) that filter at least 95% of particles of 1 μ or larger, with less than 10% face seal air leak, were first recommended in 1994 [64]. Respirators meeting these standards are referred to as N95. Given that TB bacilli are 3–5 μ in length, these masks should filter at least 95% of TB bacilli out of the air inhaled by HCWs. Modeling studies have concluded that personal respirators should work well [65], although there is no epidemiological evidence of their effectiveness.

Ventilation can reduce the risk of transmission within buildings, such as hospitals, by removal and dilution of airborne TB bacilli [66]. However, the incremental gains diminish as air exchange rates are progressively increased [66], whereas the energy costs and construction/capital costs to achieve these higher air exchange rates increase considerably [67]. Natural ventilation through open windows and doors can achieve high air exchange rates [68], but the direction of airflow within the building is unpredictable, as it is largely determined by outdoor temperature and wind direction [21,69]. Natural ventilation also has important 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 very high, as are the operating costs. Despite solid animal evidence of efficacy, relatively low costs and clear evidence of safety for humans, authoritative agencies remain reluctant to endorse use of UVGI. As a result, UVGI remains sadly underutilized.

Avian influenza

Avian influenza was considered an occasional cause of conjunctivitis or mild influenza-like illness (ILI) up until 1997, when the first outbreak of human fatal disease caused by the avian influenza H5N1virus was reported in Hong Kong [70]. Since then, other bird-to-human virus transmission, caused by this avian influenza and other subtypes, has led to sporadic outbreaks of serious disease associated with occupational exposure in poultry cullers and farmers, and veterinarians [1]. In 2003, nine Asian countries were affected by an avian influenza outbreak [71], and in 2005, outbreaks reached other Asian and European countries.

Transmission to humans occurs from inhalation or mucosal contact of infectious droplets from birds, most commonly ducks, cocks, domestic poultry and wild birds [72]. Data from Thailand in 2004 indicated that the risks of H5N1 outbreaks, and infections were significantly higher for workers in large-scale commercial poultry operations than workers with backyard flocks [73]. Transmission from captive or wild birds to captive tigers, leopards and other mammals has also been documented [1,74,75]. H5N1 does not transmit from human to human effectively, and only in a few instances has human-to-human transmission been documented. Airborne transmission to HCWs can occur with performance of aerosol-generating procedures in infected patients [76•]. However, there have been no documented episodes of transmission from patients with avian influenza to HCWs who were using appropriate personal protective equipment (PPE, see below). Thus, avian influenza is mostly an occupational disease for farmers and poultry workers, although zoo workers, modern industrialized food animal production workers and occasionally HCWs can be at risk [73].

The clinical picture depends on the viral subtype. The H5N1 can cause mild ILI, but among those who develop pneumonia, acute respiratory distress syndrome can develop and rapidly evolve to death [76•]. Gastroenteritis and encephalopathy are also associated with worse outcomes [76•]. Treatment is empirical, as there is little published evidence to guide management. Oseltamivir, a neuraminidase inhibitor, is the treatment of choice [77], and is recommended even for patients who have been symptomatic for several days because H5N1 viral replication is more prolonged [78]. Although a recent systematic review [79•] suggested little effect of neuraminidase inhibitors in healthy or high-risk patients with flu symptoms (reduction by half-day and 1 day to symptom alleviation, respectively), use of oseltamivir was associated with improved survival in complicated cases [80•].

Interventions to prevent animal-to-human transmission of avian influenza

Control measures include culling infected animals as well as animals with contact, restrictions on poultry movement, cleaning and disinfecting, and vaccinating poultry [74]. It is important that farmers and farm workers recognize the manifestations of avian influenza in poultry [81••]. In domesticated poultry, the disease manifestations range from reduced egg production to rapid death. PPE of clothes, gloves and masks is effective to prevent transmission to humans, and should be used by farmers, transport and zoo workers and veterinarians. Surgical masks are effective, as transmission is usually by large respiratory droplets from animals.

Despite lack of consistent evidence, oseltamivir has also been used to prevent disease after contact with infected birds. Because of the risk of acquired resistance, postexposure prophylaxis with oseltamivir (75 mg four times daily for 10 days) is recommended by the WHO only for personnel handling sick animals without appropriate PPE, patients in contact with animals, HCWs exposed to aerosol-generating procedures without PPE and laboratory personnel exposed to infective samples [81••]. Seasonal influenza vaccination of workers expected to be in contact with diseased poultry or HCWs caring for infected patients is recommended, not to prevent H5N1, but to minimize ILI from other influenza strains [77,81••,82]. Patients with suspected H5N1 should be hospitalized in respiratory isolation, with appropriate administrative and engineering control measures [81••].

Severe acute respiratory syndrome

Cases of atypical pneumonia with SARS were first reported in patients occupationally exposed to exotic animals in China in November 2002. This illness, caused by a coronavirus named SARS-CoV, caused an epidemic with over 8000 patients and 774 deaths between March and July 2003 [83]. The incubation period was longer than other respiratory viral illnesses, ranging from 1 to 14 days. Contagiousness appeared to be maximal around the 11th day after onset, with no transmission reported prior to onset of symptoms, apart from a small series in Canada [84]. Initial symptoms of fever, sore throat and myalgia were indistinguishable from those of other viral illnesses. However, rapid progression to severe pneumonia with respiratory failure occurred in a high proportion of cases [83]. Mechanical ventilation and admission to ICUs were often necessary [84].

Because of the high rate of hospitalization and progressive increase in contagiousness even after hospitalization, nosocomial transmission was intense. Overall, 1706 cases developed in HCWs accounting for 21% of all documented SARS cases [83]. In Singapore, it was estimated that 78% of cases resulted from nosocomial transmission [85]. In Hong Kong, the rate of transmission was reported to be 10 times higher among HCWs than in the community [86]. Overall, case fatality rate was 9.6%, but was as high as 50% among those with respiratory failure [87,88]. Corticosteroids and antiviral agents such as ribavirin had minimal effect on the course of the disease [84].

Interventions to prevent nosocomial transmission of severe acute respiratory syndrome

The SARS epidemic provided a very useful demonstration of the value of infection control measures. Several studies [89–92] showed that unrecognized patients resulted in substantial transmission to HCWs and other patients. In one study [93], no transmission occurred to HCWs who fully complied with recommendations for use of PPE, even though more than 20 patients with SARS were mechanically ventilated on that ward. Use of exhaust fans that produced very high air exchange rates may have also contributed to prevent transmission in this same ward [93]. In other studies [94,95], all transmission episodes could be linked to breaches in infection control procedures. In view of the high risk of nosocomial transmission, severity of disease, high case fatality rate and absence of any effective treatment or vaccine against the SARS-CoV, infection control measures were strictly enforced in healthcare facilities and the community. Within a few months after the introduction of these stringent control measures, the epidemic of this highly contagious and lethal agent subsided.

Recommendations for prevention of transmission of similar agents are based on these lessons. Administrative measures are the easiest to implement, and the most important. These include isolation of patients in ventilated rooms [81••], isolation (quarantine) of symptomatic HCWs and avoidance of aerosol-generating procedures such as bronchoscopy or nebulization, whenever possible. If absolutely needed, these procedures should be carried out in negative-pressure ventilation rooms.

PPE include disposable masks with visors, gloves, caps and gowns. These are highly recommended for HCWs and other caregivers dealing with known or suspected cases [96]. Hand washing is important, so facilities for hand washing should be readily available, especially in high-risk areas. If soap and water are not available on-site, alcohol-based gel hand cleaners can be used instead. Commonly used disinfectants, such as quaternary ammonium compounds and 10% bleach solutions, will kill respiratory viruses. Studies [97,98] have shown reduction of transmission of SARS with use of masks, although whether N95 respirators are needed or surgical masks are adequate remains unsettled [98,99]. N95 masks are effective to prevent transmission by airborne microdroplets, whereas surgical masks are adequate to prevent aerosol and droplet transmission. Evidence of airborne transmission of SARS was provided by the transmission from one symptomatic patient to persons living in different buildings, but downwind. Given the seriousness of the illness, it would seem prudent to use N95 respirators if SARS is suspected [81••,100], and HCWs should be meticulous in their use of complete PPE [81••]. The use of UVGI was not evaluated in the SARS epidemics.

Swine influenza

After the report of the first few cases of the swine-origin H1N1 influenza virus (S-OIV) in Mexico in late March 2009 [101], the S-OIV spread quickly to all continents, affecting millions of patients within a few months [102]. This pandemic is still ongoing [102]. The incubation period is shorter than for SARS, as is the usual duration of contagiousness (7 days) [102,103]. Asymptomatic and mild cases of ILI can occur, and transmission can occur 24 h before the onset of symptoms [103,104]. These factors may have contributed to the rapid spread of this virus globally. Hospitalization and mechanical ventilation may be required in some young children and adults, particularly in pregnant women [102]. The case fatality among patients requiring mechanical ventilation is high, although not as high as with SARS or H5N1 infection. Oseltamivir-resistant viruses, although uncommon, are associated with high mortality [105]. Symptoms and signs of influenza include fever, sore throat and dry cough [102]. Dyspnea, mental confusion, hypotension and hypoxia should prompt hospitalization and use of antiviral drugs [77]. Treatment options include oseltamivir and zanamivir; oseltamivir is preferred for severe cases and pregnant women because zanamivir is only available in inhalational form with minimal systemic effect [77]. In randomized controlled trials of these agents for other viral influenza strains, treatment reduced symptom duration in nonsevere cases [79•] and improved survival in patients with pneumonia [80•].

Interventions to prevent community transmission of H1N1 influenza virus

Community control interventions for influenza pandemic should include special vaccination [91•] and education programs directed to swine farm workers and veterinarians, as they are at very high risk for swine influenza virus infection [92] and may contribute to transmission to others in their rural communities [91•,106,107••]. These workers should be aware of signs of flu in pigs, should use PPE (gloves, coveralls and boots, and ideally goggles and N95 respirators) that are disposable or can be disinfected after use and should seek medical attention if they develop ILI. Equipment and surfaces that have been in contact with sick pigs should be thoroughly cleaned and disinfected.

Interventions to prevent nosocomial transmission of H1N1 influenza virus

Specific vaccines against H1N1, with high immunogenic effect and low adverse event rate [77,106,107••,108•], are already available. HCWs are considered a priority target for vaccination by WHO and Centers for Disease Control [107••]. Transmission of influenza virus among HCWs and from HCWs to patients in nursing homes, ICUs and other medical facilities has been well documented [109•,110], and vaccination can effectively reduce this [91•,109•].

Administrative, engineering and self-protective measures are all important to prevent nosocomial transmission of S-OIV [111••]. Administrative measures include implementation of universal precautions, rapid triage of patients with ILI and their placement in isolation. Engineering measures include adequate ventilation of rooms, including directional airflow, and increased outdoor air exchanges, and adequate cleaning [111••]. For personal protective measures to be effective, HCWs must be trained in use of PPE, especially during aerosol-generating procedures [111••], as well as hand washing after contact with respiratory secretions and after complete PPE removal. Use of masks is important, but based on a recent trial [112••], surgical masks appear adequate . However, HCWs exposed to aerosol-generating procedures, such as bronchoscopy, respiratory tract aspiration, intubation and resuscitation should wear complete PPE, including disposable N95 (or greater) filtering respirators [111••]. Patients, family and HCWs should also be instructed to wear medical masks when in contact with others within a distance less than 1 m [111••]. Patients must be instructed on cough etiquette. Standard laboratory safety rules should be followed for handling and transport of samples [113•]. Chemoprophylaxis with antivirals is only recommended for groups at high risk of complications of influenza [111••]. Transmission, prevention and outcome characteristics of emerging occupational respiratory viral infections are summarized in Table 2 [72–75,77,79•,81••,82,84,87, 92,102–104,106,107••,111••,114,115•,116].

Conclusion

HCWs and workers dealing with animals, mainly poultry and pigs, are at high risk for acquiring occupational respiratory infections. Many lessons regarding prevention of nosocomial transmission have been learned from institutional experiences with TB. Administrative, personal and engineering measures to control infection are effective and should be implemented in healthcare facilities. The simplest and cheapest measures are the administrative ones, including triage and isolation of patients with suspected contagious respiratory infections. The use of N95 personal respirators by HCWs who are caring for pulmonary TB patients is strongly recommended. The use of masks, preferably N95 respirators, and other PPE such as gowns, gloves and goggles is also recommended for HCWs caring for patients with respiratory viral infections, particularly during aero-

Table 2 Transmission, prevention and outcome characteristics of emerging occupational respiratory viral infections

	SARS	Avian influenza	Swine influenza
Infectious agent	Corona virus A (SARS-coV)	H5N1, H7N7, H7N1	H1N1
Main mode of transmission	Direct mucous membrane contact with infectious respiratory droplets and/or through exposure to fomites [114]	Inhalation or mucosal contact from ducks (usually asymptomatic reservoirs), cocks, domestic poultry and wild birds [72]	Highly efficient human-to-human and animal-to-human transmission [102]
Incubation period	1–14 days [103,114]	1–4 days [103][a]	1–7 days [102]
Transmission during incubation period	Not confirmed [84,114]	1 day before onset of symptoms [102,104][a]	
Total duration of spreading	Up to 2 weeks (maximal at 11th day) [114]. Super spreaders reported [116]	Typically 4 days, up to 3 weeks in young children and immunocompromised patients [104][a]	
Main professionals at risk	HCW, food handlers and workplace contacts (including healthcare settings) [114]	Farmers and poultry workers [72], industrialized food workers [73]	Swine workers [92], veterinarians, HCW [102]
Preventive measures			
Vaccine	Not available	Nonspecific (seasonal) [81••,82]	Specific vaccine liscenced [115•]. HCW are priority [107••]. Seasonal vaccine for swine workers [82,106]
Personal protective equipment	Complete, N95 recommended [96]	Complete, N95 recommended [81••]	Complete, N95 recommended [111••]
Administrative measures	Isolation in NP room, cleaning [96]	Education, isolation [81••]	Engineering and administrative isolation
Others	Any object carried to room placed in cleaned bag [96]	Chemoprophylaxis [81••]	Chemoprophylaxis in restricted situations [111••]
Clinical presentation	Severe disease [84,88]	From ILI to multiorgan failure [77]	From ILI to respiratory failure [102]
Fatality rate	9.6% [87], up to 50% if ventilation required	60% (89% in children) [77]	Variable

HCW, healthcare worker; ILI, influenza-like illness; NP, negative pressure.
[a] Information for any influenza subtype.

sol-generating procedures. UVGI is largely underused at present, despite the evidence of its safety and potential efficacy in reducing nosocomial transmission of TB and other respiratory agents. Influenza vaccination (including H1N1 vaccination) is strongly recommended for HCWs, as this can reduce morbidity and mortality among patients, as well as reducing morbidity and absenteeism among HCWs.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 290).

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