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Engineering control of respiratory infection and low energy design of healthcare facilities

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ABSTRACT

Indoor microorganism and infection have become an emerging direction in indoor air quality research science. Airborne droplet nuclei can serve as carriers of respiratory infectious diseases. The study of expiratory droplets and their exposure control has received particular attention since the 2003 SARS epidemics and the 2009 influenza pandemics.

Little is known about how effective the commonly-used indoor environment control strategies are for infection control. Significant questions also exist on what are the ventilation requirements for airborne infection control. There is a broad range of relevant important issues including the exposure risk, and effective control methods in various indoor settings such as hospitals, homes, schools and offices. What is known is that the minimum required ventilation rate for infection control in hospitals can be much higher than the general health and comfort requirement in homes and offices. This has resulted in significant energy efficiency issues in healthcare facilities.

This review considers the current knowledge on airborne transmission of infection and the potential implications of a move to low energy design, particularly in hospitals, on the risk of infection. The review outlines active research and development on reducing hospital energy use while improving infection control and discusses the potential for conducting "clinical trials" to gain the necessary evidence to support changes in hospital ventilation design.

CURRENT PRACTICE AND GUIDELINES IN INFECTION CONTROL

About 7% of total annual worldwide deaths, i.e. 4 million people, are due to viral respiratory infections (WHO, 2004). Among them, influenza is a serious threat; influenza epidemics occur worldwide each year and the 2009 avian flu and H7N9 outbreaks have heightened awareness of the risk posed by new strains of the virus. With many serious respiratory diseases associated with transmission in high occupancy indoor environments, the design of the environment and particularly the ventilation is understandably a key feature of infection control in healthcare settings worldwide. However with a global move to reduce the energy consumption of all buildings through measures such as improving airtightness to reduce uncontrolled infiltration, ventilation of healthcare buildings has come under scrutiny and questions are being raised as to whether such high ventilation rates are indeed necessary. It is imperative to consider how a change in healthcare building design policies may impact on infection transmission. To discuss the implication of low energy design in healthcare facilities on infection control, it is useful to review first the current knowledge, practice and guidelines in infection control.

Microorganisms are believed to be transmitted from person to person or between animals and people through a number of mechanisms including physical contact, large droplets, or through fine aerosols. Infection control guidelines worldwide for all approaches are typically based on a three-stage hierarchy (CDC 2005): Administrative control; Environmental control; Personal protective equipment. In the case of transmission by aerosols and droplets, identification and separation of infectious patients remains the first line of defence (CDC 2005), however environmental control approaches and application of personal protective equipment have a particularly important role to play depending on the disease and its transmission. The distinction between airborne and droplet transmission is based on assumed behavior of different sized particles in air. The designation of fine particulates as those with a diameter< 5 µm, those >10 µm as large particles or droplets, has long been the basis of fundamental infection control strategies; as developed by the Association of Professionals for Infection control (APIC 2013), Centers for Disease Control (CDC) and World Health Organization (WHO 2007).

Simplistically, droplet precautions recommend wearing surgical masks within 6 feet (2m) of patients with an infection. The basis for this approach is the theory of settling times by particle size; large droplets will rapidly deposit on surfaces in the vicinity of the infectious source. Traditionally, patients at risk for transmitting disease through large particles have not been placed in respiratory isolation. On the other hand, patients with infections believed to be transmitted by

fine aerosols through the airborne route have traditionally required far more intense protection strategies, including early identification, isolation into an airborne infection isolation room with specialist ventilation, and the use of a fit tested respirator by staff in such a room.

This distinction remains the mainstay of infection control, and ASHRAE has recently developed a position paper outlining overall engineering concerns and summarizing implications for engineers of many of the infectious diseases transmitted by airborne route and by large droplets (ASHRAE, 2013). ASHRAE fundamentally relies on cognizant authorities in the development of its formal positions; the importance here being the implications for control strategies. Only in healthcare have control strategies explicitly considered infections in ventilation requirements, with ahierarchy of measures recommended by guidance. Local exhaust ventilation can facilitate source control in high risk procedures, pressurization minimizes transport of airborne microorganisms and other pollutants between spaces, a high ventilation rate dilutes and removes airborne microorganisms and well defined ventilation patterns can minimize transfer within a space. Air cleaning through filtration or other means can provide local control and enable recirculation of air. Guidance on these approaches is set out in a range of standards and guidance including ANSI/ASHRAE/ASHE Standard170 (2013), FGI Guidelines for Design and Construction of Hospital and Outpatient Facilities (2014) and various CDC guidance including those on TB (2005) in the US and Health Technical Memorandum 03-01 (Department of Health, 2007) in the UK. For example all these standards stipulate that patient and ward areas should have higher than average ventilation rates to minimize opportunist transmission from undiagnosed sources, while high risk areas such as operating rooms and isolation rooms have ventilation rates in excess of 10 ACH. Other buildings such as schools, public access buildings, and offices have mostly ignored any consideration of infectious hazards, although even here there is increasing awareness of the relationship between the building and health, and filtration, dedicated exhaust to the outside and ultraviolet germicidal irradiation (UVGI) have been explored in some studies.

Nevertheless, in practice, this distinction between fine and large particles as separate modes of transmission is becoming ever harder to maintain. Ten years ago, a review of the topic in a premier journal in medicine suggested that although there were clearly agents that relied on only one or only the other mode of transmission, i.e., large or small particles, there was a third group, organisms that were “facultative” users of both (Roy and Milton 2004). Shortly thereafter, a CDC review suggested that a common agent, influenza A, might fit that description and that the critical issue was then not whether airborne, droplet, or both but in what proportion transmission occurred (Tellier 2006). The

issue has smoldered for many years in other common viral illnesses, including even the common cold, where despite widespread beliefs to the contrary, experimental arrays show airborne transmission (Dick et al 1987). Recently, Nielsen and Li have modeled particle movement over short distances and suggest that airborne transmission of infectious diseases over short range might in fact follow the same pattern as large droplet transmission (Liu et al 2010, Li 2011)

The problem has come to a head with the increase in international travel and the threat of pandemic migration, no less important because the degree and importance of airborne transmission of influenza and the risks posed by new strains remains unknown. There is also concern over other infections, particularly virulent or emerging diseases. It is long established that smallpox, a now eradicated disease, was transmitted through the airborne route (Milton 2012). In fact, careful review of older literature has raised questions about even hemorrhagic fever cases resulting from airborne transmission (Carey et al 1972; Roels et al 1995), a phenomenon reinforcing the current biosafety laboratory precaution recommendations. The 2003 SARs outbreak demonstrated only too well the challenge of dealing with a global outbreak of a new disease and the importance the environment can play in transmission (Li et al 2005). Preventing airborne transmission in pandemic settings and ensuring infrastructure is sufficiently robust to deal with current and new threats requires far more intense approaches and represents a growing challenge for engineers.

EXPOSURE TO EXPIRATORY DROPLETS AND RESPIRATORY INFECTION

Although the relative importance of large versus fine particle transmission drives protection strategies in usual and pandemic settings, little research has explored the content of those droplets and the implications for transmission.

The source represents the primary factor in transmission, although others modify the transmission process. These factors may be grouped as follows:

- The infector and source (expiratory droplet number and size, respiratory activity, virus concentration, social contact),
- The environment (air/surface temperature, moisture, contamination, air flow pattern, ventilation rate, usage – ward, consulting room, waiting room, isolation room, operating theatre etc.),
- The virus (survival, site of infection),
- The susceptible (immunity, age, social contact) etc.

While controlling the source is desirable, it is challenging particularly in health care facilities (Menzies 2000). Approaches such as masking infectious patients while they are moved within a hospital building (CDC, 2009) and applying local exhaust ventilation in certain respiratory procedures are advocated. However in the wider hospital environment controlling transmission focuses on the transmission route, and the ventilation and building design becomes a major factor. With the growing threat of pandemics, since the early 2000s, from SARS, H5N1, and H1N1, engineering control strategies become not only relevant but of growing importance in defining the environment factor in the transmission process.

Understanding the mechanism of exposure is important to develop and understand an effective control strategy. For example, ventilation intervention decreases airborne transmission by extracting, directing the flow of airborne infectious agents away from susceptible persons and/or by diluting and removing airborne infectious agents from room air. If airborne transmission represents more of a hazard than previously considered, general dilution ventilation and approaches such as air cleaning represent more important aspects of ventilation for public health than previously considered. It also follows that a reduction in ventilation rates, as may be desired in low energy healthcare buildings, potentially poses an increasing hazard. However this is only part of the picture. Ventilation impacts particles that remain airborne, but the influence on droplet transmission or deposited particles and the subsequent exposure of susceptible persons to infectious agents through contact exposure is unclear. There is some evidence that air cleaning approaches reduce surface contamination but the impact on infection risk and the effectiveness of this as an intervention are largely unknown.

The uncertainty of the airborne route for many respiratory diseases remains a crucial bottleneck of using ventilation as a community intervention measure. In the case of influenza, the US$ 8 million project Evaluating Modes of Influenza Transmission (EMIT) is one of the most recent studies that may offer the first evidential result soon (EMIT 2013). However such studies are complex and challenging, and in most cases evidence has to be derived from studies exploring specific aspects of the transmission process. More than 10 studies explore the size distribution of expiratory droplets due to coughing, sneezing, speaking and talking (e.g. Morawska et al 2009; Chao et al 2009; Xie et al 2009). The data by Duguid (1946) has been widely used in risk assessment models in the literature (e.g. Nicas et al 2005; Yang and Marr 2011). Substantial uncertainty and differences exist in these measurements, possibly due to individual inhomogeneity, instrumentation, and factors such as study control. Moreover, these studies generally characterize

healthy volunteers, so while they yield valuable information on potential for human dispersion of particles, infection risks can only be inferred by extrapolation. Survival of viruses and bacteria has been studied as a function of RH and temperature in air (Harper 1961; Yang and Marr 2011) and on surfaces (Nicas and Jones 2009; Weber and Stilianakis 2008) yet it can be hard to link this data to infection risk in humans.

More recently researchers have explored the implications of specific viral content at various particle sizes. In a small study of patients presenting with influenza-like-illness, i.e., influenza A or B virus confirmed by rapid test, Fabian et al (2008) identified viral particles in the coughed secretions of three (60%) of the five patients infected with influenza A virus and one (14%) of the seven infected with influenza B virus. Exhaled influenza virus RNA generation rates ranged from <3.2 to 20 influenza virus RNA particles per minute. Over 87% of particles exhaled were under 1 micron in diameter, with unambiguous airborne potential.

Bishoff et al (2013) recently studied patients with influenza-like illness to measure viral particles at ≤0.305 m (1 foot), 0.914 m (3 feet), and 1.829 m (6 feet) from the patient's head. Twenty-six patients (43%) released influenza virus into room air, with 5 (19%) emitting up to 32 times more virus than others. Emitters surpassed the airborne 50% human infectious dose of influenza virus at all sample locations. The primarily small influenza virus particles (diameter, <4.7 μm) showed decreasing concentrations with increasing distance from the patient's head ($P < .05$). The authors questioned the current paradigm of localized droplet transmission during non-aerosol-generating procedures

NIOSH researchers (Noti 2012) studied influenza generation in a simulated patient room and recovered particles in all aerosol fractions (5.0% in >4 μm aerodynamic diameter, 75.5% in 1-4 μm, and 19.5% in <1 μm; n = 5). They demonstrated that tightly sealed masks (glue, not so practical in living workers) to the face blocked entry of 94.5% of total virus and 94.8% of infectious virus (n = 3). A tightly sealed respirator blocked 99.8% of total virus and 99.6% of infectious virus (n = 3). A poorly fitted respirator blocked 64.5% of total virus and 66.5% of infectious virus (n = 3). A mask documented to be loosely fitting by a PortaCount fit tester, to simulate how masks are worn by healthcare workers, blocked entry of 68.5% of total virus and 56.6% of infectious virus (n = 2).

Milton (2013) studied the effect of placing surgical masks on patients to capture influenza virus in large droplet spray. Fine particles contained 8.8 (95% CI 4.1 to 19) fold more viral copies than did coarse particles, supporting Bischoff et al (2013). Surgical masks reduced viral copy numbers in the fine fraction by 2.8 fold (95% CI 1.5 to 5.2) and in the

coarse fraction by 25 fold (95% CI 3.5 to 180). Overall, masks produced a 3.4 fold (95% CI 1.8 to 6.3) reduction in viral aerosol shedding.

Finally, Lindsley et al (2010) showed that such airborne particles, of influenza A, influenza B, and RSV, migrated from an urgent care clinic throughout a health care facility. These results supported the possibility that influenza and RSV can be transmitted by the airborne route and suggest that further investigation of the potential of these particles to transmit infection is important.

The bottom line from these recent particle size and content studies is that fine particles contribute substantially to the airborne particle load especially in the "facultative" airborne viruses; however the contribution to the burden of disease remains unclear. No arrays of studies are under way to develop predictive tests on which aspect is more important and therefore which transmission prevention strategy should be primary.

To assess the impact and magnitude of such risks, engineers will need to engage and work with a multi-disciplinary team of physicians and hospital infection control teams (HICTs) to make such an assessment.

REDUCING HEALTHCARE BUILDING ENERGY USE WHILE MAINTAINING OR IMPROVING EFFECTIVE AIRBORNE INFECTION CONTROL

Given the current climate, it is clear that low-energy considerations will eventually need to be applied to hospitals. So, on what basis should there be concern about the risks of increases in airborne hospital-acquired infections (HAIs), if we change design and introduce new technology to save energy? Is there any risk at all? Although not systematically investigated in a controlled manner, there are a large number of reviews and case reports that demonstrate that an effective ventilation system, working at a minimum number of ACHs is required for both thermal comfort and good airborne hygiene levels in hospitals (Li et al 2007; Eames et al 2009; Aliabadi et al 2011).

However in a hospital environment it is not simply the ventilation alone that adds to the energy cost. As well as higher ventilation rates, infection control generally leads to a higher usage of related environmental control strategies such as use of HEPA filters which add pressure losses and higher fan power, greater water quality control (for legionella),

more control of moisture level due to the impact of moisture content on survival of pathogens etc (ASHRAE, 2013). The question is, "is it possible to develop low-energy design without compromising infection control?"

To answer this question, we need to examine different low energy design strategies. It may be useful to categorize low energy design strategies into three categories.

- Category A - those with direct impact on infection control (such as reducing ventilation rate, air disinfection, use of natural ventilation; see WHO 2009)
- Category B - those with indirect impact on infection control (such as use of displacement ventilation, use of separate dehumidification control system, use of the liquid desiccant dehumidification systems etc.)
- Category C - those with no impact on infection control (such as good housekeeping measures like turning off lights when not in use, using renewable or CHP energy sources or installing energy efficient control systems such as variable speed drives) .

Within all categories, good design and maintenance of any technology is the first step in ensuring energy efficiency. For example a well constructed isolation room with a good level of airtightness, well designed airflow pattern and pressurization and properly commissioned ventilation and control system is likely to require less energy to operate than one with poor flows that requires post-construction modifications to create an acceptable environment for comfort and infection control. Similarly where filters are required, conducting lifecycle cost analysis as part of the design process benefits both the effective operation of the system and the protection provided to patients.

For Category A low energy technologies, changes to their application in hospitals need special attention. There is a growing body of experimental and laboratory evidence to inform some of these approaches, yet there remain many unknowns. Quantitative data on ventilation rates in particular is limited; however Menzies et al (2000) showed increased risk of Tuberculosis infection at ventilation rates below 2 ACH**.** Some researchers advocate reducing ventilation rates on energy grounds, but in the absence of good evidence, care should be taken when dealing with strategies which result in reducing the number of ACHs; if this results in a higher concentration of ambient, airborne infectious agents, then this might pose a hazard, particularly in environments housing more vulnerable inpatients (e.g. transplant patients, HIV/AIDS patients, premature neonates). A small number of studies have explored natural

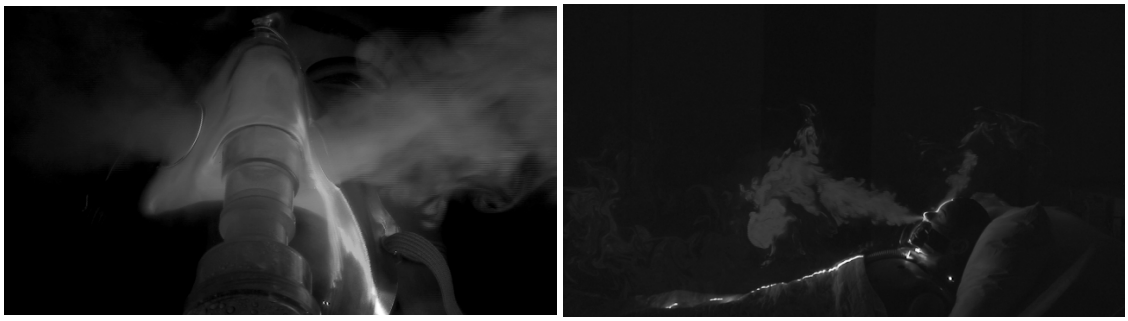
ventilation in full scale settings and have shown that some naturally ventilated hospitals can be thermally comfortable (Lomas et al 2012) and that very high ventilation rates, and hence dilution, can be achieved under certain weather conditions (Qian et al 2010; Gilkeson et al 2013). However studies also show the system can perform badly under different weather and operational conditions (Gilkeson et al 2013). Similarly there is a growing body of experimental (Xu et al 2003; NIOSH 2009) and computational (Noakes et al 2006; Sung and Kato 2011; Gilkeson and Noakes 2013) studies with a small amount of field data (Escombe et al 2009; Menzies et al 2003) that suggests ultraviolet air disinfection (UVGI) is a viable and possibly energy efficient (Ko et al 2001) approach to controlling airborne infection. Personalized ventilation is another approach where there could be some potential benefits in both energy and infection control. In the case of the short-range airborne route, traditional methods such as ventilation dilution are not effective, but there may be a role for alternatives such as personalized ventilation to provide near occupant protection (Sekhar et al 2005; Melikov 2004).

For Category B technologies, it can be even more difficult to judge if a particular technology is suitable for infection control. The use of displacement ventilation can be a good example (Li et al 2011). Displacement ventilation is known to provide better ventilation efficiency when certain conditions are met. Hence displacement ventilation has also been considered as a possible energy efficiency solution in hospital wards. Guity et al (2009) suggested that displacement ventilation at 4 ACH performed equally or better than overhead ventilation (mixing ventilation) at 6 ACH for thermal comfort, ventilation effectiveness and contaminant concentration in a single-patient ward. However, displacement ventilation has not been widely applied in hospitals, and it is difficult for a practical engineer to decide if such a system can be non-harmful to infection control. Based on the simple engineering principle, Li et al (2011) argued that “further field data on the locking-up phenomenon, weak plume trapping, particle deposition in the thermally stratified layers, the effect of occupant height variation, plume strength, droplet size and human movement, total exposure and risk analysis are needed”. “If a study focuses only on the preferable conditions, it is likely that displacement ventilation will be found to perform superior to traditional mixing ventilation and other designs.” “Based on the available data and as our understanding at present, and for protecting both the health care workers and/or other patients/visitors, we do not recommend the use of displacement ventilation in hospitals in either single-patient or multiple-patient wards for control of

exhaled substances or any harmful infectious aerosols." Other technologies where there is uncertainty over risk include those focused on thermal control. Ventilation systems that separate sensible and latent loads are known to have lower energy requirements, requiring smaller centralized air handling units and less ductwork. Provision of ceiling mounted radiant panels for local heating have become increasingly popular as they do not have the burn risk or tendency to trap dust that conventional wall mounted radiators do. Chilled beams offer a low energy approach to local cooling and are included in ANSI/ASHRAE/ASHE Standard 170 (ASHRAE, 2013). Concerns have been expressed over possible infection risks linked with cleaning and the potential for condensation to promote microbial growth, although the limited research evidence doesn't support these fears (Devlin, 2011).Understanding of all these low-energy technologies in terms of infection control presents a challenge, particularly given the uncertainties over transmission routes. Researchers have focused on building an understanding based on engineering principles, using proxy methods such as tracer experiments and computer simulation (Tang et al 2010) and comparing technologies through risk analysis approaches such as the so-called Wells-Riley equation (Riley et al 1978), and its various modifications (e.g. Beggs and Sleigh 2003; Fennelly and Nardell 1998). Engineers and building operators also need to understand the basic principles of non-engineering control strategies such as administrative measures and personal protection methods such as use of masks and respirators.

A SPECIFIC EXAMPLE – RELATIONSHIPS BETWEEN RESPIRATORY ASSIST DEVICES AND THE BUILT ENVIRONMENT

Oxygen masks are a frequently used and essential respiratory support device in hospital wards, worldwide. They are also a potential source and disseminator of airborne respiratory pathogens (**Figure 1**), principally because many of the patients that need to use them are likely to be infected with such pathogens.



A **B**

Figure 1. Illustrating the jet-like exhalation flows generated by the use of oxygen masks on a simulated patient: A) close-up view showing the emanation of exhaled airflows from the mask vents that can potentially carry airborne pathogens; B) more distant 'room' view demonstrating the capability of the oxygen mask to disseminate airborne pathogens beyond the immediate vicinity of the patient to other occupants of the room. (Images courtesy of Dr David Hui, Department of Medicine, The Chinese University of Hong Kong; experimental set-up described in Hui et al 2006a, 2006b).

After the severe acute respiratory syndrome (SARS) outbreaks of 2003, a series of airflow visualization studies on respiratory assist devices, clearly demonstrated the potential for human exhalation flows to generate and disseminate airborne pathogens (Somogyi et al 2004; Hui et al 2006a, 2006b, Ip et al 2007). Indeed, one of the largest hospital ward outbreaks of SARS described in Hong Kong was likely to have been caused by the use of a nebulizer by an undiagnosed patient with SARS (Wong et al 2005; Li et al 2005). Particle sampling studies conducted on a respiratory ward (Hathway et al 2013) also indicate that the use of patient ventilators and nebulisers changed the particle size distribution; respiratory assist devices were correlated with higher numbers of smaller particles indicating greater potential for airborne transmission.

The fate of particles released by such patients is determined by the built environment. For those in a single-bedded negative-pressure isolation room, continuously exhaling aerosols of pathogen-laden air, dilution and removal by the ventilation system combined with personal protective equipment protect healthcare workers who enter the room and the dilution combined with designed pressure relationships minimize the risks to those outside. If this ventilation system is inadequate, risks to those within the room may be excessive and leakage out of the room upon opening the door (resulting in a transient flow reversal, despite the negative pressure) may pose a real threat to other healthcare workers

and visitors outside the room (Tang et al 2005, 2013). While the risks of airborne pathogens being present on a general ward environment is lower, outbreaks are reported and it is only the diluting and removal functions of an adequate ventilation system that can keep the concentrations of such airborne pathogens within the room to a safe level.

Such factors must be considered in low energy hospital design. With respiratory assist devices likely to enhance any airborne pathogen release at potentially smaller particle sizes, the ventilation in both ward and isolation facilities will still be required to be maintained at an adequate rate to prevent the build-up of airborne pathogens to a level that poses a danger– and this concentration may vary according to different pathogens (Franz et al 1997). The reverse situation is also of concern, where isolation facilities are maintained at positive pressure using filtered air to protect vulnerable patients (e.g. bone marrow transplant patients) from potentially contaminated air entering the room from outside, particularly when healthcare workers and visitor are entering and leaving the room. Thus, before a reduction in ventilation rates or changes to ventilation design are considered as a means to reduce the energy cost of such healthcare facilities, a careful assessment of the patient group and clinical needs is required to ensure that patients and healthcare workers are not put at any increased risk as a result.

FUTURE NEEDS

Is current knowledge sufficient for future managers and designers to be concerned about the consequences of reducing the ventilation rate across a hospital facility? One might hope so, and certainly, new hospital designs seem to have taken the risks of contact transmission of infectious agents, such as MRSA (methicillin-resistant staphylococcus aureus), seriously, to some extent, at least. Yet, even such design and cost concessions for the sake of infection control require constant attendance and vigilance on the part of the microbiologists involved (Wilson and Ridgway 2006).

In comparison to airborne transmission, the evidence for contact transmission as a route of HAIs is stronger but relies mostly on “bundled” interventions (Gurieva et al 2013). Nevertheless, hand hygiene campaigns have taken the world by storm (Boyce et al 2012; Syed et al 2013; Allegranzi and Pittet 2009; Monistrol et al 2012; Allegranzi et al 2013), appropriately become an international effort, sponsored by the World Health Organization. Must the evidence for the clinical significance and impact of airborne transmission risks need to reach the same level of awareness in the professional and popular culture and media to be able to significantly influence hospital design? Does this require more than one or two multi-unit but not multi-hospital experimental studies? Given the plethora of recent studies suggesting

a significant contribution of the airborne route for influenza (Tang et al 2006; Tellier 2006, 2009), SARS-CoV (severe acute respiratory syndrome-associated coronavirus (Tang et al 2006; Li et al 2007) and other more ancient pathogens like tuberculosis (Tang et al 2006; Menzies et al 2007; Li et al 2007), one might argue that it already has. The very visible use of face masks in some affected countries (well publicized by national and international media) certainly contributed to the awareness of the airborne route of transmission for these pathogens.

Yet, there is still data lacking from a more direct, interventional study, at a hospital level. In the majority of cases the benefits of technology have to be inferred rather than directly measured, and even those studies that are conducted in the field generally rely on an existing building rather than a designed intervention. There has therefore been discussion among experts if there is a need for "clinical trials" of energy control strategies such as reducing or increasing ventilation rate. Does this really matter? On the one hand, given the current uncertainties of the proportion and clinical significance of the airborne route in causing HAIs, managers and designers could just ignore any potential implications of reduced ventilation rate or introduction of new technology– and see what happens. Yet in many instances this will be contrary to healthcare design guidance and in this increasingly litigious climate, this same evidence may be interpreted as indicating the potential for such infections to occur more frequently in a reduced ACH environment. If there is evidence available in support of a technology, any design team also have the challenge of interpreting that evidence, determining the quality of the findings and establishing whether the approach can be applied to their scenario. These difficulties with evidence-based design have been acknowledged by ASHE (2008).

However, clinical type trials are feasible in some cases, and for example have been conducted to investigate the potential benefits of air cleaning technology. Escombe et al (2009) showed that both UVGI and negative air ionisers reduced the transmission of TB from humans to guinea pigs in a clinical setting, while Kerr et al (2006) showed that the installation of ionisers in an ICU reduced the incidence of acinetobactor infections. Both trials had their challenges. Escombe's study still relies on a proxy measure (guinea pigs) although has a very comprehensive set of data including ventilation measurements and molecular typing of guinea pig infections and patient samples. Kerr's study demonstrated reduction in infection rates, but was unable to conclude the mechanism for transmission and hence show that the intervention acted on an airborne route. In both cases the trial was conducted in a single clinical environment, measured sufficient infections for statistical significance and relied on switching an intervention on or off with a comparable patient cohort.

So how would one go about designing a more direct interventional study to test the hypothesis: Does a reduced ventilation rate increase the risk of acquiring HAIs via the airborne route? And secondarily, if yes, how much can the ventilation rate be reduced to save energy and not increase the level of HAIs? On paper, it might seem very simple: compare infection rates over the course of a year between comparable patient cohorts with different ventilation rates. However there are a great number of factors that would need to be considered. Which patients? Which infections? How to measure and/or adjust ventilation?

Conducting a study in a single hospital ward, comparing standard with reduced or increased ventilation rate, and focusing on a small number of target HAI's would enable good data collection in terms of patient details and environmental characterization. However this approach may not have the numbers of infections needed to give reliable data and may not be translatable to other climates, infections, patient groups or ventilation designs.

Perhaps an alternative approach is to identify a number of hospitals from different countries with different climates and patient case mixes that could participate. Ask the Healthcare Infection Control Teams (HICTs) to document all suspected HAIs for one year to capture all seasonal variations. Next, ask the hospital engineers to adjust overall ACHs across the hospitals by a certain amount (say 10-20%) and ask the same HICTs to document the rate of HAIs for a second year. Finally, return the ventilation rates their original level in the third year and ask the HICTs to document all suspected HAIs to see if this rate has returned to a similar level as in the first year of the study. This approach, which treats the entire hospital environment as a 'black-box' has a number of advantages and disadvantages.

Advantages include, not having to detail every type of clinical activity taking place in the hospital, but just assuming that the patient case-mix and the healthcare staff involved will remain more or less the same during the three years of the study. Such a study would also have the advantage that it is able to track multiple different infections across multiple climates and can therefore give a greater insight into which effects are context specific and which are generalizable. Disadvantages with this approach include that it may not be clear exactly where the greatest impact of the reduced ACH intervention is being seen and that a broad study may well reduce the ability to collect detailed information on the environments and patients.

Planning such a study is a large and complex task. Conducting a study to assess the impact and magnitude of such risks would require an international multi-disciplinary team. In each participating hospital an Infection Control Risk

Assessment (ICRA) team with expertise in infectious disease, infection prevention, patient care, engineering, epidemiology, facility design, construction and safety (FGI, 2014) would be involved. These local teams would need to work with an international research team with engineers, epidemiologists, statisticians,physicians, microbiologists and infection control specialists. Participating hospitals would have to be selected carefully, i.e. avoiding those with planned major renovations or relocations of key services and personnel during the study period. Unforeseeable events such as major climate events (earthquakes, volcanic eruptions, tsunamis, major forest fires, etc.), or unpredictable political or economic changes could impact the results– so participating hospitals in countries that are politically and economically stable should be selected. When identifying spaces to adjust ventilation clinical risks would have to be considered. In the case of areas such as circulation zones, waiting rooms, outpatients and wards, the particular patient group, design of the building and minimum ventilation rates specified in the guidance for the particular setting need to be considered. In high risk environments such as isolation rooms, operating theatres and those wards with the most vulnerable patients (i.e. immune compromised, transplant etc.) airflow characteristics as well as ventilation rates are important and it is likely these spaces would all be excluded from any study. Feasibility and control would also be a factor; the study would only be able to compare spaces where ventilation can be reliably adjusted and maintained at a particular flow rate. Flow rate measurements would be required in order to adjust for variation between different hospitals and a study would have to control for any other infection control interventions that may be implemented in the hospital over the study period. Another potential confounder is which infections the various HICTs would agree are a result of HAIs, and in particular, a result of an airborne HAI. Differences between these definitions may confound any conclusion from the study, but this problem is not insurmountable and a consensus could be reached between the participating HICTs involved in the study.

While there are considerable challenges, such a study could be definitive if enough of the participating hospitals' conclusions agree, and should provide evidence, either way, for the impact of reduced ventilation rate on HAIs. This data would then hopefully support (or not) the concerns about this energy-saving option, on patient and staff welfare in these types of healthcare facilities.

However, if we were to conclude that such a study is impossible to conduct with feasible resources and within the constraints, then as a community we need to agree to take seriously the evidence from the past and ongoing studies investigating transmission mechanisms and control using proxy methods. In the absence of full trial data, we have to

accept this as the best evidence to support infection control in healthcare building design and work to implement the outcomes from such studies rather than insist on clinical data or nothing. To achieve this will require a multi-disciplinary effort to identify the key research and development needs, ensure that studies address as far as possible both engineering and clinical aspects and work to establish collaborative approaches to tackle the practical implications of turning research findings into new innovation. For example a lot of energy efficient design is done nowadays using computer modeling. Designers need to be careful in how such modeling results are interpreted. Input from engineers will be required to assist with this, especially in defining the appropriate starting condition parameters. Clinical and infection control experts also need to be involved to ensure that models and interpretations properly capture how the building will be used. As a collaborative team this enables consideration of parameters which may have not been identified by any party working in isolation.

SUMMARY

Infection control is an important design factor in hospitals, elderly care homes, and other healthcare facilities. Low energy design has a useful potential in healthcare facilities, but needs to take into account any potential risks in terms of infection control.

In many situations, the uncertainty of the transmission route for a respiratory pathogen remains a crucial bottleneck in choosing the most effective engineering control strategies. The effect of environmental conditions such as air temperature and humidity is also incompletely understood for most pathogens.

There is a complete lack of integrated studies on low energy healthcare building design for infection control. Some studies of individual energy efficient technologies and their potential impact on infection control issues are available. Balancing the infection risk and low energy design requires a multi-disciplinary effort, knowledge sharing between different experts and developing approaches to better translate research into practice. For new technologies, ultimately, well-designed and controlled field studies should be able to provide robust evidence for their applicability to infection control, in particular for their use at the community level.

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