INTRODUCTION

Airborne transmission of disease in hospitals

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Hospital-acquired infection (HAI) is an important public health issue with unacceptable levels of morbidity and mortality, over the last 5 years. Disease can be transmitted by air (over large distances), by direct/indirect contact or a combination of both routes. While contact transmission of disease forms the majority of HAI cases, transmission through the air is harder to control, but one where the engineering sciences can play an important role in limiting the spread. This forms the focus of this themed volume.

In this paper, we describe the current hospital environment and review the contributions from microbiologists, mechanical and civil engineers, and mathematicians to this themed volume on the airborne transmission of infection in hospitals. The review also points out some of the outstanding scientific questions and possible approaches to mitigating transmission.

Keywords: droplet evaporation; dispersion; hospital-acquired infection

1. INTRODUCTION

Healthcare-acquired infection has been the subject of a very high level of public, media and government attention in the last 5 years, when unacceptable levels of morbidity and mortality became associated with poor hand hygiene and inadequate cleaning. In many countries, central initiatives addressing education, cleaning and audit, together with compulsory reporting of infections, have brought benefits in terms of reduction of headline rates, such as methicillin-resistant Staphylococcus aureus (MRSA) bacteramia. Although evidence is not extensive, the major vector of transmission is assumed to be contact between the patient, the staff and the environment. A number of studies have shown that outbreaks can be terminated by improved hand hygiene compliance and better cleaning of the environment. However, transmission of infection by the air has been less well investigated, at least with respect to MRSA and Clostridium difficile.

Tuberculosis (TB; Mycobacterium tuberculosis) is clearly transmitted in the air and can be a source of outbreak in hospitals. Healthcare workers infected with TB can spread the infection widely and extensive screening of patients and other staff may be necessary. Similarly Norovirus is transmitted by aerosol and is difficult to contain in a hospital ward without sufficient single rooms with en suite toilets. Historically, natural ventilation was seen to be beneficial in hospital wards and was part of hospital design. With the advent of sealed high-rise buildings and forced ventilation, expensive negative pressure rooms have been introduced to house patients with infections thought likely to be transmitted by aerosol. The spread of tuberculosis among HIV patients was a recent dramatic example of the problems with enclosed rooms and prisons. To ensure sufficient dilution of the bacterial load around an infected patient, room air should be changed 10–12 times every hour. Actual room air changes in negative pressure rooms often fall below this level because of poor plant and maintenance. In general ward air changes may reach 8 h⁻¹ but more usually 4–6, or are sometimes absent in communal areas. In these circumstances high levels of aerosol contamination can develop.

MRSA can survive on surfaces or skin scales for up to 80 days and spores of Clostridium difficile may last even longer. MRSA can be transmitted in aerosol from the respiratory tract but commonly attaches to skin scales of various sizes. The distance of travel depends on the size of the scale, the larger falling to the floor within 1–2 m, the smaller travelling the entire length of the

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One contribution of 10 to a Theme Supplement ‘Airborne transmission of disease in hospitals’.
ward. Establishing colonization depends not only on the number of organisms but also the site of inoculation, e.g. an open wound or mucous membrane could generate colonization with under 10 organisms compared with several hundreds on intact skin. MRSA disseminates widely throughout the ward and is commonly found in dusty, inaccessible high surfaces. *Clostridium difficile* spores are thought to spread in the air and can be found near a patient carrying the organism (Roberts et al. 2008). However, unlike MRSA, they are rarely isolated from air samples.

Single room accommodation, with or without separate ventilation, has been used in hospitals as the principal means of preventing airborne transmission, as well as encouraging hand hygiene. Frequently, this is compromised by poor hand hygiene and staff fixing the door to the room open so they can see the patient at all times. Further, very few hospital wards have sufficient single rooms to accommodate all infected or colonized patients. A risk assessment is generally performed such that those patients with simple skin colonization are nursed in the open ward and those with respiratory or wound infection are allocated single rooms preferentially. Consequently, improvements in rates of hospital-acquired infection have been achieved slowly and with great effort. Recently, the UK Department of Health has designed temporary isolation units that can be assembled within a single bed space to provide some degree of airborne isolation. Although these may prove beneficial, there are problems with internal access in an emergency and with preventing ingress of airborne MRSA from the surrounding bay.

Research in both the laboratory and the ward is needed urgently to define better the influence of hospital design on airborne spread of these diseases. Certainly, much of the past and future research in this area has and will benefit from a close interaction between clinical scientists (such as microbiologists and infection control specialists) who can assess risk (and treat patients), and engineers (material scientists, civil and mechanical engineers) who have the potential to design improved systems to manage the spread of infection.

The purpose of this themed volume is to provide a snapshot of some of the current developments in the area of airborne transmission, focusing specifically on the hospital environment. The hospital environment is usual, being specifically a place where there is a mixture of sick, infected and immunocompromised individuals sharing the same building, and where there is some element of building design (such as different ventilation strategies for different areas) and a management plan to limit the spread of infection. While such systems are in place, transmission by air still occurs and is the focus of many research groups internationally.

The original research that is presented in this volume is separated into the generation mechanism, the engineering context and suggestions for remediation.

### 2. GENERATION OF FOMITES IN THE AIR AND THEIR MICROBIOLOGICAL COMPONENT

The key steps discussed here are understanding the sources of pathogens in the air, the effect of environmental factors on their survivability and the potential for expressing infection. Pathogens in the air are spread on particles or droplets. The solid matter may come from skin, while the droplets may be generated from the upper or lower respiratory tract, mouth, nose and circumstances such as vomiting, dripping water taps and diarrhoea. The physical mechanism of the generation of droplets and particles carrying pathogens is largely unknown, though indirect measurements are reported in this volume.

Respiratory droplets can carry microorganisms such as bacteria and viruses and constitute a medium for the transmission of infectious diseases. Flugge (1897) showed that droplets from the nose and mouth contained bacteria, but did not travel more than 2 m. Wells (1934) characterized the concepts of airborne transmission and large droplet transmission based on the droplet sizes. In his classical study of airborne transmission, Wells (1934) revealed the relationship between droplet size, evaporation and falling rate by studying the evaporation of falling droplets, and this is referred to as the Wells evaporation-falling curve of droplets by Xie et al. (2007). Wells postulated a now widely accepted hypothesis of the distinction between droplet size and airborne transmission routes. Small droplets start to evaporate after release, and thus change their size resulting in droplet nuclei that are sufficiently small to remain suspended in the air for a long time and still be infectious. Large droplets (larger than 100 μm) can settle on the ground before they become droplet nuclei.

The majority of the respiratory droplets are less than 100 μm in diameter (Duguid 1946; Loudon & Roberts 1967; Papineni & Rosenthal 1997), and these evaporate rapidly in the surrounding environment (Wells 1934) and become droplet nuclei, which suspend in the air or are transported away by airflow. The size distribution of the droplets is a matter of great debate, largely because their size distribution spans the limit of measurement techniques. Xie et al. (2009) provided for the first time data for when the food dye was not used. Thus, there are many possible steps between the production of droplets by a human source or index case and the resulting infection and disease in another individual. Droplets that carry infectious agents can be formed in many ways. Natural means include breathing, talking, sneezing, singing and, in particular, coughing. In this volume, coughing is explored using an artificial cough machine by Pantelic et al. (2009) and using human volunteers by Xie et al. (2009) and Tang et al. (2009). Artificial means of producing potentially infectious aerosols are abound in hospitals, particularly when taking high-risk respiratory samples.
like nasopharyngeal aspirates or when using respiratory assist equipment, such as nebulizers (Hui et al. 2009), ventilators (Hui et al. 2006a,b) or oxygen masks (Hui et al. 2006a,b, 2007; Ip et al. 2007) for patients in respiratory distress.

The survivability of pathogens in the air depends on many factors, including residence time in the air, the level of moisture (which in part depends on temperature), atmospheric pollutants and UV light (if outdoors in the sun, for example). Both temperature and humidity affect the lipid envelope and protein coat, affecting the period of survival. Temperature and humidity will work together to either destroy the organisms or stabilize them. Chemical pollutants in the air such as carbon monoxide and sulphur dioxide, together with UV light, will add to this disruption and may decrease survival in such an environment (Cox 1989, 1998). And, although movement in air may play a role in moving pathogens between spaces, they have a potential to act as secondary sources when they sediment onto inanimate or animate surfaces.

The survival of any infectious agent (viruses, bacteria or fungi) depends partially on ambient environmental factors such as temperature and humidity (relative or absolute), as well as UV light and other atmospheric pollutants, as summarized by Tang (2009). The transport of such airborne droplets can be driven by various other environmental factors, such as local ventilation airflows (reviewed by Nielsen 2009 and simulated by Eames et al. 2009), as well as the movement of people (and their clothing) and thermal gradients produced by various pieces of electrical equipment (as discussed by Clark & de Calcina-Goff 2009). At the same time, there is not always a consensus among infection control specialists about which infectious agents are significantly transmitted by the long-range aerosol or truly airborne route. The argument in favour of this is made for influenza by Tellier (as discussed by Clark & de Calcina-Goff 2009). Other factors, in particular, the specific infectious dose for a specific organism for any particular individual is very difficult to define as everyone has a different history of exposure and therefore differing immunological histories (Tang et al. 2006). Although some infectious doses have been estimated for some agents (that may be of particular interest to bioterrorists; Franz et al. 1997), these are not commonly encountered by most people in their everyday lives.

Another issue of interest is the pattern of receptors required for some infectious agents to initiate successful infection and, eventually, disease. Whilst bacteria and fungi can exist independently of host cells, viruses require specific receptors to which they can bind before entering and replicating within particular host cells. This has been offered as one of the explanations for why certain individuals may have been infected with avian influenza A(H5N1) and perhaps why others have not. Differing patterns of receptor distribution between different individuals in the upper and lower respiratory tracts will affect the ease with which inhaled, airborne viruses can cause infection and disease (Shinya et al. 2006; van Riel et al. 2006). This is because different species of influenza viruses (avian versus human) target different receptor molecules that are present on different cell types (Matrosovich et al. 2004). The pattern of distribution of these different cell types in the human respiratory tract probably differs between individuals.

Finally, the nature of the infecting agent and the human respiratory activity itself may cause a different variety of organism to be expelled with differing effects on secondary cases. The physiology of a cough suggests that it is more likely to bring up and expel deep-seated organisms from the lower respiratory tract in the chest (Eccles 2005; McCool 2006) than the sneeze (Eccles 2005; Baraniuk & Kim 2007) or normal speech (Inouye 2003), both of which are more likely to expel organisms inhabiting the upper respiratory tract. Generally, the latter organisms (e.g. rhinoviruses and coronaviruses) are of less severe clinical consequence (causing most cases of the common cold) than the former (which may include influenza, *Staphylococcus* and *Streptococcus* bacterial species). However, any of these organisms can move up and down the respiratory tract quite freely, especially if the cilia ladder mechanism that constantly wafts debris from the lungs to the mouth to be swallowed (and destroyed by the stomach acid) is damaged. This is one mechanism by which an initial viral infection can lead to the more serious secondary bacterial infections that may have caused the majority of deaths in the 1918 and subsequent influenza pandemics (Brundage & Shanks 2008; Morens et al. 2008).
(ii) airflow direction, i.e. the overall airflow direction in a building, which should be from clean zones to dirty zones, and
(iii) air distribution or airflow pattern, i.e. the external air should be delivered to each part of the space in an efficient manner and the airborne pollutants generated in each part of the space should also be removed in an efficient manner.

Hence there are two basic physical principles behind the roles of ventilation in infection control. The first is through dilution of airborne pathogens, and the second is the control of movement of airborne pathogens from one space to another. Wells (1955) wrote: ‘Airborne epidemics are absent from an ecological population provided with adequate air hygiene.’ The well-known Wells–Riley equation (Riley et al. 1978) was applied for evaluating the effect of ventilation, filtration and other physical processes on the transmission of airborne diseases (Fennelly & Nardell 1998). Although the use of the Wells–Riley equation demonstrates clearly the impact of ventilation or its relative impact against other engineering control measures (Nardell et al. 1991), its scientific basis has remained controversial, and it also needs the quanta data for input.

In theory, if a disease can be shown to be airborne, the importance of ventilation becomes obvious. However, the relative importance of building ventilation as compared to quarantine, vaccine, use of masks, etc. is difficult to determine. The ventilation requirements are also difficult to define and other transmission routes may coexist with the airborne route.

4. MITIGATING TRANSMISSION

To reduce the spread of any infectious disease, the route of transmission needs to be known. With influenza, there is still a controversy about the most clinically significant route of transmission, whether it be via direct (via touching contaminated human secretions on people or fomites) or close contact (i.e. within 1 m) of a source (or index case) of infectious droplets. Updated reviews on the survival of airborne infectious agents (Tang 2009) as well as, more specifically, the airborne transmission of influenza (Tellier 2009) are included in this volume.

In addition, several articles in this volume demonstrate the extent to which ambient and ventilation airflows can contribute to the enhancement as well as the mitigation of aerosol and airborne transmission of infection (Clark & de Calcina-Goff 2009; Nielsen 2009; Eames et al. 2009; Noakes & Sleigh 2009). Yet, how can we apply these findings to reducing the transmission of airborne infection in hospitals?

As with most aspects of infection control, it is likely that a combination of the various interventions investigated in this volume will contribute to any final practical solution (Rampling et al. 2001), since different areas of a hospital will require different methods of reducing aerosol of airborne infection. For example, in communal areas (e.g. corridors, stairwells, cafeterias, lifts, waiting areas, etc.) ventilation will play an important role in maintaining a steady exchange of clean air for potentially contaminated air. For many people moving through such areas and large open spaces, their infectious status will be unknown and a bulk airflow approach to aerosol infection control may be the most effective and all-encompassing. This has the additional benefit of contributing to the thermal comfort of the large numbers of people moving through such areas when a relatively high air change rate is used.

At the more personal, intimate level of a bedside ward round, clinic visit, radiological and other investigations, where patients and doctors or technicians are within close proximity (i.e. conversational distance), more specific means of personal protection can be effectively applied, e.g. personalized ventilation (Nielsen 2009; Pantelic et al. 2009) or wearing masks (Tang et al. in this volume). However, both types of intervention (bulk airflows and individualized personalized protection) are subject to some important provisos. A ventilation system needs to be well maintained in order for the required air change rate to be achieved and sustained. Clogged filters, leaking or even contaminated ducts may lead to a build up of the infectious agents they were designed to remove. Thus, poorly maintained ventilation systems may eventually act as a source of, rather than as a defence against, aerosol/airborne infection (Cotterill et al. 1996; Kumari et al. 1998; Oztoprak et al. 2006). Personalized ventilation works best if the individual to be protected is stationary, e.g. a doctor sitting at a desk in a clinic (Pantelic et al. 2009), or if the potentially infectious exhaled breath of an infected individual is to be contained, e.g. a patient lying in bed (Nielsen 2009), as it is not easily transportable. However, in reality, the doctor may move from his desk to examine the patient, and infected patients will walk around the ward, including visiting the toilets.

Although Tang et al. (2009) have shown with Schlieren airflow imaging that wearing both surgical and N95 masks should be effective in containing infectious aerosols produced by the wearer, there are many complex issues surrounding mask-wearing. First, there is the actual physical filtering effectiveness of the mask in blocking the passage of bacteria and viruses. Some older studies have reported variable effectiveness against viral and bacteria-sized particles (Chen & Willeke 1992; Weber et al. 1993; Chen et al. 1994). Even though the materials, methods and mask designs may have changed since then, later studies on N95 masks still show variable effectiveness against viral and bacteria-sized particles (Qian et al. 1998; Lee et al. 2008; Johnson et al. 2009). Second, the actual act of wearing masks and keeping them on in a proper position is very difficult, as multiple studies on healthcare workers (who wear masks to protect themselves from patients and patients from themselves) have shown (CDC 2009; Jacobs et al. 2009, Scale et al. 2009, Gershon et al. 2009, Machtyre et al. 2009). Even patients (perhaps not surprisingly when they are sick) are poor at maintaining proper and consistent mask use in an effort to contain their infection and protect others (Longtin et al. 2009).

Other strategies of mitigation (which are hotly debated) lie outside the scope of this volume. They include post-exposure prophylaxis with antibiotics or antivirals, isolation and quarantine, and contacting...
tracing, social distancing (including school closures) and immunization.

5. CONCLUSIONS
Airborne infection control provides a number of challenging questions to the building ventilation community, and most of these questions need input from multiple disciplines: e.g. How are pathogen-laden droplets released, dispersed and evaporated in the room air? How do such dispersions interact with the room air flow, body air flow and inhalation/exhalation flows? What are the most effective ventilation methods for homes and offices? What are the roles of simple ventilation methods in resource-limited countries? Is it possible to develop more effective and advanced ventilation methods? How are the ventilation requirements for infection control differ from that for comfort and general health, etc. Among these questions, the most basic should be what the ventilation requirements are for airborne infection control and what personal measures should be collectively applied to remediate transmission. This still presents a fascinating and exciting area of research that is likely to go through enormous developments over the next few years.

REFERENCES


