Editorial

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The Threat Posed by Airborne Micro-Organisms

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Over the past 20 years there has been increasing interest in the quality of air in buildings. Initially this interest was focused mainly on the perceived problem of 'sick building syndrome'. However, as time has passed, many building designers and scientists have come to realise that indoor air quality has a profound effect on both the performance and health of building occupants, since people spend most of their lives indoors. Most of the work undertaken in this field has concentrated on non-viable chemical air pollutants such as radon, carbon monoxide, asbestos fibres and volatile organic compounds while the work on viable pollutants has tended to focus on the allergenic properties of fungi and dust mite excreta. In comparison, relatively little work has been undertaken on the microbiological aspects of indoor air quality. The relative lack of research into the airborne transmission of bacteria, fungi and viruses is, in part, due to the fact that aerobiology is a little understood science and also because the threat posed by airborne microbes has been greatly underestimated. In addition, some infectious diseases that have an airborne route of transmission have become difficult to treat because of the emergence of antibiotic-resistant bacterial strains. Furthermore, some of these infections are undergoing a resurgence of worrying proportions. Tuberculosis (TB), naively thought by many to be a disease of the past, is still endemic in many parts of the world and is on the increase in the UK with 6,750 new cases being reported in 1999 [1]. Nosocomial infection (i.e. infection originating in hospital) has increased to such an extent that the National Audit Office has recently estimated the cost of dealing with the problem to be in excess of £1 billion per annum in the UK alone [2]. Finally, there is the ever-present global threat of biological weapons, which rely on the airborne dispersion of pathogens. There is thus a clear need to raise general awareness of the threat posed by airborne microbes and to undertake more research into the physical and microbiological behaviour of bio-aerosols.

The Tuberculosis Threat

TB is an archetypal example of a disease that is transmitted by the airborne route. Primary pulmonary TB is caused by the inhalation of droplet nuclei of <5 μm diameter which carry the causative agent *Mycobacterium tuberculosis*. Droplet nuclei, which are produced by infected individuals during coughing and sneezing, settle slowly and remain suspended in air for long periods. Because of their size they bypass the innate host defence mechanisms of the upper respiratory tract and are deposited in the alveoli in the lung. Transmission of TB occurs in situa-

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tions where infected persons come into close contact with others, such as in overcrowded housing, prisons or shelters for the homeless. It is, therefore, not difficult to understand why TB is often considered to be a disease of the poor, which spreads in crowded areas and confined buildings, typically among those who have inadequate access to medical treatment.

The world-wide occurrence of TB is very high, with approximately one third of the world's population thought to be infected with *M. tuberculosis* [3]. Worldwide deaths from TB are currently 3 million per year, and this is predicted to rise to 5 million by the year 2050 [4]. Such is the magnitude of the problem that, in 1993, the World Health Organisation declared the disease a global emergency [5]. Although the TB problem is greatest in the developing world, there has been a steady increase in cases occurring in Europe and the USA, with the UK and the USA seeing a 17% rise in cases between 1987 and 1993 [6]. Unfortunately, despite these depressing figures, ignorance of the TB threat persists. Indeed in 1992 the then UK Health Minister, Mrs Bottomley, stated: 'Tuberculosis has been virtually eliminated' [6].

Human immunodeficiency virus (HIV) is endemic in sub-Saharan Africa and is threatening many other parts of the world. TB acts synergistically with HIV and increases the risk of primary TB infection developing into active disease by a 100-fold [4]. In some parts of Africa, the lifetime risk of dying from AIDS is 50% [4]. The seriousness of the situation is compounded by the emergence of new multiple-drug-resistant strains of *M. tuberculosis* (MDR-TB). Multiple-drug resistance is defined as resistance to two or more antimycobacterial antibiotics. Many MDR-TB strains are resistant to isoniazid and rifampicin, two of the first-line antibiotics used in therapy of this infection. Some strains, however, are resistant to up to 7 anti-TB agents. The reasons for the emergence of multiple-drug resistance in *M. tuberculosis* are complex, but non-compliance with therapy is of major significance in this respect. Non-compliance occurs because many anti-TB drugs are associated with unpleasant side-effects. Other patients discontinue therapy because they experience a marked improvement in symptoms soon after commencing drug therapy and may fail to see the need for completing the course of medication – typically 6 months for uncomplicated cases. In countries where incomes are low and where individuals must bear the cost of their own treatment, patients may opt to purchase only 1 or 2 drugs (standard therapy commences with 4 anti-TB antibiotics) or may buy only enough drugs for a very short course of treatment.

Case-to-fatality rates of up to 93% have been rec with MDR-TB [7] underscoring the gravity of the posed by this condition. Recently, several outbre UK hospital buildings have highlighted the ever-p potential for transmission of MDR-TB in the nosoc setting [8, 9]. The measures required to control the s of MDR-TB represent a significant financial burd healthcare providers. It has been estimated that UK, the treatment of one MDR-TB patient costs be £100,000 and £200,000. In the USA, a recent incre MDR-TB transmission in hospital buildings has ale healthcare authorities. In a study of eight US hos undertaken by the Centers for Disease Control anc vention in the USA, it was found that between 198 1992, more than 100 health care workers had ski conversions following exposure to patients with TE that at least 17 had developed MDR-TB [10]. In York City, which has experienced the largest incre TB cases in the USA, it appears that hospital transmi has played a major role in the resurgence of the di with almost two thirds of MDR-TB cases being link four hospitals [11].

Nosocomial Infections

Nosocomial infection is a major problem in healthcare facilities, with approximately 1 in 10 pat acquiring an infection during a hospital stay [12]. T infections cause much misery and are associated wit nificant morbidity and mortality. In addition, the nomic impact of nosocomial infection on healthcare tems is considerable. A 1985 study in the USA estim that the total annual cost of nosocomial infection wa billion (1985 dollar rate), with 8 million lost bed da was estimated that 20,000 deaths were directly 60,000 deaths partly attributable to these infections In the UK there are at least 100,000 hospital-acqu infections each year, costing the NHS in the region c billion [2]. Given these statistics, it is not surprising healthcare authorities around the world are very cerned about nosocomial infection and are continuc seeking innovative methods to control the problem. fortunately, many of the micro-organisms responsibl nosocomial infections are difficult to eradicate, and become drug resistant. Notable examples are methic resistant *Staphylococcus aureus* (MRSA) (the so-ca super bug) and glycopeptide-resistant enterococci, bo which are found in many hospital buildings in the UI

The contribution made by airborne pathogens to nosocomial infection has often been underestimated. Many nosocomial infections of bacterial, fungal or viral aetiology are transmitted via an airborne route. Indeed, it has been calculated that the airborne route of transmission accounts for 10% of all sporadic cases of nosocomial infection. For example, pulmonary aspergillosis results from the inhalation of spores of *Aspergillus* spp. The spores are widespread in the outdoor environment and often enter hospital buildings through mechanical ventilation ducts which have inadequate filter protection. Immunocompromised patients are particularly vulnerable to infection from *Aspergillus* spp., especially bone marrow transplant recipients in whom case-to-fatality rates of 85% are typical [14].

MRSA is a major problem in many hospitals throughout the world. Although infection with MRSA is generally associated with person-to-person contact, airborne transmission of *S. aureus*, including MRSA, has occurred in a variety of settings, including intensive care, burns and orthopaedic units [15–17]. Airborne dispersal of this bacterium has been documented in individuals with MRSA respiratory tract colonisation [18]. Gram-positive bacteria, such as *S. aureus*, possess a peptidoglycan-rich cell wall, which confers relative resistance to desiccation, thus allowing them to survive for considerable periods in the environment and facilitating their distribution around buildings by air currents.

In contrast to the gram-positive bacteria, an airborne route of transmission has not been considered important in the epidemiology of gram-negative infections in the hospital setting. There is, however, accumulating evidence to suggest that the important gram-negative nosocomial pathogen, *Acinetobacter* spp. can be spread in this manner. In an investigation of an outbreak of *Acinetobacter* infection involving three neurosurgical wards, a medical ward and an intensive care unit of a district general hospital, extensive air contamination by the outbreak strain was reported [19].

In addition to bacterial infection, it should not be forgotten that nosocomial viral infections may also be spread via the air. Although respiratory viruses are most obvious in this respect, it is now evident that the airborne route is a significant mode of spread in outbreaks of acute viral gastroenteritis [20]. A 30-ml bolus of vomit has been estimated to liberate 30,000,000 virus particles into the environment and, as air currents may cause these particles to be widely distributed in some hospital areas, it is not surprising that attack rates in some viral infections are very high [21].

The Importance of Ventilation

Given that bio-aerosols remain suspended in air for long periods of time, the role of ventilation in buildings is critical. Clearly, in room spaces which are both crowded and poorly ventilated, such as found in many Russian prisons [22], the risk of acquiring an infection like TB is markedly increased. However, even in so-called well-ventilated spaces, people can be at risk if the ventilation system is poorly designed and maintained. There have been a number of celebrated cases in which mechanical ventilation systems have successfully distributed pathogens around buildings. For example, in an AIDS treatment clinic in Florida [23], widespread cross-infection to the staff occurred from patients with unsuspected TB. Investigations revealed that the building had a centralised mechanical ventilation system which was recirculating contaminated air so that it was widely distributed throughout the clinic.

Another example of the importance of ventilation systems in the transmission of TB is provided by investigations following an outbreak of this disease on board the USS *Richard E. Byrd* in 1966 [24]. In this incident, a seaman, whose TB went undiagnosed for 6 months, despite signs and symptoms suggestive of the disease, was the index case in an outbreak in which 147 of 308 enlisted men were infected. It was concluded that individuals who had little or no contact with the index case had acquired the infection through inhalation of droplet nuclei which had been widely dispersed throughout the vessel by the recirculation ventilation system.

That mechanical ventilation systems are implicated in the distribution of pathogens around buildings should come as no surprise given that it is common practice to recirculate most of the air extracted from room spaces and that many air filters are of an inferior specification and are often replaced infrequently. High-efficiency particulate air (HEPA) filters are rarely used in buildings, even in hospital ventilation systems. When it is considered that air speeds in excess of 5 $m \cdot s^{-1}$ (faster than a man can run) are usual in ventilation ducts, it can be seen that many buildings possess what can be considered as efficient pathogen distribution systems. In our own experiments at the Leeds General Infirmary, we have recovered coagulase-negative staphylococci which have travelled considerable distances down ventilation ducts.

The cases of TB in the Florida clinic and on the USS *Richard E. Byrd* illustrate one very important point, namely that the threat posed to the general public from TB-infected persons is greatest while the latter are undiag-

nosed. When diagnosed, TB patients can be isolated in negatively pressurised rooms. However, before diagnosis, a TB-infected individual may spend many hours sitting in various doctor's or hospital waiting rooms, producing large numbers of droplet nuclei containing *M. tuberculosis*, which are then inhaled, not only by other patients, but also by health care personnel [10]. Therefore, in hospital buildings, equal care should be taken when designing the ventilation systems for secondary areas (i.e. waiting rooms, corridors etc.) and primary care areas. Unfortunately, in many healthcare facilities, infection control considerations have been ignored and recirculating ducted air systems are common.

Aerobiology

For the past 18 months, a multi-disciplinary team at the University of Leeds has been investigating the application of various engineering technologies to reduce or eliminate the threat posed by bio-aerosols in clinical environments. Technologies under investigation include ultraviolet germicidal irradiation (UVGI) lamps and negative air ion generators. During our research it has become clear that the general understanding of the physical and microbiological science associated with bio-aerosols is limited. Many fundamental issues are not well understood. In particular, knowledge of the influence of temperature, relative humidity and oxygen toxicity on various micro-organisms in aerosol form is far from complete. These are important issues that must be understood when investigating, for example, the extent to which gram-negative bacteria are able to survive in a hospital ward. Much more work needs to be done in the general field of aerobiology if we are to understand fully the role which airborne pathogens play in infectious diseases.

Finding Solutions

There are a number of engineering devices cur available, which have the potential to reduce the posed by bio-aerosols. HEPA filters can be used to nate particles as small as 0.3 μm, and UVGI can effe ly kill pathogens such as *M. tuberculosis*. Howeve knowledge base concerning how these technologies s be applied in practice is very low. For example, w when and how should UVGI lamps be used in ho buildings? This is a complex question and one wh often ignored! Hospital wards are dynamic places variable occupancy patterns and variable air conve currents. By contrast, a laboratory environment is paratively static and can be easily controlled. It is a easy to make the mistake of placing a UV device, v has performed well in the laboratory, next to a ceilin ply air diffuser in a hospital ward, with the result tha small fan in the UV device is 'swamped' by the co tion current from the diffuser. Consequently, althoug UV device appears to be working well, in reality it is This is a potentially dangerous situation, because pat and staff are relying on the UV device to ensure tha ward environment is safe. This simple example illust just one of the complexities involved in applying neering technologies to clinical spaces. The control o aerosols within buildings is essentially an applied mechanics problem. Unfortunately, this fact is ignored, either through ignorance of the issues involv simply because it is considered too difficult to ur stand.

The threat posed by airborne micro-organisms is and all too often ignored. In many ways our underst ing of how micro-organisms interact with the phy environment is very limited. Much more research wo required, if we are to develop effective technologies w will protect people in vulnerable situations.

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