The Influence of Sunlight and Ventilation on Indoor Health: Infection Control for the Post-Antibiotic Era

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1. Summary

In the developed world people now spend about 90 per cent of their time indoors. Most of the air they breathe is indoor air. Infections caught in buildings are a major global cause of sickness and mortality. Understanding how they are transmitted is pivotal to public health. Yet current knowledge of how infections spread indoors is poor. So, there is only a limited understanding of how to control or prevent them doing so.

This report surveys the literature on the subject. It looks at how the indoor environment can affect outbreaks of contagious diseases. In particular, it examines the role of ventilation and natural light in infection control. This is timely, because preventing the spread of infections is going to become more of a concern in the years ahead. There is a consensus that the threat to global public health posed by drug-resistant bacteria, new viruses and other pathogens will increase. There will be more of them; and they will be more difficult to treat. This means infection control must become a higher priority.

Before the development of antibiotics, ventilation was one of three pillars of infection control. The others were natural light and cleanliness. All three were considered key in preventing diseases spreading in buildings. But then, thanks to antibiotics, bacterial infections became treatable. And for a time there was a widespread belief that infectious diseases had been defeated. So there was less emphasis on fresh air, light and hygiene in buildings than there had been. Further, over the last hundred years, expert opinion has changed markedly on the airborne transmission of diseases. It has swung from belief to denial; and then begun to move back. This, in turn, has had a direct influence on the design of buildings. Currently, there are few incentives for designers to arrange lighting or ventilation to protect building occupants from airborne contagion.

The airborne route of infection has been, and continues to be underestimated. All viral respiratory infections should now be considered airborne. Ventilation rates and standards of environmental hygiene in buildings should reflect this. At present, they are based on inadequate research. The findings of this report also suggest the modern practice of designing buildings for human comfort rather than health may increase susceptibility to communicable infections. Before antibiotics became widely available, healthcare buildings were often designed to create an environment that prevented airborne diseases spreading. Typically, they had extensive south-facing glazing, cross-ventilation via windows, and tall ceilings. The findings of this review support such an approach.

It has been known for more than a century that direct sunlight kills germs in buildings. Hospitals and tuberculosis sanatoria used to admit the sun for this purpose. The findings of this study suggest sunlight may prevent communicable diseases spreading in buildings both directly, and indirectly. First, solar radiation is the primary germicide in the environment. Second, direct sunlight may increase resistance to infection in those who receive it; even behind glass. Research suggests this preventive effect could be due to the the intensity of sunlight, or the sun's infra-red rays, or both. Light from the sun helps to synchronise the body's biological rhythms. In doing so, it may improve the immune function of occupants and their resistance to pathogens. In addition, there is evidence that the sun's infra-red radiation, via window glass, may improve immunity to infection. Other findings include:

- Increasing ventilation rates may significantly reduce airborne infections in buildings.
- The minimum amount of ventilation needed to prevent them is unknown.
- Natural ventilation may be more effective than mechanical air handling systems in preventing disease transmission.
- Outdoor air is toxic to bacteria and viruses.
- Sunlight has a marked germicidal effect in the environment; and indoors.
- Guidance recommends direct sunlight should be excluded from healthcare buildings.
- The evidence-base for cleaning as an infection control measure is lacking.
- The environment within modern buildings may encourage the growth of pathogens.
- No one infection control measure is effective in isolation.
- Those examined in this report have been under-researched for decades.

The post-antibiotic era may be upon us. Pandemic influenza is a continuing threat to global health. Then there is the prospect of severe acute respiratory syndrome (SARS) returning; of old diseases coming back in more virulent forms, or new ones that prosper indoors. Without a large body of scientific evidence to draw on, practical experience and common sense should form the basis of infection control. Together they suggest in future, a high standard of personal and environmental hygiene must be an absolute requirement in healthcare buildings. A greater appreciation of sunlight penetration, cleanliness and natural ventilation would help in this.

2. Introduction

There is evidence that building ventilation can influence the spread of infectious diseases such as measles, tuberculosis, influenza, smallpox, chickenpox, anthrax and SARS.[1] There is also evidence that daylight, and especially sunlight, kills the bacteria and viruses that cause these and other diseases.[2] However, far less importance is now given to ventilation and sunlight in preventing infections in buildings than was the case in the past. One reason for this is that during the 1960s and 70s, the belief grew that infectious diseases had been conquered.[3] Thanks to antibiotics, bacterial infections were amenable to treatment. An over-reliance on antibiotics meant there was less emphasis on infection control.[4] Also, the transmission of airborne diseases in buildings was not considered as important as it had been. So today, there is less fresh air, light and cleanliness than there was during the pre-antibiotic era. Then, all three were considered important hygienic safeguards.[5]

Worldwide there is now an epidemic of antibiotic resistance.[6] And the development of new antibiotics has stalled.[7] So the `golden age' of antibiotic therapy may soon be at an end. In 2010, the European Centre for Disease Prevention and Control published the results of a survey on communicable diseases. They concluded micro-organisms that are resistant to antibiotics are the most important disease threat in Europe.[8] And in 2011, the World Health Organisation warned the situation had reached a critical point. If no action was taken, *'the world is heading towards a post antibiotic era, in which many common infections will no longer have a cure and, once again, kill unabated.'* [9] The only protection left in this post-antibiotic age would be infection prevention and control of the first order.[10] Unfortunately, the evidence base for some infection control measures is lacking. For example, finding proof of the benefits of keeping surfaces clean in the control of infection is difficult.[11] Similarly the roles of ventilation and lighting, which used to be the mainstays of infection control, has received little attention from the scientific community.

2.1 New and Re-emerging Diseases

To compound the problem, over the last three decades outbreaks of new viruses and other pathogens have become more common. Many of them have come from animals. Recent outbreaks of SARS, avian influenza, and others suggest zoonotic diseases - those that can pass from wild or domesticated animals to humans - are now major threats to global health.[12,13] New and potentially lethal viruses are on the rise due to population growth and increased contact between humans and animals. In an article in the New York Times in 2009, the American epidemiologist Dr. Lawrence Brilliant argued we may soon be entering an `age of pandemics'. He stated:

`*In our lifetimes, or our children's lifetimes, we will face a broad array of dangerous emerging 21st-century diseases, man-made or natural, brand-new or old, newly resistant to our current vaccines and antiviral drugs. You can bet on it.'* [14]

In the years ahead, there will be challenges from other directions; including healthcare associated infections, multidrug-resistant tuberculosis, and pandemic influenza.[15] So infectious diseases are set to become more of a public health issue than they have been. And many of them are diseases of the indoor environment.

Bioterrorism poses a further potential threat to public health indoors.[16] The anthrax attacks

that occurred in the USA in 2001 showed the vulnerability of building occupants to airborne pathogens.[17] There is concern that other more virulent biological agents could be used for bioterrorism.[18] Given this background, it is timely to examine infection control in the built environment. There are ways to design or adapt buildings to limit the damage from infections. As this review will show, much that was known about this comes from the pre-antibiotic era; and much of it has since been overlooked.

3. How Infections Spread in Buildings

In order to control infections it is necessary to know how they spread. This report is mainly concerned with respiratory tract infections. These are common, often debilitating, and sometimes fatal. Their economic cost in terms of medical care and lost productivity is vast. Yet surprisingly little progress has been made in understanding how many of them pass from one host to the next.[19] Broadly, since the 1930s, four mechanisms of transmission have been recognised. They are: contact; dust; respiratory droplets and droplet nuclei.[20] Unfortunately, the way these mechanisms are defined in the literature can be can be confusing. For example, contact can mean the inhalation of large droplets from a contagious individual when they cough, sneeze or talk. This is also known as droplet transmission. But contact also refers to infection from contaminated surfaces.[21]

Large respiratory droplets from coughs and sneezes can cause environmental contamination once they fall onto horizontal surfaces, or the ground. They can then form a part of the viral or bacterial component of dust. This, in turn, can be suspended and re-suspended by activities such as dressing, sweeping, or bed making.[20] It is said that the range of such droplets is generally no more than about 1 metre.[22] So, in theory, anyone standing more than this distance from an infected person would be protected. But this is by no means certain.

Smaller respiratory droplets quickly evaporate, leaving residues which, in turn, become minute suspended particles (droplet nuclei). They can contain any organism originally present in the droplet. In contrast to larger droplets, these smaller particles can stay airborne for minutes to hours depending on size and density. And they can reach deeper lung tissues than droplets.[24] Droplet nuclei are also exhaled during normal breathing and talking, as well as in aerosols during coughing and sneezing.[20] The importance of airborne transmission (the spread of infection by droplet nuclei or dust) has been a matter of dispute for decades and remains controversial. The relative importance of droplets, and of droplet nuclei initially in the air, and those raised again as dust in the spread of respiratory infections is not known. All three modes of spread probably occur.[25] Significantly, there is no agreed classification of airborne droplets.[26] The particle cut-off diameter at which transmission changes from exclusively droplet to airborne, or vice versa, has never been set. Potentially all pathogens that colonise or replicate in the respiratory tract could cause airborne infections.[27] Nevertheless, current infection control procedures make a clear distinction between droplet and airborne transmission. The latter requires more demanding precautions.

In healthcare premises, a disease known to spread via the air, such as *Mycobacterium tuberculosis,* requires the use of negative pressure isolation rooms if it is to be contained. Anyone who enters an isolation room must wear a special, high filtration respirator; not just a surgical face mask.[28] These precautions do not apply to diseases thought to be spread by droplet transmission such as the influenza virus, rhinoviruses, adenoviruses, and respiratory syncytial virus (RSV). [29] However, activities such as breathing, coughing, sneezing, and talking generate different sizes of particles. So infectious particles do not exclusively spread as droplets or as droplet nuclei. Rather, both are produced simultaneously. The authors of a recent literature review of the subject concluded that infection control precautions should be updated. Particles in a cough or sneeze can spread both as droplets and as droplet nuclei. This means controls should include airborne

precautions whenever there is a risk from an infectious aerosol. [24]

3.1 Contact Infection

For centuries, contaminated air was regarded as the main cause of most infectious diseases.[30] By the the middle of the 19th century, the dominant theory was that the spread of disease was miasmic. Leading figures in the movement for sanitary reform were adherents. They believed infections were caused by foul atmospheric emanations from stagnant water, human waste, rotting vegetable and animal matter. So they campaigned for closed drainage and sewage systems, clean water, refuse collection, public baths, and improvements in housing and hospital design. Such improvements included high levels of natural ventilation and sunlight admission. While the sanitarians were mistaken in attributing so much disease to contaminated air, their reforms brought major improvements in public health.[31]

Gradually, scientists discovered water, food, insects and direct contact could pass diseases. When the germ theory became established, the focus moved to identifying and controlling single infectious agents and away from environmental causes. The miasmic theory fell into disrepute; and with it went the idea that diseases could contaminate air. By the start of the 20th century there was an almost total denial of airborne transmission of respiratory infection; other than that due to droplet spray within close range of an infectious individual.[32] For the next fifty years, the dominant view was that prolonged intimate contact, including droplet infection, was responsible.[20]

In the 1890s, the German scientist Carl Flügge showed infective droplets expelled during coughing had a limited range of about about 1metre. He also showed guinea-pigs could be infected much more easily by having tuberculosis patients cough on them than by the inhalation of dried infected sputum.[33] At the time there was a widespread belief that tuberculosis and other respiratory infections could be caught by the inhalation of dried infective material floating in the air. Florence Nightingale, a leading sanitarian, was a strong advocate of damp-dusting and -sweeping for getting rid of dust. As she said:

`No ventilation can freshen a room or ward where the most scrupulous cleanliness is not observed'.[34(p86)]

However, Flügge's work led to the doctrine of the spray or droplet spread of respiratory diseases. The thinking was that transmission was only by close contact, instead of an aerial spread. Although droplets do travel short distances through the air, they came to be seen as an intrinsic aspect of contact infection. Further support for the contact theory came in 1910, when the influential American epidemiologist Charles V. Chapin published a review of the evidence for and against airborne spread.[35] He concluded respiratory infections were transmitted by large droplets over short distances or through contact with freshly contaminated surfaces; not via the air, or dust.

Chapin believed germs had little viability outside the body. Their virulence was reduced by drying and exposure to sunlight. In his view, people were the source of infection; not the inanimate environment. So the contamination of walls, floors and other surfaces was not important. Tuberculosis was the only exception to his contact theory. Even then, Chapin was not convinced tuberculosis was chiefly airborne and thought contact infection played a large part in infections. In all other cases, Chapin held infections spread by direct

transference of fresh secretions, or excretions, from the sick to the well. This occurred either immediately as in kissing, or mediately on fingers, cups, spoons, etc. As he wrote in 1907:

`We must teach those who have the care of the sick not to waste so much time on the invisible, dry and dead micro-organisms of the air, but to use more soap and water on their hands.' [36(p62)]

Chapin's doctrine went unchallenged until the 1930s, when the American engineer William Firth Wells produced the first experimental evidence for droplet nuclei in airborne contagion. He demonstrated that a variety of pathogens, including streptococci, pneumococci, diphtheria and *staphylococcus aureus*, could be atomized into a chamber and remain viable in the resulting aerosols for hours or days.[37] Wells argued that droplet infection was essentially localised and concentrated; while infection by droplet nuclei was dispersed and dilute.[23] The denial of airborne spread derived from Carl Flügge's lack of understanding that his experimental techniques were incapable of detecting it.[38] As Wells concluded:

`Failure to discover air-borne infection bacteriologically no more proves its absence, therefore, than failure to isolate B. typhosus from a sewage polluted water proves that typhoid fever cannot be conveyed by drinking water.' [23(p618)]

Wells's research on the infectivity of measles undermined Chapin's concept of contact transmission. But he lacked epidemiological evidence to support it.[38] So contact remained the dominant model for most communicable respiratory disease. In 1946, at the annual meeting of the American Public Health Association, a research committee reported there was not enough evidence to show the airborne transmission of infection was predominant for any disease.[39] By the 1950s, investigators had demonstrated airborne transmission of tuberculosis by droplet nuclei. They did so by exposing guinea pigs to exhaust air from a tuberculosis ward and infecting them.[40,41] By the 1960s, airborne infection had regained some scientific acceptance. In addition to measles and tuberculosis, there was evidence of the airborne transmission of *staphylococcus aureus*.[42] Nevertheless, Chapin's views on the primacy of contact infection prevailed.[43]

3.2 Airborne Infection

In the following decades, relatively little research work was done on the airborne transmission of bacteria and viruses. It seems that the threat to health posed by airborne microbes was underestimated. More attention is now being paid to airborne infection following the severe acute respiratory syndrome (SARS) epidemic in 2003. But there is still scepticism about airborne transmission.[44] For a common disease such as influenza, the role of airborne infection is still a matter of debate. There is agreement that it is at least possible. But there is strong disagreement about its importance.[45] So infection control is based on the assumption that large-droplet transmission is the predominant mode of transmission. However, there is evidence to the contrary. A recent review of the literature concluded infection-control protocols must take airborne transmission into account; especially during a pandemic. And aerosol transmission may be responsible for the most severe cases of influenza involving viral infection of the lower respiratory tract.[46] So in practice, special air handling and respirators should be used to prevent influenza spreading.

Each year, epidemics of this highly contagious disease cause three to five million cases of severe illness, and about 250,000 to 500,000 deaths.[47] There are also pandemics of influenza. The largest of these was in 1918-19. It was the most severe outbreak of pestilence the world has seen to date. Between 50 and 100 million people may have died. Should the next pandemic prove to be as pathogenic as that of 1918, there could be 180 million to 360 million deaths globally.[48] Influenza continues to have a major impact on global health, but knowledge of its transmission and control is poor.

The current H5N1 avian influenza virus has high virulence and lethality. So far it has not readily transmitted from person to person.[49] Until recently, this form of influenza could only pass between humans via close physical contact. Most of the reported cases have been traced to contact with diseased poultry and other birds.[50] But researchers have modified the H5N1 strain of avian influenza so that it can be transmitted through the air.[51] And another highly infectious respiratory disease has been modified in the laboratory in a similar way; and that is smallpox.

3.2.1. Smallpox

At one time endemic in many parts of the world, smallpox was greatly feared because of its high mortality rate and painful disfiguring symptoms. At the beginning of the last century, smallpox was more widely believed to be airborne than any other disease.[35] It was thought to be capable of spreading over long distances; such as from a hospital to its neighbourhood.[52] But by the 1960s, when the World Health Organisation launched its campaign to eradicate smallpox it did so on the basis that the virus spread by face-to-face contact.[53] Confidence in this assumption was shaken following a smallpox outbreak in a hospital at Meschede, Germany in 1970. A patient was admitted to the hospital who was suspected of having typhoid fever. He was placed in a separate room of the isolation wing of the hospital under the sole care of two trained nurses. Strict isolation techniques were enforced. Six days later a diagnosis of smallpox, rather than typhoid, was confirmed. Within a few days, 17 people contracted smallpox and three of them died. All three floors of the hospital were affected. The pattern of spread suggested airborne transmission of the virus. This was later confirmed by smoke tests. The flow pattern matched the distribution of smallpox cases within the hospital. No alternative mechanisms of transmission were identified.[54]

One factor in this outbreak was the design of the hospital building. This seems inadvertently to have led to relatively strong air currents being set up when the heating system was on. These currents seem to have spread the virus particles throughout the building. Further evidence of the airborne transmission of smallpox came in 1978. A medical photographer at the University of Birmingham, England contracted the disease and died. The virus passed from a research laboratory to a room above, in which the victim spent much of her time. An investigation concluded the virus may have travelled in air currents up a service duct from the laboratory.[55]

There was also an accidental outbreak of the disease in the former Soviet Union in 1971. A naval scientist caught smallpox on a ship while offshore from a smallpox testing site at Aralsk, on the Aral Sea in Kazakhstan. It seems the virus travelled downwind over a distance of at least 15 kilometers to reach the ship. This has raised concerns that scientists in the former Soviet Union not only `weaponised' smallpox, but succeeded in

aerosolising it. And they may have hardened the virus so that it stays infectious once airborne.[56]

3.2.2 SARS and Hantavirus

Another example of the airborne route being underestimated is the SARS epidemic of 2003. The official investigation that followed the outbreak did not consider airborne infection to be important.[57] As with influenza and other respiratory infections, the current paradigm supports the belief that most of them are transmitted by means of large droplets over short distances, or through contact with contaminated surfaces. At the time of the SARS outbreak it was assumed that contact was the main route of transmission.[57] Most of it was. Healthcare workers who avoided face-to-face contact with SARS patients while caring for them did significantly reduce the risk of contracting the virus. This may have been due to decreased exposure to infected droplets.[58] But an analysis of the initial spread of the disease at an apartment block in Hong Kong suggests longer range airborne transmission was also involved. An infected individual developed diarrhoea and used a lavatory in one of the apartments. This person `shed' the virus in their faeces. A virus-laden aerosol from the contaminated sewage passed through faulty floor drains into apartment bathrooms, where initial exposures occurred. The virus-laden air then rose up a ventilating shaft and prevailing winds carried it to adjacent buildings. The outbreak affected 321 residents and caused 42 deaths.[59,60]

Meanwhile, faulty ventilation may have played a role in the spread of the SARS virus during the outbreak in the Prince of Wales Hospital of Hong Kong.[61] And the transmission of SARS on aircraft suggests that airborne droplets may have infected passengers during the flights.[62] Prior to the SARS outbreak, the dynamics of virus-laden aerosols had attracted little research.[19] So controlling and preventing SARS spreading was difficult. As yet, there is no definitive proof that it can be transmitted successfully by air. But if it is, healthcare architecture and engineering will have to adapt.[63] One thing the SARS epidemic confirmed was the mechanisms of respiratory disease transmission are still poorly understood:

`...it is quite astonishing to encounter exactly the same questions asked decades ago in an area that is important not only to well being, but also to the survival of people worldwide: infection spread.' [19(p335)]

Viruses such as SARS can be shed in large numbers. Some of them can survive for long periods on surfaces or objects commonly found indoors.[64] Hand-washing and surface hygiene plays a major part in preventing outbreaks.[65] But ventilation may also have a considerable impact on their control and prevention. The SARS virus was the first new lethal pathogen of the 21st century. Ten years before SARS emerged, another virus had jumped from animals to humans and was claiming lives. This time there was no question that it was airborne and could travel over distances. The hantavirus spreads to humans through the inhalation of aerosolised excreta and saliva from chronically infected wild rodents.[66] Infection can cause haemorrhagic fever, with renal syndrome. There were some 2,500 cases of hantavirus cardiopulmonary syndrome in 1993-2007, with an overall mortality of 30 per cent. This is comparable to the fatalities among 8096 cases of SARS during the 2003 epidemic.[67] A key preventive measure is ventilating rooms or buildings showing signs of rodent infestation. The airing should last for at least 30 minutes before anyone occupies the space. Cross-ventilation should be used if possible. During the airing-

out period, those involved should stay upwind. And when cleaning after ventilation, they are advised to use disposable respirators and gloves.[66,68]

3.2.3 Staphylococcus Aureus

Drug-resistant bacteria pose an increasing threat to health. The most notorious of them is methicillin resistant s*taphylococcus aureus* (MRSA). This has long been a serious problem in wards and nursing homes where it infects patients weakened by disease or injury. But strains have emerged that can infect healthy young people who have had no prior hospital exposure. Such infections are increasing in the wider community, and these strains have now entered the health care setting.[69,70] Hand-hygiene by healthcare workers is thought to be the most important method of control of MRSA and other hospital infections.[71] Healthcare workers' hands are the most common vehicle for the transmission of pathogens from patient to patient.[72]

The airborne transmission of staphylococcal infection has been known about since the 1960s.[42] There is strong evidence that the nasal cavities of susceptible adults can become colonized with staphylococcus aureus by inhaling particles from the air.[73,74] Transmission is likely when there is movement in patient rooms or during activities such as bedmaking.[75,76] The dispersal of staphylococci into the air can also be increased by a concurrent viral upper respiratory infection. This turns a carrier into a so-called `cloud shedder.' [77] Changing the dressings of burns patients can generate MRSA aerosols. Airborne transmission has been implicated in infections in hospital burns and surgery units.[78-80] And, staphylococci can travel long distances on air currents and still remain viable.[81] Case studies suggest airborne infection has been underestimated in hospital infections. It could also be a factor in the growing prevalence of MRSA infections in the community. Resistant strains of airborne MRSA have been found in higher concentrations inside homes than outside them. And the bacterium is present on hand-touch sites in otherwise healthy homes.[82,83] Contamination of household surfaces may play a major role in community-acquired MRSA transmission.[84] But the health effects associated with indoor residential exposure to airborne *S. aureus* appear not to have been investigated. There is renewed interest in the the aerial spread and environmental contamination in hospitals by other pathogens. *Acinetobactor* has been linked to airborne transmission.[85,86] *Clostridium difficile* has been found in the air of hospital wards.[87,88] Research suggests there is a risk for *C. difficile* contamination via the air, particularly in patients with active symptoms.[89]

3.2.4. Gastro-intestinal Diseases

As with respiratory infections, the global burden from infectious intestinal diseases is vast. Microbes responsible include *Salmonella, Campylobacter* and adenovirus. In the developed world, the most significant cause of infectious gastrointestinal illness is probably norovirus.[90] This highly infectious organism is easily transmitted by contact between individuals, by contact with contaminated surfaces and objects, in food, and as airborne particles.[91,92] A recent review of documented outbreaks of norovirus in hospitals concluded 18.5 per cent were person-to-person infections, while 3.7 per cent of the total were food-borne. For the remaining 77·8 per cent the route of infection was unknown.[93]

A large proportion gastrointestinal diseases are spread within households. They can be transmitted in food prepared in the home by an infected person. Direct hand-to-mouth transfer is another route.[94] Intestinal infection can also be transmitted by aerosolised particles from vomiting or fluid diarrhoea. A sick person can produce 10^7 virus particles per

millilitre of vomit. And faecal material can contain up to 10^{12} viruses per gram.[65Barker] Projectile vomiting is probably a major source of cross-infection. And the droplets generated by flushing toilets can be inhaled or deposited on surfaces.[95] The high attack rates during norovirus outbreaks may be due to dispersion via aerosols.[96]

The airborne route could be important in the transmission of *C. difficile;* but this is not adequately addressed by current control measures.[97] Patients infected with *C. difficile* shed large numbers of spores in faeces. These can contaminate their skin, clothing, bedding, and nearby surfaces. Skin scales are a source for airborne dispersal of spores. As many as 10^{6}-10^{7} skin squama are shed in a 24 hour period.[98] One potential source of airborne spread are the lidless toilets commonly used in hospitals. When a toilet is flushed without a closed lid, aerosol production can contaminate the surrounding environment with *C. difficile*.[99]

As with communicable respiratory illness, even small decreases in incidence of gastroentiritis, diarrhea or other intestinal infections would result in large savings from reduced medical costs and increased productivity. Some of it could be reduced by improved personal hygiene. Reducing indoor contamination and airborne transmission would also reduce the burden to society.

3.2.5 Tuberculosis

Many potentially lethal respiratory diseases have been linked to housing. They include diphtheria, scarlet fever, pneumonia, meningitis, whooping cough, measles, mumps, and rubella.[100] But perhaps the most significant is tuberculosis. This used to be the leading cause of death in developed countries. At the end of the 19th century, it claimed more than 1 million lives in Europe each year.[101] Figures for the Britain show that tuberculosis caused the deaths of about 1 in every 8 of the population at this time.[102] An earlier estimate, from 1840, put the figure at 1 in 5 deaths.[103]

A number of theories have been put forward to explain the steady decline of tuberculosis in Britain from the mid-19th century onwards. One was that improved standards of living, especially better nutrition, were responsible. Others have argued the sanatarians' pre-bacteriological public health campaign was decisive. For some, it was improved housing, rather than better nutrition, which was the major factor.[104] During the 19th- and into 20th century, there was a belief that people who lived in sub-standard, overcrowded housing were at higher risk. Statistical evidence supported this view. Improvements in ventilation, lighting, and crowding are credited with helping to reduce the prevalence of the disease.[105-107]

In the 1970's, TB was thought to have been nearly eliminated; but it has re-emerged as a major health concern. Tuberculosis is now the world's most deadly bacterial infectious disease.[108] One reason is co-infection with the human immunodeficiency virus (HIV). The two diseases act synergistically and so magnify the burden.[109] Another reason is the increase of resistant TB strains. There are an estimated half a million cases of multidrug-resistant TB worldwide, including so-called extensively resistant TB (XDR-TB).[110] There are high rates of MDR-TB in Asia, parts of Eastern Europe and countries of the former Soviet Union.[111]

Tuberculosis is mainly passed in the air by droplet nuclei.[112] Transmission of *M. tuberculosis* bacteria to a non-infected person is more likely if there is overcrowding and

poor ventilation. So there is a greater risk of contracting the disease in confined environments such as prisons, shelters for the homeless and long-term care facilities.[113] And anyone who lives and sleeps in the same household as an infected person is at risk. However, there are no studies that address ventilation in private houses in terms of tuberculosis transmission.[114] Indeed, there do not appear to any for any respiratory disease. In a similar manner to hospitals, the potential for airborne transmission in non-healthcare settings has received little attention.

The transmission of tuberculosis, like human viral diseases, is chiefly an indoor event. The economic burden of this is huge. One estimate for the United States, published in 2002, put the heath-care costs of building-influenced communicable respiratory infections (influenza, cold, tuberculosis) at $10 billion. There were also $19 billion from absenteeism caused by illness, and a further $3 billion in other performance losses. There were some 52 million cases of influenza and common cold a year in the USA of which 10-14 per cent (5-7 million cases) could have been prevented. This would, in turn, have resulted in a saving of $3-4 billion.[115]

3.3 Dust-borne Infection

Charles Chapin attached little importance to the infectivity of dust. But experiments and observations made during the first half of the 20th century led many experts to consider whether dust and disintegrating sputum were major sources of infection.[64walther] While there was no absolute proof, there was strong circumstantial evidence that large secreted droplets drying on bedclothes, floors, dressings and elsewhere could be harmful.[116] Large numbers of hemolytic streptococci, staphylococci, pneumococci, diphtheria bacilli, and tubercle bacilli had been isolated in the floor dust on hospital wards. And it was known that the dispersion of these micro-organisms into the air from floor sweeping, bedmaking, and dressing, resulted in a general contamination of the whole ward environment.[25] However, in spite of much laboratory evidence that the dust in scarlet fever, diphtheria and ear-nose-and-throat wards could contain many millions of haemolytic streptococci or diptheria bacilli, clinicians were reluctant to believe that dried bacteria were capable of causing infection.[117]

There were few instances in which hospital infection could directly be attributed to dust. One study of infected burns implicated dust. This showed that 11 per cent of newly-admitted patients to hospital had small amounts of haemolytic streptococci on their burns. But within 3 to 6 days 66 per cent were grossly infected with the haemolytic streptococcus. And two out of every 100 patients developed scarlet fever. Haemolytic streptococci were found in considerable numbers in the air and dust of the burns wards.[118] Another example of probable infection via dust was that of someone developing acute tonsillitis having swept the floor of a room that had been vacated by a patient with streptococcal puerperal fever three days earlier. The sweeper was infected with the same strain of streptococcus as the fever patient.[119]

During the 1940s, research work was done on dust suppressive measures in wards. There was good evidence this reduced the amount of bacteria in the air. However, few reports of the successful control of disease emerged. Dust-borne infection was hard to prove because of the many modes of transmission of infection which exist at the same time. One study from 1944 showed a dramatic reduction during a measles epidemic. At the time, a serious hazard for measles patients was secondary infection with *haemolytic streptococcus*. The virus-damaged mucous membranes of their respiratory tracts were

highly vulnerable to the pathogen. Also, the catarrhal nature of measles favoured heavy contamination of bed-clothes and garments. On movement, infected dust particles were released into the air. These factors, together with the overcrowding of patients in hospitals at epidemic times, favoured the acquisition and spread of streptococci. The complications of streptococcal infection for measles patients, who were mostly children, were severe. They included otitis media, mastoiditis, and broncho-pneumonia. During the measles outbreak reported in the 1944 study, rigorous anti-dust measures were taken in one of two identical wards. In the ward where dust was controlled, the cross-infection rate was 18.6 per cent. In the other ward, where dust was not controlled, secondary infections with streptococcus rose to 73.3 per cent.[120]

It was also in 1944 that Dr. Lawrence Garrod published the results of a study in which he tried to determine how far dust was responsible for streptococcal cross-infection in surgical wards.[121] At the time, Garrod was the professor of bacteriology at the University of London University and bacteriologist to St. Bartholomew's Hospital. Dr. Garrod was unable to find direct evidence that dust caused infection. But he did show that dust could remain highly infective for long periods. Garrod's study was prompted by an outbreak of scarlet fever in a hospital. With the aid of a vacuum cleaner he took dust samples from wards and tested them for haemolytic streptococci. He concluded there were enough bacteria in the dust in some of the wards affected to have caused the epidemic. Garrod found dust could contain these organisms in large numbers, particularly near infected patients' beds, and in floor dust. But he discovered there were no streptococci in many specimens of dust in the same wards collected from sites on or close to the windows. Garrod also found more streptococci in dust from dark wards than in comparable specimens from normally lit wards. So he then carried out a series of experiments to find out if daylight was killing the streptococci. He found it was.[121] At the time, a number of studies of the bactericidal effectiveness of natural light on bacteria were published. The findings are reviewed later in this report.

3.3.1 Staphylococcus Aureus in Dust

In the years that followed Dr. Garrod's experiments, staphylococci replaced streptococci in hospitals. Other pathogens have emerged such as vancomycin-resistant *enterococci* (VRE), *Pseudomonas aeruginosa*, *Acinetobacter spp*., and *C difficile*. The results of an international survey published in 2001, showed *staphylococcus* was the most common cause of hospital- and community-acquired skin, soft tissue, bloodstream, and lower respiratory infection in many parts of the world.[122] Patients infected with *staphylococcus aureus* can shed large numbers of infected scales.[123] And *staphylococcus*, like other dangerous hospital pathogens, can survive for months in dust.[64] Hospital floors can have high levels of staphylococcus contamination, especially the area around beds.[124] Dust particles with staphylococcus on them can be transmitted to near-patient hand-touch surfaces via air currents.[75]

Some studies suggest removing dust may reduce the risk of infection. One example followed a 21-month outbreak of infection and colonization with MRSA on a male surgical ward. Despite aggressive measures being introduced, including isolation of affected patients and the closure and cleaning of ward bays, it could not be controlled. What finally ended the outbreak was cleaning the ward to almost double the usual level; with the emphasis on continuous removal of dust from ward surfaces, floors, furniture and medical equipment. The authors of this study concluded that a dusty ward is an important source of

MRSA infection for surgical patients. They also concluded that no one measure, on its own, is enough:

`Control of hospital-acquired infection with MRSA requires a combination of measures, none of which are completely effective in isolation.' [125(p109)]

Similarly, an outbreak of MRSA in a Scottish surgical unit also responded to cleaning. The outbreak, which involved fourteen patients, ended following a major cleaning programme in all areas of the unit; and improvements in the ward fabric. The conclusion drawn from this was resources should be directed to cleaning, and the improvement and maintenance of wards, rather than being diverted to the retro-active control of MRSA outbreaks.[126]

There are also reports of hospital patients becoming infected by MRSA-contaminated dust from mechanical ventilation systems.[127,128] In one case, the system in question was working on an intermittent cycle from 4 pm. to 8 am. The daily shut-down temporarily caused negative pressure. So air from the ward was drawn into the ventilation system and contaminated the outlet grilles. It seems contaminated air was then blown back into the ward when the ventilation system started up. Cleaning the system, and putting it on a continuous running cycle, prevented further outbreaks of the MRSA infection.[128] In another incident, researchers identified MRSA in the exhaust duct of an isolation room as the source of an outbreak in an adjacent intensive care unit. MRSA bacteria in exhaust air were coming back into the unit through a partially open window. The infections stopped once the ventilation system was repaired and the window was sealed.[129] Similarly, dust may have been a factor in an outbreak of *Bacillus cereus* in a neonatal intensive care unit (NICU) in a Japanese hospital. Vigorous cleaning of the NICU, adequate ventilation and covering air vents to prevent dust falling from them ended the outbreak.[130]

3.3.2 Dust in Vacuum Cleaners

Research shows vacuum cleaners are effective collectors of contaminated dust. And pathogens can survive in them for long periods. An investigation of salmonella infections in young children has shown this. Historically, salmonella infection has been linked to contaminated food or direct contact with animals. But some cases of infant salmonellosis in the home may result from contact with contaminated dust or dust aerosols. In one study researchers found salmonella in 3 of the 76 household vacuum cleaners they examined. And they found the bacterium could survive in dust in a vacuum cleaner for up to two months.[131] A similar study from the United States found 15 of 55 vacuum cleaners tested were contaminated with salmonella.[132] While vacuum cleaners are an aid to hygiene, emissions from them can contribute to indoor exposure to biological aerosols if dust is not filtered properly.[133]

3.4 Ventilation and Infection

There is a growing body of evidence that the aerial dispersion of pathogens may be contributing to the spread infection in hospital wards. But the minimum amount of ventilation needed to prevent the spread of infectious diseases, such as SARS, influenza and tuberculosis, is unknown. As a World Health Organisation report recently concluded:

`Despite more than 100 years of ventilation and infection study, the information is still sparse and incomplete. There are insufficient data to estimate minimum ventilation requirements in isolation rooms or in non-isolation areas in hospitals to prevent the spread

of airborne infection. There are also insufficient data to estimate the minimum ventilation requirements in schools, offices and other non-hospital buildings to prevent the spread of airborne infection.' [134(p19)]

Down the years, building design and ventilation have been linked to infectious disease outbreaks. But there have been few recent well-designed studies. One explanation for the dearth of published data is the challenging nature of this kind of research. Another is a lack of dedicated funding.[135] Whatever the reason, there is little scientific basis for current ventilation standards regarding infection. This was the conclusion of an expert panel that reviewed the literature following the SARS pandemic. Of the 40 papers that met their selection criteria, they considered ten to be conclusive. Overall, the panel found there was strong evidence of a link between ventilation, air movement in buildings, and the spread of infectious diseases. These included smallpox, anthrax, measles, chickenpox, influenza and SARS.[1] However, in 2006, another multidisciplinary expert panel convened to review the literature on ventilation and health. They judged that 27 peer-reviewed papers published in scientific journals gave enough information to inform the relationship. Of these 24 were conclusive; of which just three were on ventilation and communicable respiratory infections. The panel members were divided as to whether the evidence was strong or only suggestive. Finally, they concluded the three papers in question only suggest infection rates increased with lower ventilation rates in the building environments studied.[135]

The first of them was published in 1988. This large study of US Army recruits compared the prevalence of respiratory illness among trainees living in barracks. The results showed rates of acute respiratory illness with fever were 50 per cent higher among recruits housed in newer barracks than in older ones. The newer buildings had low rates of mechanical outside air supply, extensive air recirculation and closed windows. The older barracks had frequently open windows, or higher rates of mechanical air supply with less recirculation.[136] The second paper, again from the United States, describes an outbreak of pneumococcal disease in a jail. During the epidemic, the disease attack rate was 95 per cent higher in jail cells with the lowest volume of outside air supply per inmate.[137] The third paper, from Canada, reported on tuberculosis infection among workers in hospitals. This was strongly associated with inadequate ventilation rates - below two air changes an hour - in general patient areas.[138]

Taken together, epidemiological evidence and reports of airborne transmission of viral and non-viral diseases points to a causal relationship between ventilation rates and respiratory infections. One recent study has shown the amount of potentially pathogenic airborne bacteria in a ventilated space decreases with increased airflow rates.[139] However, opinion has been, and continues to be divided on the subject. So at this point, it might be useful to examine what happened in British hospitals from the 19th to the 21st century. Ventilation and infection control were at the forefront of hospital design for much of this period.

3.4.1 Mechanical or Natural Ventilation

In 1864, Britain's Chief Medical Officer John Simon presented a report on hospital hygiene to the Privy Council. In it, he wrote that ventilation of wards was of the utmost importance. It should be perfect; leaving no corner untouched by its currents.[140] At this time, natural ventilation was thought to be the best way to achieve this. Simon stated the open window was the essential inlet for fresh air. Windows were also the preferred outlets for used air in most circumstances - working in conjunction with chimneys. Like Florence Nightingale

before him, Simon recommended oblong wards with windows on the two long sides. These were to be sash windows reaching to the top of the ward. Between each two windows there should be enough space for one bed-head.

His report describes how ventilation in hospitals had changed in the preceding years. Many British hospitals had originally been built with mechanical ventilation. But, in Simon's words, artificially ventilated wards had been *`costly and fatal failures.'* [140(p66)] York County Hospital had to close because it was so unhealthy. Other hospitals, such as Bristol General Hospital, the West Kent Hospital, Maidstone, the Liverpool Royal Infirmary, and the Edinburgh Royal Infirmary tried mechanical ventilation and abandoned it. The system at Guy's Hospital in London was judged a failure because of the poor sanitary condition of the wards. By the time of Simon's report, no British hospital used artificial ventilation; except as a supplement to natural ventilation.[140] However, by 1971 the position had changed. Mechanical ventilation was thought superior to natural ventilation.

In 1971, a Scottish study showed patients had fewer wound infections in a new type of artificially ventilated ward than in the old fashioned Nightingale type.[141] The new ward design had controlled ventilation with 40 per cent of its patients isolated in single rooms. Following the transfer of patients from the old ward to the new, postoperative staphylococcal wound infections fell by about 55 per cent. At first sight, this demonstrated the superiority of the new design. But one could argue it was not a fair comparison. First, by the 1970s the crowding of open wards seems to have become common practice; and a recurring infection hazard. So the aim was to tackle overcrowding. And the only way to do this was to design the new wards so that extra beds could not be fitted in. Second, there is no mention in this study of the respective ventilation rates. Nightingale wards were designed for cross ventilation via open windows. But in this case, smoke tests showed the old ward had no set ventilation pattern. There were, however, reports of `wild' air streams from occasionally opened windows. So it seems the old ward was not being used as the designers intended: there were too many beds and not enough fresh air.[141]

Recently, the position has changed again. Current guidance recommends passive ventilation in British hospitals. The aim now is to reduce the need for mechanical ventilation or air-conditioning. But this seems to be driven more by the need to control energy use and reduce carbon emissions.[142] Significantly, a recent review of ventilation in hospital wards concluded relatively little research work has been done on the clinical benefits. While the the risks of airborne transmission of infection are recognised in specialist facilities, such as operating theatres, bronchoscopy suites, and isolation rooms they are not in wards. Guidance on the ventilation of patient rooms, general ward spaces, and intensive care units does not consider the impact of ventilation on the transmission of infection. Rather, ventilation is specified in terms of patient comfort and minimising energy costs.[143] Meanwhile, there is growing evidence that the part played by airborne transmission in the spread of infection within wards has been underestimated.[76,144] If so, the potential of ward ventilation to control infection needs to be reassessed.

Field studies have shown that ventilation systems in many hospitals fail to work properly because of poor design or construction, or because of poor maintenance. Such failings have been implicated in several outbreaks of tuberculosis.[145-150] Contaminated hospital ventilation systems have been implicated in outbreaks of fungal infections.[151,152] The source of an outbreak of *Serratia marcescens* infection in a baby unit of a hospital in

United Arab Emirates was traced to an air conditioner duct.[153] And, as noted earlier, faulty and contaminated ventilation has been linked to MRSA outbreaks.[127-129,154]

Britain's hospitals are adopting passive ventilation; to reduce energy consumption. Paradoxically, new housing in Britain and other countries now makes increasing use of mechanical ventilation. Again, this is to meet demanding energy and carbon emissions targets. Until recently, little published research was available on the health effects. But there have been concerns. And there are doubts about the technology. In 2012, the findings of a study of 299 mechanically ventilated Dutch homes confirmed some of them. This work, commissioned by the the Dutch Ministry of Housing, identified major problems with the installation, operation and maintenance of the ventilation systems in homes.[155] Researchers found dust and dirt in the air supply ducts in 67 per cent of houses fitted with mechanical ventilation heat recovery (MVHR). Air filters were dirty in almost half of them. And a third had dirt in their ventilation units. In addition, exhaust air was being recirculated in more than half of all homes with MVHR. And about half of the homes had at least one room with insufficient ventilation. Most occupants did not control ventilation systems as recommended. They often did not know how to. And many of them did not use the highest ventilation settings because of noise levels.[155]

So, as in hospitals, mechanical ventilation has not always performed as well as it should. This was a small study. And there is no published evidence that mechanical ventilation has been a factor in the spread of infection in houses. However, a wide range of micro-organisms, including some potentially pathogenic ones, are commonly found indoors.[156] And the airborne ones could become more virulent. Figures from Germany, Canada, and the United States show that people spend most of their time indoors in private homes.[157-159] It follows from this that most of the air people breathe is indoor air. According to one estimate, more than half of the body’s intake during a lifetime is air inhaled in the home.[160] Leaking or contaminated ductwork, and clogged filters favour the build up of the bacteria, viruses and fungi. As in hospitals, poorly installed and maintained ventilation systems may aid the spread of infectious agents. And mechanical ventilation may not be capable of delivering enough air changes to dilute airborne pathogens such as avian influenza or SARS.

4. Mechanisms for Reducing Infection

This section of the report reviews evidence that ventilation, light and cleanliness can neutralise or remove the pathogens in buildings.

4.1 Cleaning

The role of the inanimate hospital environment, such as surfaces and equipment, in the spread of infection remains controversial; and its significance is unclear.[161] In particular, the the precise role of environmental cleaning in the control of hospital infections is unknown.[162] While there is general consensus that environmental cleanliness is important for controlling infection, the scientific evidence for this is limited.[163]

Charles Chapin's model of infection emphasised hand hygiene; and this continues to be the focus of infection control in hospitals, and not only those targeting MRSA. Some studies show this to be effective. But others have failed to find a significant link between hand hygiene and MRSA acquisition rates.[164] Indeed, recent studies suggest increasing hand hygiene may not reduce MRSA infection.[165] One explanation for this is that with so much emphasis on clean hands, less is paid to the surfaces they touch.[166] Like other pathogens, MRSA contaminates surfaces.[167] A recent study of MRSA on nurses' hands found more on them after contact with the environment than following contact with patients.[168] So it would appear both hand hygiene and cleaning are needed to reduce the risk of infection. Yet experts continue to debate the importance of cleaning to prevent hospital acquired MRSA. In common with other recent research on infection in buildings, the findings on this are contradictory. Some studies show cleaning reduces MRSA infections. Others seem to show it does not.[161]

The part played by environmental contamination in the spread of MRSA is not well documented.[169] But as noted earlier, the presence of contaminated dust, and its removal, seems to affect the course of hospital outbreaks. The risk of catching another type of hospital pathogen, vancomycin-resistant *enterococcus*, has been reduced when cleaning and hand hygiene are combined.[170] Years ago, these measures formed the basis of infection control. It is worth noting that in her *Notes on Nursing* Florence Nightingale insisted on rigorous environmental cleaning and regular hand washing to prevent hospital infections.[34]

Recent studies do confirm what Florence Nightingale, Professor Lawrence Garrod and others from the past suspected but were unable to prove. Putting patients in rooms previously occupied by patients infected or colonised with hospital pathogens is potentially dangerous. They have an increased risk of acquiring the same pathogen compared to patients not occupying such rooms.[171,172] But many other unsolved problems remain. For example, the extent to which reducing the contamination of environmental surfaces from prior room occupants reduces the risk of infection. One recent study shows aggressive cleaning may reduce MRSA and VRE transmission. It may also eliminate the risk of MRSA acquisition due to an MRSA-positive prior room occupant. But aggressive cleaning was not able to eliminate the increased risk from VRE. Reasons put forward for this included a higher burden of VRE contamination; and that such contamination may be a major factor intransmission. It may also be due to a greater difficulty in eliminating VRE contamination.[173,174]

4.2 Ventilation

A century ago, building codes and standards set high ventilation rates to dilute air to minimise the risk of airborne contagion. Figures from the period show recommended air change rates were about ten times higher than they are now. For example, in 1914 a British Admiralty Ventilation Committee recommended the air change rate on the Royal Navy's ships should be some 3,000 cubic feet (85 m^3) per man per hour.[175] This was also recommended for British housing.[176,177] By the 1920s, scientific opinion had turned against airborne infection; the contact route assumed greater importance. Natural cross-ventilation remained popular in hospitals. The sanatorium regimen of treating diseases, such as tuberculosis, in the open air had a direct influence on hospital design.[178] But gradually, the rationale for ventilation changed. Tuberculosis, smallpox and other common infectious diseases posed less of a threat to public health than they had done. So rather than prevent infection, the aim was to create comfortable conditions and remove odours produced by building occupants. Standards based on comfort remained in place until the Arab Oil Embargo in October 1973, when energy efficiency became a priority. Air change rates fell further to save fuel. Soon the phenomenon that became known sick building syndrome (SBS) appeared. This was characterised by a range of temporary symptoms and conditions, such as headache, dry eyes, nasal congestion, fatigue and nausea. The syndrome was linked to poor ventilation and was sometimes called ‘tight building syndrome’.[179]

In 1976, an outbreak of respiratory illness at a hotel in Philadelphia proved a turning point. Delegates at an American Legion convention suffered 182 cases of pneumonia and 29 deaths. The infection was caused by a previously unrecognised bacterium later named *Legionella pneumophilia*. The hotel’s ventilation and humidification system was later found to be the source of the bacterial exposure.[180] This outbreak revived interest in indoor air quality and health in buildings.[181] Then the 1980s saw an epidemic of tuberculosis in New York City and a resurgence of the disease in other urban centres in the USA. These outbreaks included new strains of difficult-to-treat, multiple-drug-resistant *M. tuberculosis* (MDRTB).[182] They stimulated further interest in the control and prevention of airborne disease.[113] Then, in the wake of the 2003 severe acute respiratory syndrome epidemic, it became clear the potential for airborne transmission in hospitals has received little attention. And there are still insufficient data on which to base minimum ventilation rate guidelines for this. Those that are in place are not based on sound scientific evidence.[183]

4.2.1 Ventilation and the Common Cold

Typically, adults have between two and five common colds each year, and children between four and eight colds.[65Barker] Rhinoviruses cause the great majority of them.[184] Despite many years of study, the preferred route rhinovirus takes to inflict the common cold on susceptible individuals remains controversial. The conventional view is that most transmission is by contact.[185] Sharing office space increases the risk of the common cold.[186] And a study carried out in mechanically ventilated office buildings found evidence supporting aerosol transmission of the rhinovirus. The results suggested an increased risk of inhaling infectious droplet nuclei in buildings when the supply of outdoor air is low.[187] A more recent study, one of the first of its kind, looked at the number of colds among students in college dormitories. There was a strong link between infection rates, ventilation rates and crowding. Students in 6-person rooms were twice as likely to have common colds 6 or more times a year than students in 3-person rooms. There was a also a dose-

response relationship between infections with colds and outdoor-to-indoor air flow rates. Some 35 percent of students caught more than 6 colds each year when the ventilation rate was 1 litre a second per person. With a ventilation rate of 5 litres a second, the number of students catching colds 6 times or more fell to 5 per cent. So strong was the evidence in this study, the authors concluded that airborne transmission may be the main route for colds.[188] If this is the case, droplet nuclei could be a major route for other acute respiratory infections. So, ventilation may be more important in diluting and dispersing the viruses that cause them than is currently appreciated.

4.2.2 Preventing Infection: Natural or Mechanical Ventilation?

Recent measurements of air change rates suggest that the risk of transmission of airborne diseases can be significally lower in naturally ventilated spaces than in mechanically ventilated ones. Older buildings with large windows and high ceilings may be far safer than more modern designs in this respect. In 2007, researchers measured natural ventilation in 70 different rooms in hospitals where tuberculosis patients were being treated. They compared air exchange rates in respiratory wards, general medical wards, outpatient consulting rooms, waiting rooms and emergency departments with those in mechanically ventilated, negative-pressure respiratory isolation rooms. They then used an airborne infection model to predict the effect of these ventilation rates on tuberculosis transmission. The highest risk of infection was in closed, unventilated spaces. By contrast, clinical rooms in hospitals built before the 1950s with high ceilings and large windows on more than one wall gave the greatest protection.[189]

There was an increased risk of airborne contagion in modern wards with low ceilings and small windows. Mechanically ventilated rooms with sealed windows posed an even greater risk, despite being ventilated at the rates recommended by guidelines. The results from the model suggested that, after 24 hours of exposure to untreated tuberculosis patients, some 39 per cent of susceptible individuals in mechanically ventilated rooms would become infected. This compared with 33 per cent in modern, naturally ventilated clinical rooms with windows and doors open; and just 11 per cent in pre-1950 ones. Overall, natural ventilation, with windows and doors opened, was more than double that of mechanically ventilated, negative-pressure rooms. And even at the lowest wind speeds, natural ventilation performed better than mechanical ventilation. This research also showed that protective rates of ventilation are achievable with windows only partially open.[189]

The large windows and high ceilings of many older buildings allowed up to 40 air changes per hour. However, these and other ventilation rates this study will have been influenced by climatic conditions, such as wind velocity and direction. But no details of this were reported. The study also assumed that the mechanical ventilation plant would deliver 12 air changes per hour. However, a subsequent inspection found poorly maintained electric motors, corroded fan blades clogged with deposits, and air extraction and supply fans unprotected by filters. In practice, the mechanically ventilated rooms in this study only achieved half the air changes they should have. This is not unusual. As the authors of the paper noted, respiratory isolation rooms often do not deliver the recommended air exchange rates.[189]

A recent study of hospitals in Hong Kong also shows naturally ventilated wards can achieve higher air change rates than those with mechanical systems. Measurements in a tuberculosis hospital and an outpatient clinic found much higher rates than the 12 air

changes an hour specified for isolation rooms. In a ward with all the doors and windows open, cross ventilation occurring, and a strong breeze the maximum rate was 69 air changes an hour. Even without cross-ventilation, rates were between 14 and 31.6 air changes an hour.[190] A study from Thailand also reported high air change rates in naturally ventilated facilities; and that mechanical ventilation failing to meet performance standards.[191]

It is notable that when a new lethal virus did emerge in 2003, patients were safer in cross-ventilated wards. Case studies from China following the SARS outbreak indicate cross-ventilation is one of the most effective ways of controlling SARS infection in hospitals. And there were no reports of SARS cases caused by cross-infection in hospitals with high ventilation rates.[192] Another study of isolation wards in Chinese hospitals showed those with a high proportion of openable windows were more effective in preventing outbreaks of SARS among healthcare workers than other designs.[193]

There is, as yet, no direct epidemiological evidence to support, or challenge, the superiority of ventilation through open windows over that achieved with mechanical systems. Historical evidence suggests high rates do have a protective effect. To cite just one example, during the notorious 1918 influenza pandemic, patients with severe symptoms who were cared for outdoors survived in greater numbers than those indoors. Some of the worst affects of the virus were seen below decks on troop ships.[194] According to one report, those who suffered most on ships were in the most badly ventilated spaces. And patients put outside in tents survived in greater numbers than those treated indoors.[195,196] Eighty years later in Saudi Arabia, during Operation Desert Shield, respiratory disease among military personnel followed a similar pattern. Upper respiratory tract infections were more frequent in troops housed in air-conditioned barracks than among those housed in tents.[197]

4.2.3 The Open Air Factor

During the Second World war, far more emphasis was placed on ventilating hospital wards than is the case today. In 1944, Britain's Medical Research Council published a memorandum on the control of infections in hospitals. It included guidance on ventilation, as follows:

`This should be as free as possible, winter and summer, day and night. Wards should be thoroughly aired immediately before and after blackout, and several times during the night.' [198(p17)]

The protective effect may be more than just high ventilation rates diluting germs. What the Nightingale ward, and tuberculosis sanatorium had in common was they were designed to make conditions indoors as close to those outdoors as possible. This was thought to both therapeutic and hygienic. The majority of bacteria and viruses that cause airborne infections in humans cannot tolerate sunlight, oxidants or the temperature extremes that occur outdoors. In the 1960s, scientists at the Chemical Defence Establishment, at Porton Down, Wiltshire discovered that outside air was much more lethal to micro-organisms than indoor air. They used the term Open Air Factor (OAF) to describe the agent or agents in outdoor air that reduce the survival and infectivity of airborne pathogens, and their transmission by the airborne route.[199] Research continued into the 1970s, showing this ephemeral property of outdoor air had an adverse effect on viability and virulence of both

airborne viruses and bacteria. One of them was *Francisella tularensis* which is a potential bioterrorist agent.[200]

However, the natural disinfecting characteristics of outdoor air were then ignored for more than two decades.[26 Weber] One early research finding was the OAF disappeared rapidly in any form of enclosure. It was subsequently shown that experimental containers could be ventilated at rates that enabled the toxic properties of open air to be fully preserved.[201] So far there is no scientific evidence that maintaining high natural ventilation rates in buildings preserves OAFs and reduces the survivability of pathogens. This has not been investigated. But it seems reasonable to suggest designing to admit outdoor air at high rates may decrease microbial survival. Historical evidence supports this. The greatest of hospital reformers, Florence Nightingale, said the first rule of nursing was to keep air indoors as pure as that outside, without chilling the patient:

`Always air from the air without, and that, too, through those windows, through which the air comes freshest.' [34(p13)]

4.2.4 Open Windows

Natural ventilation has a number of advantages, including relatively low cost and low maintenance. However, the mere presence of doors and windows is no guarantee they will be opened to encourage air movement. And natural ventilation usually depends on climatic conditions being favourable for its use. Regarding infection, one advantage it has over mechanical ventilation is that air can enter a building by more than one route. With mechanical ventilation it comes in through an outdoor intake. As Florence Nightingale was keen to point out years ago, there is no guarantee that incoming air does not mix with contaminated air. Also, mechanical ventilation could be used to spread biological agents. Following the anthrax attacks of 2001, relocating air intakes to publicly inaccessible locations was recommended. Ideally, intakes on large buildings should be put on secure roofs or high sidewalls.[202]

A recent review of design strategies for infection prevention in US hospitals concluded that it was unlikely that natural ventilation would be used in future acute care facilities. First, the North American climate precluded its use, except in a few temperate regions. Second, natural ventilation compromised the integrity of the building envelope, allowing in unfiltered air with outdoor air contaminants such as fungal spores. A further obstacle to the use of natural ventilation was that it:

`...is not compatible with modern life safety and infection prevention principles.' [202(pS6)]

In British hospitals, staff and patients can only partially open windows because of safety concerns. So natural ventilation is not as easy to achieve as it used to be. A maximum opening of 100 mm is recommend for windows within reach of patients.[203] But the risk of unsupervised patients injuring themselves has to be weighed against hazards of cross-infection due to inadequate ventilation. Virulent pathogens have been less of a problem in modern hospitals than they were during the pre-antibiotic era. Ventilation rates have fallen. But they may need to increase significantly. In the days when hospital windows were left open, wards were often designed so that one nurse could see all the patients. So one solution to present day concerns about the safe use of widows would be to ensure patients are watched at all times. Alternatively, windows could be designed both for ventilation and

patient safety.

It is true that outdoor pathogens can come straight into hospital wards in through open windows. But a recent investigation found that the amount of potentially pathogenic bacteria was no higher in window-ventilated patient rooms than in mechanically ventilated rooms.[139] Significantly, the modern practice of designing buildings for human comfort rather than health could influence the ecology of indoor microbes. And not for the better. As the authors of this study noted:

`... reducing direct contact with the outdoor environment may not always be an optimal design strategy for bacterial pathogen management.' [139(p9)]

4.3 Natural Light and Disinfection

The idea that sunlit spaces are healthier than those in shadow and darkness is ancient. Scientific confirmation of this belief came in 1877, when Arthur Downes and Thomas Blunt reported to the Royal Society that sunlight inhibited the growth of bacteria in test tubes.[204] Their classical investigations showed sunlight has a bactericidal effect; even behind glass. This has been described as one of the most influential discoveries in all of photobiology.[205]

From 1877 to 1895, a series of studies showed sunlight could kill a range of bacteria. This research coincided with the discovery that bacteria could cause potentially fatal diseases such as typhus, typhoid fever, anthrax, cholera, diphtheria and tuberculosis. [2] In 1882, the German physicist and bacteriologist Robert Koch identified the tubercle bacillus, or *M.tuberculosis*.[206] By doing so, Koch disproved the widely held belief that tuberculosis was inherited and non-infectious.

In 1890, Koch gave an address at the International Medical Congress in Berlin where he announced sunlight was lethal to the tubercle bacillus. He stated that direct sunlight could kill the bacillus in a few minutes, or several hours, through glass. The time depended on the thickness of the layer of bacteria exposed. Also, ordinary diffuse daylight, such as is found near windows in houses, could kill the bacterium in five to seven days.[207] Even before Koch's discoveries it was recognised by many that transmission of the disease was less likely to occur in clean, well-lit, well-ventilated houses or hospitals; even in those for tuberculosis patients.[208]

In the years that followed Koch's observations, other scientists investigated the effects of natural light on the tubercle bacillus. In general, they supported Koch's findings. This early research showed direct sunlight was more bactericidal than had Koch proposed; but diffuse light was less effective in killing the bacillus in dust.[209] What is notable from the literature of the time is how few studies were made. According to one estimate, at the beginning of the 20th century, tuberculosis was killing one-seventh of the human race. Yet there was little research into the survival of the bacillus.[210] Four decades later, in 1942, the results of more tests appeared. They followed an investigation of the risk of tuberculosis infection among staff and patients at the Barlow Sanatorium, Los Angeles California. Patients at the sanatorium were treated according to the `open air' regimen. So they were exposed to the elements day and night. When daylight and sunlight entered their rooms it did so *`for the most part unfiltered by glass'*. It had only to pass through a wire screen. [211]

The rooms and immediate surroundings of patients were tested for viable tubercle bacilli.

Cultures were made from swabbings of bed-side tables, lamps, bed frames and other hand-touch sites. Cultures were also made from room dust and sweepings; and from cotton filters through which room air had been sucked. Without exception, all of the results were negative. So a series experiments then followed to see how effective diffuse daylight was at making tubercle bacilli non-viable and non-infectious. The results showed dried bacilli exposed in an unglazed north window died within four or five days; depending upon the mass of the dose. In a drawer in the same room they survived for two or three months, and in a refrigerator for over six months. The results also showed the bacillus survived longer in winter than in the spring and summer.[211]

There do not appear to be any further studies on the direct effects of daylight on the survivability of *M. tuberculosis.* Given the global upsurge in tuberculosis, fostered by the human immunodeficiency virus (HIV) pandemic, and new multidrug-resistant strains, this is surprising. The WHO does refer to sunlight in some of its guidance on preventing hospital infections. For infections transmitted by the airborne route, such as tuberculosis, one of their documents recommends patients should be placed in single rooms that ideally have sunlight, negative air pressure and 6-12 air changes per hour. However, the reasons for sunlight exposure are not made clear.[212] Other guidance on infection control in hospitals makes no reference to it. The WHO does recognise there is value in the germicidal effect of light in homes - but only in lavatories. And direct sunlight is not mentioned. Their guidance on healthy housing states natural lighting should be provided to water closets wherever possible because it kills bacteria. It also says special glass, which transmits a higher proportion of ultraviolet rays, should be used. Where it is not, and ordinary window glass is fitted, windows should be left open in warm weather for at least three hours. This is to allow shorter wavelength ultraviolet radiation to enter and help in bactericidal action.[100Ranson]

4.3.1 Daylight and Streptococci

In 1944, Dr. Lawrence Garrod published the results of the study in which he tried to determine how far dust was responsible for streptococcal cross-infection in surgical wards.[121] As noted earlier, he discovered there were no streptococci in many specimens of dust taken from sites on or close to the windows. He also found more streptococci in dust from dark wards than in comparable specimens from normally lit wards.

During the Second World War the ground floor windows of many British hospitals were protected against bomb-blast by by brick walls. So they were poorly daylit. The windows in the upper wards were unprotected. Of the samples Garrod took from ground floor wards, 72 per cent yielded haemolytic streptococci, whereas only 18 per cent of samples from the upper floors were positive. Close to unobstructed windows, even thick dust was consistently free from bacteria. Here was circumstantial evidence of the bactericidal activity of daylight through glass. But other factors may have influenced his findings, such as ventilation, and variations in the composition and degree of pollution of the dust. So Professor Garrod then carried out a series of experiments to find out why there was less bacteria in upper wards. He put dust samples and films of dried pus containing haemolytic streptococci under different lighting conditions. He found sunlight had the strongest bactericidal effect. Diffused light from a north window was capable of killing streptococci, even though filtered through two layers of glass. By contrast, streptococci in dust kept in the dark at room temperature survived for 195 days. So, in his view, given the right conditions infected dust could easily cause prolonged epidemics in hospitals; with long

intervals between fresh cases. The results of Professor Garrod's investigation were reported in the British Medical Journal in 1944. They were:

`...placed on record in order to draw attention to the possible importance of good natural illumination as a hygienic safeguard, and in the hope that they may lead to further study of this subject. Although good lighting is universally recognised as desirable, it has never, so far as I am aware, been insisted on as a prime necessity in wards for septic surgical cases. This study suggests that in such wards it has an important part to play, particularly if no special measures...are taken to prevent the atmospheric diffusion of dust... Preoccupation with the ultraviolet part of the spectrum has led to a common belief that only direct sunlight is usefully bactericidal; it must now be recognized that ordinary diffuse daylight, even on a cloudy day and even in winter in England, can be lethal to bacteria, and that glass is no absolute bar to this effect.' [121(p247)]

Dr. Garrod was already aware that between 1941 and 1942, Dr. Leon Buchbinder and a team of investigators at Columbia University in New York, had already assessed the lethal effect of sunlight and daylight on streptococci and made similar findings.[213-215] Dr. Buchbinder believed the spread of respiratory infections could not be explained by the contact theory alone; and the indoor environment might play a role in their dissemination. [215] So tests were carried out under conditions simulating natural room conditions. A technique was used to measure the lethality of daylight in which bacteria were sprayed into the air and allowed to settle on filter paper in open Petri dishes. They were then covered with their glass tops. The dishes were then exposed to daylight or sunlight coming through closed windows for a given length of time. At the end of each test, agar was poured into the dishes. They were then incubated and the colonies developed were counted. Death rates were compared with for the same organisms kept in the dark. The results showed that in the absence of light, streptococci could survive with practically undiminished virulence for long periods indoors. They also confirmed something that Downes and Blunt suspected in 1877 but had been unable to prove, that the blue portion of the visible spectrum is the most germicidal. [215]

These tests showed that the lethal power of diffuse light through glass was significant. Its capacity to kill bacteria varied with its spectral distribution and intensity. Light from blue skies was the most effective while that of very cloudy skies the least. Again, direct sunlight was much more lethal than daylight. The median survival time (or the time necessary for 50 per cent killing) of the alpha strain of haemolytic streptococci was about 5 minutes in the sun compared to more than an hour for diffuse daylight. The stronger the sunlight the more lethal it became. The potency of sunlight per unit of intensity to be less than that of diffuse daylight; probably because there is more blue light in skylight than sunlight. They also examined the bactericidal effect of artificial light, as emitted by tubular fluorescent lamps. They killed streptococci but were not felt to be of value as disinfecting agents because their low intensity.[213]

4.3.2 Daylight and Pneumococcus

The research team at Columbia University also examined the effects of daylight on *pneumococcus*. They found diffuse light was more rapidly lethal to this pathogen than to streptococcus. Nevertheless, they considered airborne transmission of the pneumococci a possibility.[214] Fifty years earlier, several workers had found that pneumococci in dried sputum exposed to diffuse daylight remained viable and retained their virulence for

extended periods of time. This was confirmed in the 1930s.[216] More recently, a study from the 1970s found pneumococci can survive for long periods in sputum.[217] Another, from 1905, showed putting dried sputum in sunlight results in the prompt death of the organism. This study included experiments in which a spray of the bacteria was exposed to sunlight while in suspension. This destroyed the bacteria within half an hour.[218] Again, there are no recent studies on the survival of *pneumococcus* to confirm or refute such findings. Nor do there appear to be any on the airborne transmission of this bacterium. Nevertheless, it is the major cause of bacterial pneumonia and meningitis worldwide.[219] And antimicrobial resistance among pneumococci has escalated dramatically over the past three decades.[220]

4.3.3 Daylight and Menginococcus

In 1944, researchers at the University of Chicago carried out research on the *meningococcus* bacterium. First they investigated how long it could survive and remain viable outside the human body. At the time, *meningococcus* was generally regarded as a sensitive organism unable to withstand drying. Their results showed otherwise.[221] Meningococci were much more resilient than generally supposed. Virulent organisms were recovered from the surfaces of glass, wood, and cotton cloth a week or more after drying and storing them in a dark cupboard at room temperature. The virulence of the surviving meningococci was tested on mice. These were then autopsied to confirm that their deaths resulted from meningococcus sepsis; indicating the meningococci were fully virulent. The conclusion drawn from these findings was that inanimate surfaces might be able to play a role in the spread of meningococcal meningitis. It seems this was usually overlooked when considering the epidemiology of the disease at this time.[221]

Having shown dried meningococci could remain viable in the dark, they then exposed them to different intensities of natural light. Direct sunlight, which had passed through an ordinary window pane, killed the micro-organisms within a few hours. Diffuse daylight from a north window passing through two layers of glass (an ordinary window pane and a pyrex Petri dish) also killed them; though not as rapidly. Meningococci dried in films on glass beads and cotton gauze died within 30 hours. The effect was slower on cotton towelling and on wood. During cloudy weather, when the sky was overcast throughout the day, the micro-organisms died off much more rapidly close to a window than they did a distance of 12 feet from it. Also, tests with coloured filters showed red light had little impact on the viability of dried meningococci. Blue light, by contrast, was highly bactericidal. The lethality of the light transmitted by other coloured filters of orange, green and yellow was proportional to the amount of blue light each filter transmitted.[222]

4.3.4 Daylight and Staphylococci

In the 1920s, manufacturers started producing glass that transmitted a greater proportion of ultraviolet radiation than an ordinary window pane. At the time, exposure to the sun's rays were thought to be highly beneficial. So getting a greater proportion of the solar spectrum into buildings was a logical development.[223] In 1930, the results of a series of experiments were published which indicated this new type of glass might reduce the risk of infection in buildings. Tests were undertaken to find out the bactericidal power of direct sunlight, of sunlight through plate glass, and sunlight through `Vitaglass'.[224] The latter was one of the brands then on the market.[223]

Two different types of experiment were undertaken. In the first, the various light effects

were tested on *S. aureus* and two other types of bacteria growing on agar plates. The plates were placed at the bottom of wooden boxes. Each one had a removable top which allowed the sun's rays to enter unimpeded, or which could be replaced by plate glass or Vitaglass. The boxes were then positioned so that sunlight fell perpendicularly into them, and onto the plates of bacteria inside them. Exposure times ranged from 30 minutes in good weather, to three hours in variable conditions. In one typical test, a box with Staphylococcus plates was put in the sun for fifty minutes. The original number of bacteria present was 900 per plate. At the end of the test an average of 300 colonies developed in the box with no glass fitted. There were 420 colonies with a Vitaglass lid; and 620 colonies in the box with plate glass fitted. Taking an average of all of the tests, nearly three-quarters of the bacteria were killed by unfiltered sunlight. About half of them died when the Vitaglass was used. And just over a quarter with ordinary plate glass.[224]

The results were similar for the second series of experiments, in which bacteria laden air was used in place of agar plates. The boxes were exposed to sunlight with one or other of the glass covers fitted. The boxes were then sealed, and equal amounts of air drawn out of them. These samples were then used to estimate the number of bacteria left in each box. These were clearly difficult experiments; and they have not been replicated. But the results, together with those of the agar plate tests, indicate the bacterial content of room air may be lessened by sunlight. And the use of glass which is more permeable to ultraviolet radiation than plate glass increases the bactericidal effect. The researchers interpreted their findings as follows:

`They suggest...that if a glass or window tax is ever again imposed, it should not be like that of 1695, which taxed windows as such, but rather a tax which discriminates in favor of glass which transmits ultraviolet rays.' [224(p1394)]

The results of further tests on staphylococci with sunlight were published in 1992.[225] Cultures of the bacterium were exposed to mid-to-late summer sunlight for 45 minutes, in the early afternoon, at the Australian National University in Canberra. Three types of filter were put over them: photocopier paper; window glass; and perspex of the same thickness as the glass. In these tests, the glass filter had only a small effect in decreasing the killing by sunlight. The effect of perspex was a more substantial reduction in killing. Complete shading, using photocopying paper, resulted in no bactericidal effect. The experiments showed the lethal effect of sunlight on staphylococci is due to radiation between 300-380 nm, with further effects apparent at shorter and longer wavelengths. They also showed that as well as killing exposed staphylococci, solar radiation is mutagenic. The authors observed that *S. aureus* is commonly exposed to unfiltered sunlight, as about a third of humans have it in their skin:

`Thus, such older remedies for S. aureus and other bacterial infections as exposure of patients and clothing and bedlinen to sunshine may have a sound basis in fact.' [225(p247)]

Subsequent tests at the same facility in Canberra showed unfiltered sunlight killed approximately 99 per cent of staphylococci cells within 70 minutes of exposure on a cloud-free spring or early summer day.[226] Filtering out part of the the UV-B component of sunlight (280-315 nm) with perspex slightly reduced this bactericidal effect. When all of the UV-B was filtered out, so that the cells were exposed to UV-A (315-400 nm) and visible radiation, they took longer to die. And when staphylococci were exposed to visible radiation alone,

there was no measurable killing effect on the bacteria.

So, both solar UV-A and UV-B radiation kill *S. aureus.* The tests showed the effects of UV-A on staphylococci are not as immediate as UV-B. But once the UV-A in sunlight becomes lethal, it kills at about the same rate as UV-B.[226] These results broadly support those from the study from 1930 which compared the relative bactericidal power of sunlight through plate glass, and sunlight through `Vitaglass'. Ordinary window glass absorbs solar radiation below 300 nm. So it lets in UV-A and a small amount of UV-B. Given time, this would be lethal to staphylococci and, potentially, many other pathogens. But the effects of sunlight through glass on bacteria, viruses and spores are not well-documented.

4.3.5 Disinfection with Artificial Light

The germicidal effects of artificial light have been investigated. One study already mentioned, from 1941, compared kill rates of streptococcus bacteria grown in glass Petri dishes exposed to skylight, direct sunlight, and a fluorescent lamp. This was identified as a `daylight' lamp. But there are no details of its spectral output.[213] A study from 1950, showed cool white fluorescent lights can have an inhibiting effect on the growth of *S. aureus*.[227] The germicidal action appears to be equal, per unit of illumination, to that of daylight. But, again, the intensity may be too low to have a useful effect.

Daylight, or `full-spectrum' fluorescents are supposed to more closely match the spectral distribution of natural light than conventional fluorescents. Full-spectrum lamps used in a more recent study, from 1970, were designed to mimic sun and sky radiation at a colour temperature of 5,500K. About 5 per cent of their total radiant power was at wavelengths between 290 and 380 nm.[228] Cultures of two species of bacteria *S. aureus* and *S. marcescens* were put under both full-spectrum and conventional cool white lamps for up to 8 hrs. Tests were carried out with the bacteria placed at 2ft 10 inches and 7ft 6 inches from the lamps. Exposing staphylococci to cool white lamps in standard fittings produced little bactericidal effect. But after eight hours of exposure to full-spectrum light, at high or low levels, there was an equivalent degree of killing of 90 per cent. Two hours of exposure produced minimal results. Four hours gave intermediate results. Neither of the light sources in this investigation, the full-spectrum or cool white, had any effect on the second species of bacteria, S. *marcescens*. It was argued this lack of killing effect may have been due to the photoreactivity of this bacterium.[228] In these experiments, the culture plates were uncovered. So the ultraviolet component of the full-spectrum lights would have been unfiltered.

4.4 Solar Radiation and Resistance to Infection

Years ago, getting direct sunlight into buildings was thought to be an important hygienic safeguard. Sunlight may prevent communicable diseases spreading in buildings directly, and indirectly. First, the solar radiation is the primary germicide in the environment.[229] It kills pathogens that cause respiratory and other infections. Second, direct sunlight may increase resistance to infection in those who receive it; even behind glass. The reasons for this improved immunity are not clear. Research suggests it may be due to the the intensity of sunlight, or the sun's infra-red rays, or both.

In recent years it has become accepted that there is a strong link between a person’s mental health and how well their immune system works. Positive emotions protect against death and disability.[230] Negative ones are harmful. Depression is a common and

potentially dangerous condition. It acts as a form of chronic stress; and this is associated with immune dysfunction.[231] Research indicates people suffering from depression are at increased risk of infection.[232] One explanation for this is the body's natural killer cells do not function as effectively in a major depression.[233] The link between infection and depression appears to have attracted little attention from medical researchers. One of the few studies on it reported women who undergo coronary artery bypass grafting are more likely to develop an infection if they have a major depression following surgery. Compared to non-depressed women, they have reduced immune function and more pneumonias and upper respiratory infections.[234] In another study, women with metastatic breast cancer who were depressed had an impaired immune responses to bacteria, fungi and yeasts.[235] So, it follows that alleviating the symptoms of depression might prevent or improve resistance to infection.

Bright-light therapy is an effective treatment for a range of psychiatric conditions; in particular, seasonal and major depression.[236] Also, seasonal and non-seasonal depression are influenced by environmental illumination.[237] Research in hospitals shows patients in sunlit wards recover better from depressive illness and other conditions. Sunlight has a positive effect on the length of stay, mortality rate, perceived stress and pain of hospital patients.[238-241] One explanation for this is the light levels needed to regulate the body’s circadian rhythms are much higher than those needed for visual tasks.[242] They need to be over 1000 lux to have a positive impact. Electric lighting provides somewhere between 50 and 400 lux. While adequate for vision, this is close to biological darkness for the body’s circadian system. In a sunlit room there can be as many as 60,000 lux falling on a plane surface.[243] This is more than enough to reset the body's internal clock.

Experiments with bright light - using light at levels above those normally found indoors - show it has benefits beyond relieving the symptoms of depression. During the winter months it seems to be effective at improving vitality and reducing distress.[244] It may also help with dementia. In one study, increasing light levels in the day-rooms of nursing homes to 1,000 lux slowed down the rate of cognitive decline in demented patients. It also improved their sleep patterns and depressive symptoms.[245] Without proper time-cues from the sun, or other sources, the underlying rhythm of the body can become disturbed. This can cause a range of health problems. Disruption of the body’s circadian rhythms has been linked to heart disease, diabetes, obesity, and breast and prostate cancer.[246,247]

As yet, there is no direct evidence that hospital patients are better able to resist infections if they are in sunlight. However, new evidence shows the immune system's ability to detect a pathogen is controlled by the circadian system. In February 2012 researchers from Yale University School of Medicine published the results of tests on mice in which they examined the function of Toll-like receptor 9 (TLR9). This is a gene in the immune system which detects the DNA of viruses and bacteria. They found that when TLR9 was at its most active, the mice responded better to infection. The severity of their infections correlated with daily variations in TLR9 expression and function.[248] These results give the first clear evidence of a direct molecular link between circadian rhythms and the immune system. Findings such as these suggest that if hospital patients biological rhythms are entrained, and they are not depressed, they may be better placed to resist infection.

4.4.1 Infra-red Radiation and Infection

There is growing recognition that the visible part of the solar spectrum has health benefits. Natural light is more effective at entraining the body's circadian rhythms than electric sources. It provides a higher light level at the eye. And it is more closely matched to the spectral sensitivity of the eye than most artificial light sources.[249] People prefer daylight as their main source of illumination.[250,251] And they prefer lighting levels which are significantly higher than current indoor lighting standards. These match the levels at which biological stimulation of the circadian system can occur. And building users prefer lighting that follows the daylight cycle instead of a constant level of illumination.[252]

Like the visible spectrum, the sun's infra-red radiation may also have a health impact on people indoors. Solar energy is widely recognised as an effective heat source for buildings. Passive solar design provides building occupants with radiant heat. This acts on the surface of the body, but can also stimulate deeper-lying tissues. The biological effects of radiant heating extend to the internal organs, the central nervous system and enzymatic processes.[253] Infra-red radiation has been shown to assist wound healing and relieve pain.[254-257] The health benefits have been recognised for centuries. Roman villas and baths had special glazed sun-rooms called a `heliocaminus', or solar furnace. This appears to have been a solar-heated sweat room, or sauna.[258] In Scandinavian countries, saunas have been popular for hundreds of years. There is published evidence of the health benefits of using them. They appear to be effective in treating congestive heart failure and in reducing blood pressure.[259-261] Infra-red may also protect against seasonal depression.

Although light treatment in the winter is effective for seasonal depression, it does not make patients feel as well as they do in summer. The mood improvement they experience with conventional light treatment is not as complete as the spontaneous remission that happens in summertime.[262] One explanation for this, which experiments support, is that seasonal variations in the infra-red component of solar radiation affect mood states. It seems infra-red, like the visible spectrum, could have an anti-depressant effect.[263,267] So this too could, in turn, could influence resistance to infection. Direct evidence of this in humans is lacking. But tests on animals suggest it may be significant. Infra-red has been shown to enhance the natural immune response of mice against skin infection with MRSA and improves the healing of wounds infected with MRSA.[268] And in humans it inactivates MRSA in the nose of carriers; as well as fungal and other pathogens.[269]

4.4.2 Sunlight Behind Glass

There is one study which suggests sunlight transmitted through ordinary window glass can directly influence the outcome of an infection. This was published in 1933.[270] At the time, the bone disease rickets was a major health problem. Rickets is not an infectious disease; but it increases susceptibility to infection. Rickets is caused by vitamin D deficiency and affects infants. The symptoms include bending of the limbs and spine, bad teeth, muscle weakness, growth failure, lethargy, tetany, and seizures. During the 1920s, scientists proved that rickets develops when children stay out of the sun; and that sunbathing cures it. They also became aware that ordinary window glass filters out the ultra-violet radiation that produces vitamin D. The study in question found exposing rachitic rats to sunlight transmitted by window glass raised their resistance to infection. But it did not improve their rickets.[270]

In these experiments, young albino rats were raised on a diet lacking vitamin D; and kept out of sunshine. Then at midday, for four weeks, one group of them was given a direct sun

bath under window glass. A second group of rachitic rats was exposed to fresh air instead of sunlight. All other conditions were the same. And a third group was kept indoors and shielded from daylight. At the end of four weeks, all the rats were given an oral dose of a strain of Salmonella enteritidis. This `rat typhoid' is highly pathogenic to young rats. They were then observed for a further four weeks. The level of resistance to the infection was estimated by the number of rats in each group who survived. Of those exposed to the sun under window glass, 57 per cent survived for four nweeks against 32 per cent kept inside. The rats given fresh air also survived in greater numbers than the group kept inside. Some 43 per cent were still alive after four weeks. The same tests were done on rats whose diet included vitamin D. With the vitamin D added, 75 per cent of those exposed under glass survived for four weeks, against 61 per cent kept inside.

Exposure to sunshine through window glass, and to fresh air, for a short period each day, seems to have markedly raised the resistance of rats to the enteritidis infection. The authors of the study noted the beneficial effect was apparent whether vitamin D was present or absent in the diet. So they deduced the increase in resistance was not due to any improvement in the rats' rickets. They concluded with the following:

`The vital radiations from the sun should not be limited to the narrow band in the short ultra-violet region, which is antirachitic. The foregoing results show definitely that rays longer than those that are necessary to prevent or cure rickets have a marked effect on the animal organism, as evidenced by a decided increase in resistance to infection.' [270(p95)]

So the sun's visible and infra-red rays may indeed improve immunity in people indoors. A great deal remains unknown on the subject. Until recently, the same was true of vitamin D. The belief was that vitamin D was narrow acting, and that its only value was in bone mineralization and skeletal development. We now know that vitamin D is involved in the functioning of the immune system. It regulates the expression genes throughout the body. These include cells in the immune system that attack and destroy viruses and bacteria. [271,272] But it seems the impact of sunlight through window glass on immunity has not been researched since the 1930s. Clearly, it would be unwise to draw too many conclusions from the results of one study. They do point to improved resistance to disease. And it is notable that at one time a sunroom was a standard feature of hospitals.[273] There were thought to be health benefits from being in the sun under glass. Today, there is renewed appreciation that critically ill patients could benefit from sunlight.[274] But hospital architects are now advised to minimise solar gains in their designs. Glare and overheating can be harmful. But keeping sunlight out of hospitals in this way may place patients at increased risk of infection, depression and other health problems. The same may be true of housing and other building types.

If sunlight is admitted into buildings to prevent airborne infections, this must be compatible with other design requirements, such as ventilation. To be effective they will need to work in tandem. However, the ventilation requirements for airborne infection control have yet to be determined. They could differ from those for comfort and general health. [275] Then again, they may not. The same may be true of sunlight and daylight. The amount needed to influence infection rates is uncertain. Examples of older hospitals and other building types designed both for comfort and health promotion might offer some useful insights.

5. Discussion

It is clear many common infections are acquired indoors. And indoor infections are a major global cause of sickness and mortality. However, the literature shows current knowledge of how diseases spread in buildings is poor. The relationship between ventilation and infection has been studied for more than a century. Yet there are still insufficient data to work out the minimum amount needed to prevent the spread of airborne contagion. Only a handful of ventilation studies are deemed scientifically rigorous.

Some infections are known to be transmitted by the airborne route. Tuberculosis is the most important of them. For others, such as influenza, airborne transmission is thought possible. The debate about the relative importance of the different modes of infection is ongoing. Meanwhile, a belief that most communicable respiratory infections are transmitted by means of large droplets over short distances, or through contact, predominates. The majority of infection probably is passed in this way. But most of the pathogens acquired indoors are able to use more than route to infect humans. This makes it hard to show an individual infection to be airborne. The current distinction between those that are spread by contact and those that are airborne appears to be arbitrary. When people cough, sneeze and talk they produce an aerosol of droplets and droplet nuclei. On this basis, all communicable respiratory diseases should be controlled on the basis that they are airborne, as should the viral infections that cause gastro-intestinal infections.

Although there has been a revival in interest in the airborne transmission of bacteria and viruses in recent years, little research work has been done on it. The drug-resistant bacterium MRSA is a leading cause of death and disability worldwide. There is evidence that MRSA is transmitted through the air. But, so far, not enough for hospitals to ventilate their general wards to prevent MRSA infections; nor those caused by any other pathogen. The epidemic of SARS in 2003 provided evidence that a potentially lethal virus could spread between distant locations via contaminated air. During the outbreak, room ventilation was a key determinant of airborne disease transmission. Based on this and other evidence, there is a convincing argument for increased air change rates to prevent airborne infection. Cross-ventilation via windows seems to be particularly effective. By contrast, poorly designed or maintained mechanical ventilation systems can increase disease transmission.

Scientific data on the effectiveness of cleaning in reducing infections in buildings are extremely limited; and even inconsistent. Common sense would suggest keeping hospital wards clean reduces the risk of cross- and reinfection. But the evidence base for cleaning as an infection control measure is lacking. In healthcare, more emphasis is now put on hand hygiene than environmental cleanliness. But to be effective, infection control requires a combined approach. It is notable that Florence Nightingale insisted on regular hand washing, scrupulous standards of cleanliness, and high ventilation rates to prevent infection. She also insisted on direct sunlight in sick-rooms. This, she believed, both purified the air and helped patients recover.

Now it has been known for more than a century that natural light and, in particular, direct sunlight has a strong germicidal effect in buildings. The hygienic value of good daylighting

has received little scientific interest since the early discoveries were made. The benefits have been neglected. The evidence may be fragmentary: but it is compelling. So are reports of the health benefits of sun exposure. Studies show sunlight can alleviate the symptoms of depression. In doing so it may, in turn, reduce the risk of infection. Sunlight also entrains the body's circadian system. New research suggests this may increase resistance to infection too. In addition, studies indicate ultra-violet radiation has anti-depressant and other biological effects that may increase immunity to contagious disease. This merits further investigation.

Throughout history, communicable respiratory and gastro-intestinal infections have taken an enormous toll on the human population. Against this background, it is surprising how little research has been directed at their mechanisms of transmission; especially those that prosper in buildings. Today we face the resurgence of old diseases in more virulent forms. And there is a consensus that new ones will increasingly threaten global public health. Years ago, hospitals and other buildings were designed to prevent infections spreading. High levels of natural ventilation and plenty of light were absolute requirements. Today they are not. Cleanliness used to be considered pivotal to infection control. There is less support for it now. But if we are entering a post-antibiotic era, and as more pathogens are passing from animals to humans, this needs to be reassessed. Faced with the threat of untreatable infections, whether from drug-resistant bacteria or new diseases, it would be wise to take a precautionary approach. More emphasis should now be placed on prevention. Standards of personal and environmental hygiene in hospitals must be higher than they have been. Healthcare and other buildings should be arranged to stop infections spreading. And it might be prudent to assume all new diseases, and some old ones, contaminate indoor air; especially during a pandemic.

6. Recommendations

The infection control measures examined in this report have been under-researched for decades. There is evidence that high levels of natural light, natural ventilation, and cleanliness can protect against indoor contagion. It seems they can neutralise the pathogens that cause disease. But in recent years there has been little appreciation of this from a public health perspective. A research programme should be put in place to confirm this and work out how best to design buildings to stop indoor infection. Given they are a major global cause of sickness and mortality, the level of investment should be significant. But it is worth noting there is already a wealth of information from previous generations of buildings on how to prevent infections spreading. This too should be investigated.

7. REFERENCES

1. Li Y, Leung GM, Tang JW, Yang X, Chao CY, et al. Role of ventilation in airborne transmission of infectious agents in the built environment - a multidisciplinary systematic review. Indoor Air 2007 Feb;17(1):2-18.

2. Hockberger PE. The discovery of the damaging effect of sunlight on bacteria. J Photochem Photobiol B 2000 Nov;58(2-3):185-91.

3. Pier GB. On the greatly exaggerated reports of the death of infectious diseases. Clin Infect Dis 2008 Oct 15;47(8):1113-4.

4. Gould IM. Controversies in infection: infection control or antibiotic stewardship to control healthcare-acquired infection? J Hosp Infect 2009;73:386-9.

5. Nightingale F. *Notes on Hospitals.* John W. London; Parker and Son, 1859.

6. Gould IM. Antibiotic resistance: the perfect storm. Int J Antimicrob Agents 2009;34:S2-S5.

7. Piddock LJ. The crisis of no new antibiotics - what is the way forward? Lancet Infect Dis 2011 Nov 17:1-5.

8. European Centre for Disease Prevention and Control. Annual Epidemiological Report on Communicable Diseases in Europe 2010. Stockholm: ECDC; 2010.

9. Chan M. Combat drug resistance: no action today means no cure tomorrow. Statement by WHO Director-General. World Health Day 6 April 2011. http://www.who.int/mediacentre/news/statements/2011/whd_20110407/en/index.html

10. Pratt R. Preparation for a post antibiotic era must start now. Nurs Times 2010 Sep 14-20;106(36):26.

11. Dancer SJ. The role of environmental cleaning in the control of hospital-acquired infection. J Hosp Infect. 2009 Dec;73(4):378-85.

12. Daszak P, Tabor GM, Kilpatrick AM, Epstein J, Plowright R. Conservation medicine and a new agenda for emerging diseases. Ann N Y Acad Sci. 2004 Oct;1026:1-11.

13. Woolhouse MEJ, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. Emerg Infect Dis 2005;11(12):1842-47.

14. Brilliant L. The Age of Pandemics. Wall Street Journal. May 2; 2009. http://online.wsj.com/article/SB124121965740478983.html [Accessed May 8, 2012]

15. Suk JE, Semenza JC. Future infectious disease threats to Europe. Am J Public Health

2011 Nov;101(11):2068-79.

16. Wallin A, Luksiene Z, Zagminas K, Surkiene G. Public health and bioterrorism: renewed threat of anthrax and smallpox. Medicina (Kaunas). 2007;43(4):278-84.

17. Utrup LJ, Frey AH. Fate of bioterrorism-relevant viruses and bacteria, including spores, aerosolized into an indoor air environment. Exp Biol Med 2004 Apr;229(4):345-50.

18. Fleck F. Conference warns of danger of re-emergence of smallpox as weapon of bioterror. Bull World Health Organ 2003;81(12):917-8.

19. Morowaska L. Droplet fate in indoor environments, or can we prevent the spread of infection? Indoor Air 2006;16: 335-47.

20. Langmuir AD. Epidemiology of airborne infection. Bacteriol Rev 1961 Sep;25:173-81.

21. Riley RL, O'Grady F. Airborne Infection: Transmission and Control. New York; Macmillan, 1961.

22. Weiss MM, Weiss PD, Weiss DE, Weiss JB. Disrupting the transmission of influenza a: face masks and ultraviolet light as control measures. Am J Public Health 2007 Apr;97 Suppl 1:S32-7.

23. Wells WF. On air-borne infection: study II. Droplets and droplet nuclei. Am J Hyg 1934;20:611-18.

24. Gralton J, Tovey E, McLaws ML, Rawlinson WD. The role of particle size in aerosolised pathogen transmission: a review. J Infect 2011 Jan;62(1):1-13.

25. Loosli CG. Dust and its control as a means of disinfection of air. Am J Public Health 1947;37(4):353-58.

26. Weber TP, Stilianakis NI. Inactivation of influenza A viruses in the environment and modes of transmission: a critical review. J Infect. 2008 Nov;57(5):361-73.

27. Tang JW, Li Y, Eames I, Chan PK, Ridgway GL. Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. J Hosp Infect 2006 Oct;64(2):100-14.

28. WHO. Practical Guidelines for Infection Control in Health Care Facilities. World Health Organization. SEARO Regional Publication No. 41 WPRO Regional Publication, India 2004.

29. Guidelines for Environmental Infection Control in Health-Care Facilities. U.S. Department of Health and Human Services Centers for Disease Control and Prevention (CDC). Atlanta; 2003.

30. Bovalius A, Roffey R. Aerobiology and spread of microbial diseases. Def Sci J 1987;l37(2):185-204.

31. Susser M, Susser E. Choosing a future for epidemiology: I. Eras and paradigms. Am J Public Health. 1996 May;86(5):668-73.

32. Perkins JE. Evaluation of methods to control air-borne infections. Am J Public Health Nations Health. 1945 September;35(9):891-97.

33. Flügge C. Die verreitung der Phthise durch staubtormiges sputum und durch beim husten verspritzte tropfchen. Z Hyg Infektionskr 1898;29:107-124.

34. Nightingale F. *Notes on Nursing; What it is and What it is Not.* New York; Dover Publications, 1969.

35. Chapin CV The Sources and Mode of Infection. New York; Wiley and Sons 1910.

36. Chapin CV. Contact infection. Public Health Pap Rep 1907;33(Pt 1):57-62.

37. Wells WF, Stone R. On air-borne infection. Study III. Viability of Droplet Nuclei Infection. Am J Epidemiol 1934;20(3): 619-27.

38. Williams REO. Intramural spread of bacteria and viruses in human populations. Ann Rev Microbiol 1960;14: 43-64:1960.

39. Perkins JE, Gilcreas FW, Hollaender A, et al. The present status of airborne infections. Am J Public Health. 1947 January; 37(1):13-22.

40. Riley RL, Mills CC, Nyka W, et al. Aerial dissemination of pulmonary tuberculosis: a two-year study of contagion in a tuberculosis ward: 1959. Am J Epidemiol 1959 Jul 1;142(1):3-14.

41. Riley RL, Mills CC, O'Grady F, Sultan LU, Wittestadt F, Shivipuri DN. Infectiousness of air from a tuberculosis ward-ultraviolet irradiation of infected air: comparative infectiousness of different patients. Am Rev Respir Dis 1962 Apr;85:511-25.

42. Mortimer EA Jr, Wolinsky E, Gonzaga AJ, et al. Role of airborne transmission in staphylococcal infections. Br Med J 1966;1:319-22.

43. Eickoff TC. Airborne disease: Including chemical and biological warfare. Am J Epidemiol 1996 Oct 15;144(8 Suppl):S39-46.

44. Beggs CB. The airborne transmission of infection in hospital buildings: fact or fiction? Ind Built Environ 2003;12(1-2):9-18.

45.Tang JW, Li Y. Transmission of influenza A in human beings. Lancet Infect Dis. 2007 Dec;7(12):758.

46. Tellier R. Aerosol transmission of influenza A virus: a review of new studies. J R Soc Interface 2009 Dec 6;6 Suppl 6:S783-90.

47. WHO. World Health Organization Influenza (Seasonal) Fact sheet N–211. Apr, 2009. [Accessed May 9, 2012]. Available from: http://www.who.int/mediacentre/factsheets/fs211/en/

48. Osterholm MT. Preparing for the next pandemic. N Engl J Med 2005 May 5;352(18):1839-42.

49. Gambotto A, Barratt-Boyes SM, de Jong MD, Neumann G, Kawaoka Y. Human infection with highly pathogenic H5N1 influenza virus. Lancet. 2008 Apr 26;371(9622):1464-75.

50. Aditama TY, Samaan G, Kusriastuti R, et al. Avian Influenza H5N1 Transmission in households, Indonesia. PLoS One. 2012;7(1):e29971.

51. Fouchier RAM, García-Sastre A, Kawaoka Y, Barclay WS, Bouvier NM et al. Pause on avian flu transmission research. Science 27 January 2012: 400-401.

52. Mortimer PP. Ridding London of smallpox: the aerial transmission debate and the evolution of a precautionary approach. Epidemiol Infect. 2008 Oct;136(10):1297-305.

53. Langmuir LD. Changing concepts of airborne infection of acute contagious diseases: a reconsideration of classic epidemiologic theories. Ann N Y Acad Sci 1980;353:35-44.

54. Wehrle PF, Posch J, Richter KH, Henderson DA. An airborne outbreak of smallpox in a German hospital and its significance with respect to other recent outbreaks in Europe. Bull World Health Organ. 1970;43(5):669-79.

55. Shooter RA. Report of the Investigation into the Cause of the 1978 Birmingham Smallpox Occurrence. London; H.M. Stationery Office. July 1980.

56. Zelicoff AP. An epidemiological analysis of the 1971 smallpox outbreak in Aralsk, Kazakhstan. Crit Rev Microbiol. 2003;29(2):97-108.

57. Roy CJ, Milton DK. Airborne transmission of communicable infection-the elusive pathway. N Engl J Med 2004 Apr 22;350(17):1710-12. check

58. Chen WQ, Ling WH, Lu CY, Hao YT, Lin ZN, Ling L, Huang J, Li G, Yan GM. Which preventive measures might protect health care workers from SARS? BMC Public Health 2009 Mar 13;9:81.

59. Yu IT, Li Y, Wong TW, Tam W, Chan AT, Lee JH, Leung DY, Ho T. Evidence of airborne transmission of the severe acute respiratory syndrome virus. N Engl J Med 2004 Apr 22;350(17):1731-9.

60. McKinney KR, Gong YY, Lewis TG. Environmental transmission of SARS at Amoy Gardens. J Environ Health. 2006 May;68(9):26-30.

61. Wong TW, Lee CK, Tam W, Lau JT, Yu TS, Liu SF, Chan PK, Li Y, Bresee JS, Sung JJ, Parashar UD, Outbreak Study Group: Cluster of SARS among medical students exposed

to single patient, Hong Kong. Emerg Infect Dis 2004;10:269-276.

62. Olsen SJ, Chang HL, Cheung TY, Tang AF, Fisk TL, Ooi SP, Kuo HW, Jiang DD, Chen KT, Lando J, Hsu KH, Chen TJ, Dowell SF. Transmission of the severe acute respiratory syndrome on aircraft. N Engl J Med 2003 Dec 18;349(25):2416-22.

63. Tong TR. Airborne severe acute respiratory syndrome coronavirus and its implications. J Infect Dis 2005 May 1;191(9):1401-2.

64. Walther BA, Ewald PW. Pathogen survival in the external environment and the evolution of virulence. Biol Rev Camb Philos Soc. 2004 Nov;79(4):849-69.

65. Barker J, Stevens D, Bloomfield SF. Spread and prevention of some common viral infections in community facilities and domestic homes. J Appl Microbiol. 2001 Jul;91(1):7-21.

66. Kimmel M, Braun M, Alscher DM. Should we recommend precautions during a hantavirus endemic? NDT Plus 2010;3(4): 424-26.

67. Clement J, Maes P, Ducoffre G, Loock FV, van Ranst M. Hantaviruses: underestimated respiratory viruses? Clin Infect Dis. 2008 Feb 1;46(3):477-9.

68. Mills JN, Corneli A, Young JC, Garrison LE, Khan AS, Ksiazek TG. Hantavirus pulmonary syndrome-United States: updated recommendations for risk reduction. Centers for Disease Control and Prevention. MMWR Recomm Rep. 2002 Jul 26;51(RR-9):1-12.

69. Cataldo MA, Taglietti F, Petrosillo N. Methicillin-resistant Staphylococcus aureus: a community health threat. Postgrad Med. 2010 Nov;122 (6):16-23.

70. Gordon RJ, Lowy FD. Pathogenesis of methicillin-resistant Staphylococcus aureus infection. Clin Infect Dis 2008 Jun 1;46 Suppl 5:S350-9.

71. Boyce JM, Pittet D. Guideline for hand hygiene in health care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the Hand Hygiene Task Force. Infect Control Hosp Epidemiol 2003; 23(Suppl):1e40.

72. Allegranzi B, Pittet D. Role of hand hygiene in healthcare-associated infection prevention. J Hosp Infect. 2009 Dec;73(4):305-15.

73. Williams REO. Epidemiology of airborne staphylococcal infection. Bacteriol Rev 1966;30:660-672.

74. Lidwell OM, Brock B, Shooter RA, Cooke EM, Thomas GE. Airborne infection in a fully air-conditioned hospital. IV. Airborne dispersal of Staphylococcus aureus and its nasal acquisition by patients. J Hyg (Lond). 1975 Dec;75(3):445-74.

75. Shiomori T, Miyamoto H, Makishima K, Yoshida M, Fujiyoshi T, Udaka T, Inaba T, Hiraki N. Evaluation of bedmaking-related airborne and surface methicillin-resistant Staphylococcus aureus contamination. J Hosp Infect. 2002 Jan;50(1):30-5.

76. Shiomori T, Miyamoto H, Makishima K. Significance of airborne transmission of methicillin-resistant Staphylococcus aureus in an otolaryngology-head and neck surgery unit. Arch Otolaryngol Head Neck Surg 2001;127:644-8.

77. Sherertz RJ, Reagan DR, Hampton KD, et al. A cloud adult: the Staphylococcus aureus-virus interaction revisited. Ann Intern Med 1996;124:539-47.

78. Dansby W, Purdue G, Hunt J, et al. Aerosolization of methicillin-resistant Staphylococcus aureus during an epidemic in a burn intensive care unit. J Burn Care Res. 2008 Mar-Apr;29(2):331-7.

79. Rutala WA, Katz EB, Sherertz RJ, Sarubbi FA Jr. Environmental study of a methicillin-resistant Staphylococcus aureus epidemic in a burn unit. J Clin Microbiol 1983 Sep;18(3):683-8.

80. Farrington M, Ling J, Ling T, French GL. Outbreaks of infection with methicillin-resistant Staphylococcus aureus on neonatal and burns units of a new hospital. Epidemiol Infect 1990 Oct;105(2):215-28.

81. Schulz J, Formosa L, Seedorf J and Hartung J. Measurement of culturable airborne staphylococci downwind from a naturally ventilated broiler house. Aerobiologia 2011;27(4):311-318.

82. Gandara Isolation of Staphylococcus aureus and antibiotic-resistant staphylococcus aureus from residential indoor bioaerosols. Environ Health Perspect 2006;114:1859–64.

83. Scott E, Duty S, Callahan M. A pilot study to isolate Staphylococcus aureus and methicillin-resistant S aureus from environmental surfaces in the home. Am J Infect Control 2008 Aug;36(6):458-60.

84. Uhlemann AC, Knox J, Miller M, Hafer C, Vasquez G, Ryan M, Vavagiakis P, Shi Q, Lowy FD. The environment as an unrecognized reservoir for community-associated methicillin resistant Staphylococcus aureus USA300: a case-control study. PLoS One. 2011;6(7):e22407.

85. Bernards AT, Frénay HM, Lim BT, Hendriks WD, Dijkshoorn L, van Boven CP. Methicillin-resistant Staphylococcus aureus and Acinetobacter baumannii: an unexpected difference in epidemiologic behavior. Am J Infect Control 1998 Dec;26(6):544-51.

86. Allen KD, Green HT. Hospital outbreak of multi-resistant Acinetobacter anitratus: an airborne mode of spread? J Hosp Infect 1987 Mar;9(2):110-9.

87. Snelling AM, Beggs CB, Kerr KG, Shepherd SJ. Spores of clostridium difficile in hospital air. Clin Infect Dis 2010 Nov 1;51(9):1104-5.

88. Roberts K, Smith CF, Snelling AM, Kerr KG, Banfield KR, Sleigh PA, Beggs CB. Aerial dissemination of Clostridium difficile spores. BMC Infect Dis 2008 Jan 24;8:7.

89. Best EL, Fawley WN, Parnell P, Wilcox MH. The potential for airborne dispersal of Clostridium difficile from symptomatic patients. Clin Infect Dis 2010 Jun 1;50(11):1450-7.

90. Widdowson MA, Monroe SS, Glass RI. Are noroviruses emerging? Emerging Infect Dis 2005;11:735-7.

91. Aziz AM. Managing outbreaks of norovirus in an NHS hospital. Br J Nurs. 2010 May 13-26;19(9):589-96.

92. Marshall JA, Bruggink LD. The dynamics of norovirus outbreak epidemics: recent insights. Int J Environ Res Public Health 2011 Apr;8(4):1141-9.

93. Greig JD, Lee MB. A review of nosocomial norovirus outbreaks: infection control interventions found effective. Epidemiol Infect. 2012 Jan 4:1-10.

94. Carter MJ. Enterically infecting viruses: pathogenicity, transmission and significance for food and waterborne infection. J Appl Microbiol. 2005;98(6):1354-80.

95. Rusin P, Orosz-Coughlin P, Gerba C. Reduction of faecal coliform, coliform and heterotrophic plate count bacteria in the household kitchen and bathroom by disinfection with hypochlorite cleaners. J Appl Microbiol 1998 Nov;85(5):819-28.

96. Cunney RJ, Costigan P, McNamara EB, et al. Investigation of an outbreak of gastroenteritis caused by Norwalk-like virus, using solid phase immune electron microscopy J Hosp Infect. 2000 Feb;44(2):113-8.

97. Donskey CJ. Preventing transmission of Clostridium difficile: is the answer blowing in the wind? Clin Infect Dis. 2010 Jun 1;50(11):1458-61.

98. Clark RP, de Calcina-Goff ML. Some aspects of the airborne transmission of infection. J R Soc Interface 2009; 6(suppl 6):S767-S782.

99. Best EL, Sandoe JA, Wilcox MH. Potential for aerosolization of Clostridium difficile after flushing toilets: the role of toilet lids in reducing environmental contamination risk. J Hosp Infect. 2012 Jan;80(1):1-5.

100. Ranson R. *Healthy Housing: A Practical Guide.* London; Spon Press and the World Health Organization Regional Office for Europe, 1991.

101. Anon. The Practitioner. 1898;(60)6:286.

102. Bryder L. *Below the Magic Mountain: a Social History of Tuberculosis in Twentieth Century Britain.* Oxford; Clarendon Press, 1988.

103. Bodington G. *An Essay on the Treatment and Cure of Pulmonary Consumption, On Principles N, Rational and Successful.* Longmans 1840. Reprinted London; The New Sydenham Society, 1901.

104. Fairchild AL, Oppenheimer GM. Public health nihilism vs pragmatism: history, politics,

and the control of tuberculosis. Am J Public Health 1998 Jul;88(7):1105-17.

105. Stein L. A study of respiratory tuberculosis in relation to housing conditions in Edinburgh: 1 - The pre-war period. Br J Soc Med 1950;4:143-169.

106. Krieger J, Higgins DL. Housing and health: time again for public health action. Am J Public Health 2002;92:758-768.

107. Jacobs DE, Kelly T, Sobolewski J. Linking public health, housing, and indoor environmental policy: successes and challenges at local and federal agencies in the United States. Environ Health Perspect 2007;115:976-982.

108. Loddenkemper R, Hauer B. Drug-resistant tuberculosis: a worldwide epidemic poses a new challenge. Dtsch Arztebl Int. 2010 Jan;107(1-2):10-9.

109. Kwan CK, Ernst JD. HIV and tuberculosis: a deadly human syndemic. Clin Microbiol Rev. 2011 Apr;24(2):351-76.

110. World Health Organization. WHO/IUATLD Global Project on Anti-Tuberculosis Drug Resistance Surveillance. WHO/HTM/TB/2008.394. World Health Organization, Geneva, 2008.

111. Wright A, Zignol M, Van Deun A, et al. Epidemiology of antituberculosis drug resistance 2002-07: an updated analysis of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance. Lancet. 2009 May 30;373(9678):1861-73.

112. Beggs CB, Noakes CJ, Sleigh PA et al. The transmission of tuberculosis in confined spaces: An analytical review of alternative epidemiological models. Int J Tuberc Lung Dis 2003;7:1015-26.

113. Cole EC, Cook CE. Characterization of infectious aerosols in health care facilities: an aid to effective engineering controls and preventive strategies. Am J Infect Control 1998 Aug;26(4):453-64.

114. Larcombe L, Orr P. Housing conditions that serve as risk factors for tuberculosis infection and disease. An Advisory Committee Statement (ACS). Can Commun Dis Rep. 2007 Oct 1;33(ACS-9):1-13.

115. Mendell MJ, Fisk WJ, Kreiss K, Levin H, Alexander D, et al. Improving the health of workers in indoor environments: priority research needs for a national occupational research agenda. Am J Public Health 2002;92:1430-40.

116. Anon. The dangers of dust. Br Med J 1941 Jun 28;1(4199):970-1.

117. Cruikshank R. Hospital infection: a historical review. Br Med Bull 1944;2(12): 272-276.

118. Cruickshank R. The bacterial infection of burns. J Path Bact 1935;41(2):367-69.

119. White E. On the possible transmission of hemolytic streptococci by dust. Lancet

1936;(1):941.

120. Wright J, Cruickshank R, Gunn W. Control of dust-borne Streptococcal infection in measles wards. Br Med J 1944 May 6;1:611-4.

121. Garrod LP. Garrod LP. Some observations on hospital dust with special reference to light as a hygienic safeguard. Brit Med J 1944 Feb 19th; 245-257.

122. Diekema DJ, Pfaller MA, Schmitz FJ, Smayevsky J, Bell J, Jones RN, Beach M; SENTRY Partcipants Group. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. Clin Infect Dis. 2001 May 15;32 Suppl 2:S114-32.

123.Davies R R, Noble WC. Dispersal of staphylococci on desquamated skin. Lancet 1963;1:1111.

124. Walter CW, Kundsin RB. The floor as a reservoir of hospital infections. Surg Gynecol Obstet 1960 Oct;111:412-22.

125. Rampling A, Wiseman S, Davis L, Hyett AP, Walbridge AN, Payne GC, Cornaby AJ. Evidence that hospital hygiene is important in the control of methicillin-resistant Staphylococcus aureus. J Hosp Infect. 2001 Oct;49(2):109-16.

126. Corcoran GD, Kirkwood EM. Revised guidelines for the control of methicillin-resistant Staphylococcus aureus infection in hospitals. Letter. Journal of Hospital Infection 1999;41:72-74.

127. Wagenvoort JH, Davies BI, Westermann EJ, Werink TJ, Toenbreker HM. MRSA from air-exhaust channels. Lancet 1993;341:840-1.

128. Kumari DN, Haji TC, Keer V, Hawkey PM, Duncanson V, Flower E. Ventilation grilles as a potential source of methicillin-resistant Staphylococcus aureus causing an outbreak in an orthopaedic ward at a district general hospital. J Hosp Infect 1998;39:127-33.

129. Cotterill S, Evans R, Fraise AP. An unusual source for an outbreak of methicillin-resistant Staphylococcus aureus. J Hosp Infect 1996;32:207-16.

130. Shimono N, Hayashi J, Matsumoto H, Miyake N, Uchida Y, Shimoda S, Furusyo N, Akashi K. Vigorous cleaning and adequate ventilation are necessary to control an outbreak in a neonatal intensive care unit. J Infect Chemother. 2011 Oct 26. [Epub ahead of print]

131. Haddock RL, Nocon FA. Infant salmonellosis and vacuum cleaners. J Trop Pediatr 1994 Feb;40(1):53-4.

132. Haysom IW, Sharp K. The survival and recovery of bacteria in vacuum cleaner dust. J R Soc Promot Health. 2003 Mar;123(1):39-45.

133. Knibbs LD, He C, Duchaine C, Morawska L. Vacuum cleaner emissions as a source of indoor exposure to airborne particles and bacteria. Environ Sci Technol. 2012 Jan 3;46(1):534-42. Epub 2011 Dec 7.

134. Atkinson J, Chartier Y, Pessoa-Silva CL, Jensen P, Li Y, Seto W-H, et al. (Eds.) *Natural Ventilation for Infection Control in Health-Care Settings*. Geneva; World Health Organization, 2009.

135.Sundell J, Levin H, Nazaroff WW, Cain WS, Fisk WJ, Grimsrud DT, Gyntelberg F, Li Y, Persily AK, Pickering AC, Samet JM, Spengler JD, Taylor ST, Weschler CJ. Ventilation rates and health: multidisciplinary review of the scientific literature. Indoor Air 2011 Jun;21(3):191-204.

136. Brundage JF, Scott RM, Lednar WM, Smith DW, Miller RN. Building-associated risk of febrile acute respiratory diseases in Army trainees. JAMA 1988 Apr 8;259(14):2108-12.

137. Hoge CW, Reichler MR, Dominguez EA, et al. An epidemic of pneumococcal disease in an overcrowded, inadequately ventilated jail. N Engl J Med. 1994 Sep 8;331(10):643-8.

138. Menzies D, Fanning A, Yuan L, FitzGerald JM. Hospital ventilation and risk for tuberculous infection in canadian health care workers. Canadian Collaborative Group in Nosocomial Transmission of TB. Ann Intern Med 2000 Nov 21;133(10):779-89.

139. Kembel SW, Jones E, Kline J, Northcutt D, Stenson J, Womack AM, Bohannan BJ, Brown GZ, Green JL. Architectural design influences the diversity and structure of the built environment microbiome. ISME J 2012;2;1-11. doi: 10.1038/ismej.2011.211. [Epub ahead of print]

140. Simon J. *Sixth Report of the Medical Officer of the Privy Council.* House of Commons Parliamentary Papers. London; HMSO 1864.

141. Smylie HG, Davidson AI, Macdonald A, Smith G. Ward design in relation to postoperative wound infection. I. Br Med J 1971 Jan 9;1(5740):67-72.

142. Anon. Tomorrow's Healthcare Environments - Towards A Sustainable Future. 8758:0.7: England. Norwich; The Stationary Office 2011.

143. Beggs CB, Kerr KG, Noakes CJ, Hathway EA, Sleigh PA. The ventilation of multiple-bed hospital wards: review and analysis. Am J Infect Control 2008 May;36(4):250-9.

144. Roberts K, Hathwaya A, Fletcher LA, Beggs CB, Elliott MW, Sleigh PA. Bioaerosol production on a respiratory ward. Indoor Built Environ 2006;15;1:35-40.

145. Catanzaro A. Nosocomial tuberculosis. Am Rev Respir Dis. 1982 May;125(5):559-62.

146. Pearson ML, Jereb JA, Frieden TR, Crawford JT, Davis BJ, Dooley SW, Jarvis WR. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. A risk to patients and health care workers. Ann Intern Med 1992 Aug 1;117(3):191-6.

147. Ehrenkranz NJ, Kicklighter JL. Tuberculosis outbreak in a general hospital: evidence for airborne spread of infection. Ann Intern Med. 1972 Sep;77(3):377-82.

148. Pearson ML, Jereb JA, Frieden TR, Crawford JT, Davis BJ, et al. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. A risk to patients and health care workers. Ann Intern Med. 1992;117:191-6.

149. Beck-Sagué C, Dooley SW, Hutton MD, Otten J, et al. Hospital outbreak of multidrug-resistant Mycobacterium tuberculosis infections. Factors in transmission to staff and HIV-infected patients. JAMA. 1992 Sep 9;268(10):1280-6.

150. Hubad B, Lapanje A. Inadequate hospital ventilation system increases the risk of nosocomial Mycobacterium tuberculosis. J Hosp Infect. 2012 Jan;80(1):88-91.

151. Lutz BD, Jin J, Rinaldi MG, Wickes BL, Huycke MM. Outbreak of invasive Aspergillus infection in surgical patients, associated with a contaminated air-handling system. Clin Infect Dis. 2003 Sep 15;37(6):786-93.

152. McDonald LC, Walker M, Carson L, Arduino M, Aguero SM, Gomez P, McNeil P, Jarvis WR. Outbreak of Acinetobacter spp. bloodstream infections in a nursery associated with contaminated aerosols and air conditioners. Pediatr Infect Dis J. 1998 Aug;17(8):716-22.

153. Uduman SA, Farrukh AS, Nath KN, Zuhair MY, Ifrah A, Khawla AD, Sunita P. An outbreak of Serratia marcescens infection in a special-care baby unit of a community hospital in United Arab Emirates: the importance of the air conditioner duct as a nosocomial reservoir. J Hosp Infect 2002 Nov;52(3):175-80.

154. deSilva MI, Rissing JP. Postoperative wound infections following cardiac surgery: significance of contaminated cases performed in the preceding 48 hours. Infect Control 1984 Aug;5(8):371-7.

155. Balvers J, Bogers R, Jongeneel R, van Kamp I, Boerstra A, van Dijken F. Mechanical ventilation in recently built Dutch homes: technical shortcomings, possibilities for improvement, perceived indoor environment and health effects. Arch Sci Rev 2012;55(1)4-14.

156. Rintala H, Pitkäranta M, Toivola M, Paulin L, Nevalainen A. Diversity and seasonal dynamics of bacterial community in indoor environment. BMC Microbiol. 2008 Apr 8;8:56. Little known bacteria indoors.

157. Brasche S, Bischof W. Daily time spent indoors in German homes-baseline data for the assessment of indoor exposure of German occupants. Int J Hyg Environ Health 2005;208:247-253.

158. Leech JA, Nelson WC, Burnett RT, Aaron S, Raizenne ME. It's about time: a comparison of Canadian and American time-activity patterns. J Expo Anal Environ Epidemiol 2002;12:427-432.

159. EPA. Report to Congress on Indoor Air Quality, Volume II: Assessment and Control of Indoor Air Pollution. Publication number EPA 400-1-89-001C. U.S. Washington, DC. Environmental Protection Agency; 1989. pp. i, 4-14.

160. Sundell J. On the history of indoor air quality and health. Indoor Air. 2004;14 (Suppl 7):51-58.

161. Hota, B. Contamination, disinfection, and cross-colonization: are hospital surfaces reservoirs for nosocomial infection? Clin Infect Dis 2004; 39:1182–9.

162. Dancer SJ. Mopping up hospital infection. J Hosp Infect 1999 Oct;43(2):85-100.

163. Dancer SJ. Hospital cleaning in the 21st century. Eur J Clin Microbiol Infect Dis 2011;30:1473e1481.

164. Bloemendaal AL, Fluit AC, Jansen WM, Vriens MR, Ferry T, et al. Acquisition and cross-transmission of Staphylococcus aureus in European intensive care units. Infect Control Hosp Epidemiol. 2009 Feb;30(2):117-24.

165. Beggs CB, Shepherd SJ, Kerr KG. Increasing the frequency of hand washing by healthcare workers does not lead to commensurate reductions in staphylococcal infection in a hospital ward. BMC Infect Dis 2008 Sep 2;8:114.

166. Dancer SJ. Control of transmission of infection in hospitals requires more than clean hands. Infect Control Hosp Epidemiol 2010;31:958-960.

167. Boyce JM, Potter Bynoe G, Chenevert C, King T. Environmental contamination due to methicillin-resistant Staphylococcus aureus: possible infection control implications. Infect Control Hosp Epidemiol 1997;18:622-627.

168. Creamer E, Dorrian S, Dolan A, et al. When are the hands of healthcare workers positive for meticillin-resistant Staphylococcus aureus? J Hosp Infect 2010;75:107-111.

169. Sexton T, Clarke P, O'Neill E, Dillane T, Humphreys H. Environmental reservoirs of methicillin-resistant Staphylococcus aureus in isolation rooms: correlation with patient isolates and implications for hospital hygiene.J Hosp Infect. 2006 Feb;62(2):187-94.

170. Hayden MK, Bonten MJM, Blom DW, et al. Reduction in acquisition of vancomycin-resistant enterococcus after enforcement of routine environmental cleaning measures. Clin Infect Dis 2006;42:1552-60.

171. Huang SS, Datta R, Platt R. Risk of acquiring antibiotic resistant bacteria from prior room occupants. Arch Intern Med 2006;(166):1945-51.

172. Drees M, Snydman DR, Schmid CH, Barefoot L, Hansjosten K, Vue PM, Cronin M, Nasraway SA, Golan Y. Prior environmental contamination increases the risk of acquisition of vancomycin-resistant enterococci. Clin Infect Dis. 2008 Mar 1;46(5):678-85.

173. Datta R, Platt R, Yokoe DS, Huang SS. Environmental cleaning intervention and risk

of acquiring multidrug-resistant organisms from prior room occupants. Arch Intern Med. 2011 Mar 28;171(6):491-4.

174. Chemaly RF, Ghantoji SS, Stibich M. Novel intervention for eliminating VRE from the environment. Arch Intern Med. 2011 Oct 10;171(18):1684-5.

175. Ellis FP. Victuals and ventilation and the health and efficiency of seamen. Br J Ind Med 1948 Oct;5(4):185-97.

176. Mosley S. Fresh air and foul: the role of the open fireplace in ventilating the British home, 1837-1910. Planning Perspect 2003;18(1):1-21.

177. Macey FW. Specifications in detail. 3rd ed. London; Crosby Lockwood and Son, 1905.

178. Watt J. The ventilation, heating and lighting of hospital wards. Proc Roy Soc Med 1933;26(11):1411-1426.

179. Mendell M, Fine L. Building ventilation and symptoms - where do we go from here? Am J Publ Health 1994;84(3):346-48.

180. Fraser DW, Tsai TR, Orenstein W, Parkin WE, Beecham HJ, Sharrar RG, Harris J, Mallison GF, Martin SM, McDade JE, Shepard CC, Brachman PS. Legionnaires' disease: description of an epidemic of pneumonia. N Engl J Med. 1977 Dec 1;297(22):1189-97.

181. Menzies D, Bourbeau J. Building-related illnesses: current concepts. N Engl J Med 1997;337:1524-33.

182. Kamholz SL. Resurgence of tuberculosis: the perspective a dozen years later. J Assoc Acad Minor Phys 1996;7(3):83-6.

183. Knibbs LD, Morawska L, Bell SC, Grzybowski P. Room ventilation and the risk of airborne infection transmission in 3 health care settings within a large teaching hospital. Am J Infect Control. 2011 Dec;39(10):866-72.

184. Monto AS. Epidemiology of viral respiratory infections. Am J Med 2002 Apr 22;112 Suppl 6A:4S-12S.

185. Samet JM. How do we catch colds? Am J Respir Crit Care Med. 2004 Jun 1;169(11):1175-6.

186. Jaakkola JJ, Heinonen OP. Shared office space and the risk of the common cold. Eur J Epidemiol 1995 Apr;11(2):213-6.

187. Myatt TA, Johnston SL, Zuo Z, Wand M, Kebadze T, Rudnick S, Milton DK. Detection of airborne rhinovirus and its relation to outdoor air supply in office environments. Am J Respir Crit Care Med 2004;169: 1187-190.

188. Sun Y, Wang Z, Zhang Y, Sundell J. In China, students in crowded dormitories with a low ventilation rate have more common colds: evidence for airborne transmission. PLoS One. 2011;6(11):e27140.

189. Escombe AR, Oeser CC, Gilman RH, Navincopa M, Ticona E, et al. Natural ventilation for the prevention of airborne contagion. PLoS Med 2007;4(2): e68.

190. Qian H, Li Y, Seto WH, Ching P, Ching WH, Sun HQ. Natural ventilation for reducing airborne infection in hospitals. Build Environment 2010;45(3)559-65.

191. Jiamjarasrangsi W, Bualert S, Chongthaleong A, Chaindamporn S, Udomsantisuk N, Euasamarnjit W. Inadequate ventilation for nosocomial tuberculosis prevention in public hospitals in Central Thailand. Int J Tuberc Lung Dis 2009;13:454-59.

192. Jiang Y, Zhao B, Li X, Yang X, Zhang Z, Zhang Y. Investigating a safe ventilation rate for the prevention of indoor SARS transmission: An attempt based on simulation approach. Building Simulation 2009;2:281-289.

193. Jiang S, Huang L, Chen X, Wang J, Wu W, Yin S, Chen W, Zhan J, Yan L, Ma L, Li J, Huang Z. Ventilation of wards and nosocomial outbreak of severe acute respiratory syndrome among healthcare workers. Chin Med J 2003 Sep;116(9):1293-97.

194. Crosby AW. *America's Forgotten Pandemic: The Influenza of 1918*. 2nd ed. Cambridge, England; Cambridge University Press, 2003.

195. Anon. Influenza at the Camp Brooks Open Air Hospital. JAMA 1918;71:1746-47.

196. Brooks WA. The open air treatment of influenza. Am J Public Health 1918;8:746-750.

197. Richards AL, Hyams KC, Watts DM, Rozmajzl PJ, Woody JN, Merrell BR. Respiratory disease among military personnel in Saudi Arabia during Operation Desert Shield. Am J Public Health 1993 Sep;83(9):1326-29.

198. Anon. The Control of Cross Infection in Hospitals. Medical Research Council War Memorandum No.11. London; HMSO 1944.

199. Cox, C.S. The open air factor. In The Aerobiological Pathway of Microorganisms. Chichester; John Wiley 1987. pp. 218-229.

200. Hood AM. The effect of open-air factors on the virulence and viability of airborne Francisella tularensis. Epidemiol Infect. 2009 Jun;137(6):753-61.

201. Hood AM. Open-air factors in enclosed systems. J Hyg 1974;(72) 53-60.

202. National Institute for Occupational Safety and Health. *Guidance for Protecting Building Environments from Airborne Chemical, Biological, or Radiological Attacks.* Cincinnati; Department of Health and Human Services Centers for Disease Control and Prevention National Institute for Occupational Safety and Health, May 2002.

203. NHS Estates. Health Technical Memorandum No 55. Windows. 2nd edition. NHS Estates. London; 1998.

204. Downes A, Blunt TP. Researches on the effect of light upon bacteria and other organisms. Proc Roy Soc 1877;26:488-500.

205. Hockberger PE. A history of ultraviolet photobiology for humans, animals and microorganisms. Photochem Photobiol 2002;76(6):561-579.

206. Sakula A. Robert Koch: centenary of the discovery of the tubercle bacillus, 1882. Thorax. 1982 Apr;37(4):246-51.

207. Solly SE. A Handbook of Medical Climatology. Philadelphia and New York; Lea Brothers & Co.1897.

208. Ransome A, Delepine S. On the influence of certain natural agents on the virulence of the tubercle-bacillus. Proc Roy Soc London 1894 May 24; 51-56.

209. Rogers JB. Studies on the viability of the tubercle bacillus. Am J Public Health 1920 Apr;10(4):345-7.

210. Weinzirl J. The action of sunlight upon bacteria with special reference to B. tuberculosis. Public Health Pap Rep 1906;32(Pt 2):128-53.

211. Smith CR. Survival of tubercle bacilli. Am Rev Tuberc 1942 March;45(3):334.

212. *WHO Guidelines on Prevention and Control of Hospital Associated Infections.* World Health Organization Regional Office for South-East Asia. New Delhi; January 2002.

213. Buchbinder L, Solowey M, Phelps EB. Studies on microorganisms in simulated room Environments III. The survival rates in streptococci in the presence of natural daylight, sunlight and artificial illumination. J Bacteriol 1941;42(3):353-366.

214. Solowey M, Solotorovsky M, Buchbinder L. Studies on microorganisms in simulated room environments VII. Further observations on the survival rates of streptococci and pneumococci in daylight and Darkness. J Bacteriol 1942;42(5):545-555.

215. Buchbinder L. The bactericidal effects of daylight and sunlight on chained gram positive cocci in simulated room environment: theoretical and practical considerations. In Aerobiology, (ed. FR Moulton), Amer Assoc Adv Sci. Washington, Smithsonian Institute 1942, p267-270.

216. Stillman EG. Viability of pneumococci in dried sputum. J Infect Diseases 1938;63:340-345.

217. Williams SG, Kauffman CA. Survival of streptococcus pneumoniae in sputum from patients with pneumonia. J Clin Microb 1978 Jan;7(1):3-5.

218. Wood FC. The viability of the pneumococcus after drying: A study of one of the

factors in pneumonic infection. J Exp Med. 1905 Aug 25;7(5):592-625.

219. Yu VL, Chiou CC, Feldman C, Ortqvist A, Rello J, et al. International Pneumococcal Study Group. An international prospective study of pneumococcal bacteremia: correlation with in vitro resistance, antibiotics administered, and clinical outcome. Clin Infect Dis. 2003 Jul 15;37(2):230-7.

220. Lynch JP 3rd, Zhanel GG. Streptococcus pneumoniae: epidemiology and risk factors, evolution of antimicrobial resistance, and impact of vaccines. Curr Opin Pulm Med. 2010 May;16(3):217-25.

221. Miller CP, Schad D. The resistance of meningococci to drying. J Bacteriol 1944 Jan;47(1):71-7.

222. Miller CP, Schad D. Germicidal action of daylight on meningococci in the dried state. J Bacteriol 1944 Jan;47(1):79-84.

223. Beckett HE. *Ultra-Violet Window Glazing*. Building Research Bulletin No. 8. Department of Science and Industrial Research. London; HMSO 1930.

224. Broadhurst J, Hausmann TW. Bacterial destruction through glass. Am J Nurs 1930 Nov;30:1391-94.

225. Chapple RM, Inglis B, Stewart PR. Lethal and mutational effects of solar and UV radiation on Staphylococcus aureus. Arch Microbiol 1992;157(3):242-8.

226. el-Adhami W, Daly S, Stewart PR. Biochemical studies on the lethal effects of solar and artificial ultraviolet radiation on Staphylococcus aureus. Arch Microbiol 1994;161(1):82-7.

227. Lidwell OM, Lowbury EJ. The survival of bacteria in dust: III. The effect of light on the survival of bacteria in dust. J Hyg (Lond) 1950 Mar;48(1):28-37.

228. Himmelfarb P, Scott A, Thayer PS. Bactericidal activity of a broad-spectrum illumination source. Appl Microbiol 1970 Jun;19(6):1013-4.

229.Lytle CD, Sagripanti JL. Predicted inactivation of viruses of relevance to biodefense by solar radiation. J Virol 2005 Nov;79(22):14244-52.

230. Young SN. How to increase serotonin in the human brain without drugs. J Psychiatry Neurosci 2007;32(6):394-399.

231. Maes M, Kubera M, Obuchowiczwa E, Goehler L, Brzeszcz J. Depression's multiple comorbidities explained by (neuro)inflammatory and oxidative & nitrosative stress pathways. Neuro Endocrinol Lett. 2011;32(1):7-24.

232. Falagas ME, Karamanidou C, Kastoris AC, Karlis G, Rafailidis PI. Psychosocial factors and susceptibility to or outcome of acute respiratory tract infections. Int J Tuberc Lung Dis 2010 Feb;14(2):141-8.

233. Maddock C, Pariante C. How does stress affect you? An overview of stress, immunity, depression and disease. Epidemiol Psychiatr Soc 2001;10:153-62.

234. Doering LV, Martínez-Maza O, Vredevoe DL, Cowan MJ. Relation of depression, natural killer cell function, and infections after coronary artery bypass in women. Eur J Cardiovasc Nurs. 2008 Mar;7(1):52-8.

235. Giese-Davis J, Collie K, Rancourt KM, Neri E, Kraemer HC, Spiegel D. Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: a secondary analysis. J Clin Oncol. 2011 Feb 1;29(4):413-20.

236.Pail G, Huf W, Pjrek E, Winkler D, Willeit M, Praschak-Rieder N, Kasper S. Bright-light therapy in the treatment of mood disorders. Neuropsychobiology. 2011;64(3):152-62.

237. Kent ST, McClure LA, Crosson WL, et al. Effect of sunlight exposure on cognitive function among depressed and non-depressed participants: a REGARDS cross-sectional study. Environ Health 2009 Jul 28;8:34.

238. Beauchemin KM, Hayes P. Dying in the dark: sunshine, gender, and outcomes in Myocardial Infarction. J Roy Soc Med 1998;91:352-354.

239. Beauchemin KM, Hayes P. Sunny rooms expedite recovery from severe and refractory depressions. J Affect Disorders 1996;40:49-51.

240. Benedetti F et al. Morning sunlight reduces length of hospitalization in bipolar depression. J Affect Disorders 2001;62:221-223.

241. Walch JM, Rabin BR, Day R et al. The effect of sunlight on postoperative analgesic medication use: a prospective study of patients undergoing spinal surgery. Psychosomatic Med 2005;67:156-163.

242. Rea MS. Light – much more than vision? *Light and Human Health: EPRI/LRO 5th International Lighting Research Symposium*. Palo Alto, CA: The Lighting Research Office of the Electric Power Research Institute; 2002. pp1-15.

243. Burberry P. *Environment and Services.* Third Edition. London; Batsford 1977.

244. Partonen T, Lönnqvist, J. Bright light improves vitality and alleviates distress in healthy people. J Affect Dis. 2000;57(1-3):55-61.

245. Riemersma-van der Lek RF, Swaab DF, Twisk J, Hol EM, Hoogendijk WJ, Van Someren EJ. Effect of bright light and melatonin on cognitive and noncognitive function in elderly residents of group care facilities: a randomized controlled trial. JAMA. 2008 Jun 11;299 (22):2642-55.

246. Stevens RG, Rea MS. Light in the built environment: potential role of circadian disruption in endocrine disruption and breast cancer. Cancer Causes Control 2001;12(3):279-287.

247. Stevens RG, Blask DE, Brainard GC, et al. Meeting report: the role of environmental lighting and circadian disruption in cancer and other diseases. Environ Health Perspect 2007;115(9):1357-1362.

248. Silver AC, Arjona A, Walker WE, Fikrig E. The circadian clock controls toll-like receptor 9-mediated innate and adaptive immunity. Immunity 2012 Feb 24;36:251-61.

249. Boyce P, Hunter C, Howlett O. *The Benefits of Daylight Through Windows.* Troy, New York; Rensselaer Polytechnic Institute 2003.

250. Heerwagen JH, Heerwagen DR. Lighting and psychological comfort. Light Design Appl 1986;16(4):47-51.

251. Veitch JA, Hine DW, Gifford R. End-users' knowledge, beliefs, and preferences for lighting. J Interior Design 1993;19(2):15-26.

252. Begemann SHA, van den Beld GJ, Tenner AD. Daylight, artificial light and people in an office environment: overview of visual and biological responses. Int J Indust Ergonomics 1997;20(3):231-239.

253. Goromosov MS. *The Physiological Basis of Health Standards for Dwellings.* Public Health Papers, No. 33. Geneva; World Health Organization, 1968.

254. Danno K, Mori N, Toda K, Kobayashi T, Utani A. Near-infrared irradiation stimulates cutaneous wound repair: laboratory experiments on possible mechanisms. Photodermatol Photoimmunol Photomed 2001 Dec;17(6):261-5.

255. Lewith, G.T. and Machin, D. A randomised trial to evaluate the effect of infra-red stimulation of local trigger points, versus placebo, on the pain caused by cervical osteoarthrosis. Acupunct Electrother Res 1981;6:277-284.

256. Yokoyama, K. and Sugiyama, K. Temporomandibular joint pain analgesia by linearly polarized nearinfrared irradiation. Clin J Pain 2001;17:47-51.

257. Lee CH, Roh JW, Lim CY, Hong JH, Lee JK, Min EG. A multicenter, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of a far infrared-emitting sericite belt in patients with primary dysmenorrhea. Complement Ther Med. 2011 Aug;19(4):187-93.

258. Butti K, Perlin JK. *A Golden Thread - 2500 Years of Solar Architecture and Technology.* London, Marion Boyars 1980.

259. Crinnion WJ. Sauna as a valuable clinical tool for cardiovascular, autoimmune, toxicant- induced and other chronic health problems. Altern Med Rev. 2011 Sep;16(3):215-25.

260. Mussivand T, Alshaer H, Haddad H, Beanlands DS, Beanlands R, Chan KL, Higginson L, Leenen F, Ruddy TD, Mesana T, Silver MA. Thermal therapy: a viable adjunct

in the treatment of heart failure? Congest Heart Fail 2008 Jul-Aug;14(4):180-6.

261. Beever R. Far-infrared saunas for treatment of cardiovascular risk factors: summary of published evidence. Can Fam Physician 2009 Jul;55(7):691-6.

262. Postolache TT, Hardin TA, Myers FS, et al. Greater improvement in summer than with light treatment in winter in patients with seasonal affective disorder. Am J Psychiatry 1998;155: 1614-6.

263. Meesters Y, Beersma DG, Bouhuys AL, van den Hoofdakker RH. Prophylactic treatment of seasonal affective disorder (SAD) by using light visors: bright white or infrared light? Biol Psychiatry 1999 Jul 15;46(2):239-46.

264. Masuda A, Nakazato M, Kihara T, Minagoe S, Tei C. Repeated thermal therapy diminishes appetite loss and subjective complaints in mildly depressed patients. Psychosom Med 2005 Jul-Aug;67(4):643-7.

265. Chang Y, Liu YP, Liu CF. The effect on serotonin and MDA levels in depressed patients with insomnia when far-infrared rays are applied to acupoints. Am J Chin Med 2009;37(5):837-42.

266. Tsai JF, Hsiao S, Wang SY. Infrared irradiation has potential antidepressant effect. Prog Neuropsychopharmacol Biol Psychiatry 2007 Oct 1;31(7):1397-400.

267. Tsai JF. Potential antidepressant effect of infrared irradiation has seasonality. Photomed Laser Surg 2009 Dec;27(6):943-6.

268. Lee SY, Seong IW, Kim JS, Cheon KA, Gu SH, Kim HH, Park KH. Enhancement of cutaneous immune response to bacterial infection after low-level light therapy with 1072nm infrared light: A preliminary study. J Photochem Photobiol 2011 Dec 2;105(3):175-82.

269. Bornstein E, Hermans W, Gridley S, Manni J. Near-infrared photoinactivation of bacteria and fungi at physiologic temperatures. Photochem Photobiol 2009 Nov-Dec;85(6):1364-74.

270. Ross JR, Elizabeth Chant E, Tisdall FF. Effect of sunshine through window glass and fresh air on resistance to infection. Am J Dis Child 1933 Jan;45:81-95.

271. Zasloff M: Sunlight, vitamin D, and the innate immune defenses of the human skin. J Invest Dermatol 2005;125:6-17.

272. Kamen D, Tangpricha V: Vitamin D and molecular actions on the immune system: modulation of innate and autoimmunity. J Mol Med 2010, 88:441-450.

273. Atkinson W. *The Orientation of Buildings or Planning for Sunlight.* New York; J Wiley & Sons, 1912.

274. Castro R, Angus DC, Rosengart MR. The effect of light on critical illness. Crit Care 2011 Mar 22;15(2):218.

275. Eames I, Tang JW, Li Y, Wilson P. Airborne transmission of disease in hospitals. J R Soc Interface. 2009 Dec 6;6 Suppl 6:S697-702.