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## REVIEW

# Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises

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**Summary** The epidemics of severe acute respiratory syndrome (SARS) in 2003 highlighted both short- and long-range transmission routes, i.e. between infected patients and healthcare workers, and between distant locations. With other infections such as tuberculosis, measles and chickenpox, the concept of aerosol transmission is so well accepted that isolation of such patients is the norm. With current concerns about a possible approaching influenza pandemic, the control of transmission via infectious air has become more important. Therefore, the aim of this review is to describe the factors involved in: (1) the generation of an infectious aerosol, (2) the transmission of infectious droplets or droplet nuclei from this aerosol, and (3) the potential for inhalation of such droplets or droplet nuclei by a susceptible host. On this basis, recommendations are made to improve the control of aerosol-transmitted infections in hospitals as well as in the design and construction of future isolation facilities.

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## Introduction

The experience in 2003 with severe acute respiratory syndrome (SARS) highlighted the issue of aerosol transmission, both short range between healthcare workers and their patients,<sup>1–3</sup> and long

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range amongst the residents of the Amoy Gardens estate.<sup>4,5</sup> Aerosol or airborne transmission is already well recognized for many human pathogens. Much work has been performed using air-sampling techniques together with culture and molecular detection methods for viruses<sup>6–16</sup> [particularly varicella zoster virus (VZV)],<sup>17–24</sup> bacteria<sup>25–33</sup> [particularly tuberculosis (*Mycobacterium tuberculosis*, TB) and other mycobacteria],<sup>34–42</sup> and fungi (particularly *Aspergillus* spp.).<sup>43–56</sup> Beggs reviewed the importance of airborne transmission of infection in hospitals, focusing mainly on bacteria that are well known to cause nosocomial infections, i.e. *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA), *M. tuberculosis*, *Acinetobacter* spp., *Aspergillus* spp., *Pseudomonas* spp. and *Legionella* spp.<sup>57</sup> He concluded that, for these infections, although contact spread was still the main route of infection, infections via the airborne route, both direct and indirect (via the settling of airborne pathogens on fomites), were probably underestimated.

The generation of such infectious aerosols of infectious human pathogens can occur in many ways, and in many settings, although some have been studied more extensively than others due to their greater clinical significance. The literature on the risks of aerosol transmission of infection in hospital operating theatres is extensive.<sup>58–65</sup> Over 40 studies on the relationship between ventilation systems and the transmission of infection in hospitals, offices, aeroplanes and ships were reviewed recently by Li *et al.*<sup>66</sup> Studies have also been conducted on how infectious aerosols generated by various procedures in hospital environments can lead to infection in burns care facilities<sup>67–69</sup> and medical intensive care units.<sup>70,71</sup> In particular, the use of oxygen masks,<sup>72,73</sup> and power tools in dental practice<sup>74–77</sup> and orthopaedics<sup>77–84</sup> may pose a risk of aerosol infection. Aerosol dispersal of infectious agents has also been demonstrated in wastewater spray sites,<sup>85</sup> surface waves on the sea,<sup>86</sup> the flushing of the household toilet,<sup>87</sup> and even just opening a standard hinged door.<sup>88</sup>

## Definitions

True long-range aerosol transmission becomes possible when the droplets of infectious material are sufficiently small to remain almost indefinitely airborne and to be transmitted over long distances. One set of infection control guidelines for healthcare settings suggested that only TB, measles (rubeola virus) and chickenpox (VZV) should be considered as 'true' airborne infectious diseases.<sup>89</sup> However, it is likely that other infectious agents

may also behave as 'airborne', given a favourable environment, e.g. whooping cough (*Bordetella pertussis*), influenza virus, adenovirus, rhinovirus, *Mycoplasma pneumoniae*, SARS coronavirus (SARS-CoV), group A streptococcus and *Neisseria meningitidis*. Many more organisms fall into this category, as it probably includes virtually all pathogens where replication and/or colonization occur in the respiratory tract. Table I lists organisms associated with varying degrees of aerosol transmission.<sup>90</sup> Each organism can also be transmitted through direct contact with infected body fluids.

A recent systematic review demonstrated that adequate or inadequate ventilation has an effect on the risk of infection via infectious aerosols.<sup>66</sup> This interdisciplinary review, authored by a large group of engineers, microbiologists and epidemiologists, defined the following terms.

- Airborne transmission refers to the passage of micro-organisms from a source to a person through aerosols, resulting in infection of the person with or without consequent disease.
- Aerosols are a suspension of solid or liquid particles in a gas, with particle size from 0.001 to over 100  $\mu\text{m}$ .<sup>91</sup> Infectious aerosols contain pathogens.
- A droplet nucleus is the airborne residue of a potentially infectious (micro-organism-bearing) aerosol from which most of the liquid has evaporated.<sup>92</sup>

On the basis of these definitions, the following clinically applicable distinctions are made between short-range airborne infection routes (between individuals, generally less than 1-m apart) and long-range routes (within a room, between rooms or between distant locations, generally greater than 1-m distances):

- The short-range airborne infection route depends on the close proximity of the infected source and susceptible host. A study was performed recently (Xie *et al.*, unpublished observations) to define more clearly the size of the droplets originally referred to by Wells.<sup>92</sup> These terms are also in common current use. This study proposes the following size definitions: 'large-droplet' diameter  $>60 \mu\text{m}$ , 'small droplet' diameter  $\leq 60 \mu\text{m}$  and 'droplet nuclei' diameter  $<10 \mu\text{m}$ . Note that small droplets may also participate in short-range transmission, but they are more likely than larger droplets to evaporate to become droplet nuclei and then be considered as having the potential for long-range airborne transmission (see below).<sup>93</sup>

**Table I** Pathogens and diseases that have the potential to be transmitted via the airborne route

Pathogen	Aerosol route of transmission
Anthrax	Inhalation of spores
Arenaviruses	Inhalation of small particle aerosols from rodent excreta
Aspergillosis	Inhalation of airborne conidia (spores)
Blastomycosis	Conidia, inhaled in spore-laden dust
Brucellosis	Inhalation of airborne bacteria
<b>Chickenpox/shingles</b> (varicella zoster virus)	Droplet or airborne spread of vesicle fluid or respiratory tract secretions
Coccidioidomycosis	Inhalation of infective arthroconidia
Adenovirus	Transmitted through respiratory droplets
Enteroviruses (coxsackie virus)	Aerosol droplet spread
Cryptococcosis	Presumably by inhalation
Human parvovirus	Contact with infected respiratory secretions
Rotavirus	Possible respiratory spread
Norwalk virus	Airborne transmission from fomites
Hantavirus	Presumed aerosol transmission from rodent excreta
Histoplasmosis	Inhalation of airborne conidia
Influenza	Airborne spread predominates
Lassa virus	Aerosol contact with excreta of infected rodents
Legionellosis	Epidemiological evidence supports airborne transmission
Lymphocytic choriomeningitis	Oral or respiratory contact with virus-contaminated excreta, food or dust
<b>Measles</b>	Airborne by droplet spread
Melioidosis	Inhalation of soil dust
Meningitis ( <i>Neisseria meningitidis</i> )	Respiratory droplets from nose and throat
Meningitis ( <i>Haemophilus influenzae</i> )	Droplet infection and discharges from nose and throat
Meningitis ( <i>Streptococcus pneumoniae</i> )	Droplet spread and contact with respiratory secretions
Mumps	Airborne transmission or droplet spread
Nocardia	Acquired through inhalation
Paracoccidioidomycosis	Presumably through inhalation of contaminated soil or dust
Whooping cough ( <i>Bordetella pertussis</i> )	Direct contact with discharges from respiratory mucous membranes of infected persons by the airborne route
Plague ( <i>Yersinia pestis</i> )	Rarely airborne droplets from human patients. In the case of deliberate use, plague bacilli would possibly be transmitted as an aerosol
Pneumonia ( <i>S. pneumoniae</i> )	Droplet spread
Pneumonia ( <i>Mycoplasma pneumoniae</i> )	Probably droplet inhalation
Pneumonia ( <i>Chlamydia pneumoniae</i> <sup>a</sup> )	Possibilities include airborne spread
Psittacosis ( <i>Chlamydia psittaci</i> <sup>a</sup> )	By inhaling the agent from desiccated droppings, secretions and dust from feathers of infected birds
Q fever ( <i>Coxiella burnetti</i> )	Commonly through airborne dissemination of coxiellae in dust
Rabies	Airborne spread has been demonstrated in a cave where bats were roosting, and in laboratory settings, but this occurs very rarely
Rhinitis/common cold (rhinovirus, coronavirus, parainfluenza, respiratory syncytial virus)	Presumably inhalation of airborne droplets
Rubella	Droplet spread
Smallpox ( <i>Variola major</i> )	Via respiratory tract (droplet spread)
Sporotrichosis	Pulmonary sporotrichosis presumably arises through inhalation of conidia

Table I (continued)

Pathogen	Aerosol route of transmission
Staphylococcal diseases	Airborne spread is rare but has been demonstrated in patients with associated viral respiratory disease
Streptococcal diseases	Large respiratory droplets. Individuals with acute upper respiratory tract (especially nasal) infections are particularly likely to transmit infection
Toxoplasmosis	Inhalation of sporulated oocysts was associated with one outbreak
<b>Tuberculosis</b>	Exposure to tubercle bacilli in airborne droplet nuclei
Tularaemia ( <i>Francisella tularensis</i> )	By inhalation of dust from contaminated soil, grain or hay

Virtually all of these pathogens are also transmissible by direct contact. Pathogens in bold are those which are considered to have the potential to be transmitted by the long-range airborne route.<sup>89</sup> The original wording of the reference text<sup>90</sup> concerning aerosol transmission routes has been retained as much as possible.

<sup>a</sup> Now known as *Chlamydomphila psittaci* and *Chlamydomphila pneumoniae*, but the original classification has been retained here as in the original reference text.<sup>90</sup>

Exhaled air from both nose and mouth is able to enter and mix with air in the breathing zone of another person standing nearby (e.g. patients and doctors on a ward round at the bedside). Thus, short-range transmission implies that air flows between individuals may interact to infect one another.<sup>94</sup> In addition, it has been shown that the use of a simple oxygen mask may also generate a short-range (<1 m) infectious aerosol, with a potential risk to nearby healthcare workers and other patients.<sup>72,73</sup> Together with nebulizers, oxygen masks fall into this classification of potential short-range aerosol transmission sources, but some droplets generated by such masks can evaporate to become droplet nuclei that can also transmit infection over larger distances.<sup>57</sup>

- Long-range aerosol transmission refers to the potential for agents to be carried long distances by air flows to cause infection, and includes the traditional terms 'small-droplet' or 'droplet nuclei' and 'airborne'. Virtually all infectious agents that can cause infection at long range can also cause infection at short range as well as by direct contact. Therefore, use of the term 'long range' refers to the greatest distance from their source at which these agents have the potential to cause infection.

### Infectious agents transmissible by aerosols

If the pathogen has some part of its life cycle in the respiratory tract, it is more likely to be present in aerosols generated and projected into the surrounding air by breathing, talking, coughing,

sneezing and singing. For truly airborne pathogens (TB, measles and VZV), the routes of acquisition and dissemination of the infectious particles are well recognized to be via the respiratory tract. In the other pathogens listed in Table I, acquisition of the infection is also via the respiratory tract, which is the primary site of infection and replication. Therefore, these other pathogens, such as parvovirus B19, enteroviruses and the organisms of atypical pneumonias [*M. pneumoniae*, *Chlamydomphila psittaci* (previously *Chlamydia psittaci*), *Chlamydomphila pneumoniae* (previously *Chlamydia pneumoniae*), *Coxiella burnetti* and *Legionella pneumophila*], have the potential to be transmitted via aerosols as their life cycle involves replication at some point in the respiratory tract. Regarding *L. pneumophila*, replication also occurs in water systems, and human infection can occur via infected water aerosols, such as showerheads and fountains. With SARS-CoV, viral RNA as well as viable (culturable) virus has been found in air samples.<sup>95,96</sup> Therefore, SARS-CoV can potentially be transmitted by short- and long-range aerosols to cause disease, as has been strongly implicated by several studies.<sup>1–5</sup>

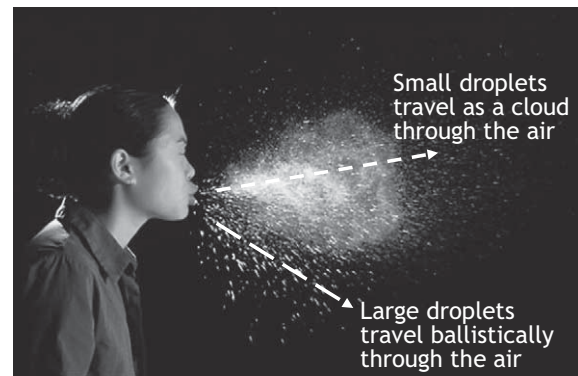
With influenza, there is ongoing debate about the nature of transmission between people. A recent review suggested that 'aerosol-generating procedures...should be performed with proper infection control precautions', but the authors do not elaborate on exactly what these precautions should be.<sup>97</sup> Recent guidelines from the UK review the evidence for aerosol transmission of influenza more comprehensively.<sup>98</sup> The report concluded that whilst close contact with infected individuals seems to be responsible for the vast majority of transmission, most reports of influenza transmission

do not provide enough temporal-spatial data to determine whether transmission is mainly due to droplet, contact or airborne spread. This is probably the most realistic assessment, and this uncertainty is reflected in the large range of values for the basic reproductive number ( $R_0$ , the number of secondary cases arising from a single index case in an otherwise totally susceptible population), ranging from 1–2<sup>99</sup> to 2–7<sup>100</sup> to <21.<sup>101</sup> However, there are reports to suggest that in pandemic or large, explosive outbreak situations, influenza can become truly airborne.<sup>12,13</sup> For comparison, the  $R_0$  values of other commonly encountered infections are shown in Table II.

In contrast, other pathogens, such as human immunodeficiency virus and hepatitis B and C viruses, replicate mainly outside the respiratory tract and are not naturally transmitted via aerosols. With other organisms that can replicate on many surfaces either inside or outside the body, e.g. *S. aureus*, the picture is not so clear-cut. Although mainly spread by direct contact, there is a suggestion that patients that carry *S. aureus* in the respiratory tract can spread the bacteria by short-range aerosols.<sup>57,106</sup> *S. aureus* on skin epithelial cells on fomites, such as bed sheets, can also be spread during bed making.<sup>57,106</sup> This becomes more important when considering resistant strains such as MRSA.<sup>57</sup>

## Sources of infectious agents

A commonly encountered source is the patient with flu-like symptoms who is coughing, sneezing and dispersing the organism (Figure 1).<sup>107,108</sup> In the diagnostic laboratory, it may be an inoculated



**Figure 1** Droplet generation. A flash photo of a human sneeze, showing the expulsion of droplets that may be laden with infectious pathogens. Sneezing can produce as many as 40 000 droplets of 0.5–12  $\mu\text{m}$ .<sup>107</sup> These particles can be expelled at a velocity of 100 m/s,<sup>108</sup> reaching distances of several metres. Smaller droplets with less mass are less influenced by gravity, and can be transported as a ‘cloud’ over greater distances and by air flows. Larger droplets with more mass are more strongly influenced by gravity and less so by air flows, and move more ‘ballistically’, falling to the ground more quickly. Reproduced with the kind permission of Prof. Andrew Davidhazy, School of Photographic Arts and Sciences, Rochester Institute of Technology Rochester, NY, USA.

culture medium that is dropped or spilt, as has been reported for laboratory-acquired SARS infection.<sup>109</sup> A more worrying possibility is the deliberate release of a biological agent, such as during the US terrorist anthrax attacks of 2001–2002,<sup>32,33</sup> or an accidental release, such as the anthrax incident in the Russian city of Sverdlovsk of 1979.<sup>110</sup>

A sneeze can generate up to 40 000 droplets (Figure 1),<sup>107,108</sup> which can evaporate to produce droplets of 0.5–12  $\mu\text{m}$  in diameter.<sup>107</sup> A cough can generate about 3000 droplet nuclei, the same number as talking for 5 minutes.<sup>111</sup> During normal breathing, exhalation can project droplets up to 1 m in room air, which may be inhaled by another person nearby (Figure 2),<sup>94</sup> whereas sneezing can project droplets several metres (Figure 1).<sup>107,108</sup> In addition, a recent study has shown that some individuals may exhale more particles during quiet breathing than others, suggesting that some people may be more infectious than others when infected with the same organism.<sup>112</sup> The way that an infectious aerosol is generated should be considered when assessing the probable distance of spread. As noted earlier, large droplets can evaporate to become small droplets that can evaporate further to become droplet nuclei and hence become truly airborne if this evaporation process can occur before the

**Table II** The basic reproductive number ( $R_0$ ) of some human infectious agents (adapted from Reference<sup>102</sup> with additional references as indicated)

Infectious disease	Basic reproductive number ( $R_0$ )
Measles	15–17
Whooping cough	15–17
Chickenpox <sup>103</sup>	10–12
Mumps	10–12
Rubella	7–8
Diphtheria	5–6
Poliomyelitis	5–6
Smallpox <sup>103</sup>	4–7
Influenza <sup>99–101</sup>	1.68–20
SARS <sup>104,105</sup>	2–3

SARS, severe acute respiratory syndrome.



**Figure 2** Smoke visualization of exhalation flow from nose of the right mannequin penetrating into the breathing zone of the left mannequin, which are 0.4 m apart.<sup>94</sup> Reproduced from Figure 12 in Reference<sup>94</sup> with the kind permission of Blackwell Publishing.

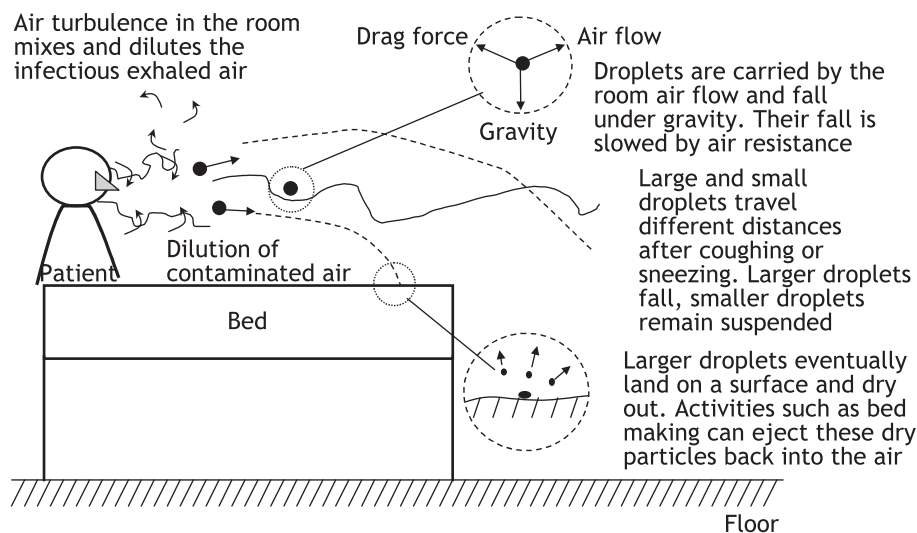
droplet lands on the ground. The 2003 SARS epidemics also revealed iatrogenic and environmental factors that might contribute to producing virus-laden aerosols, such as those produced by nebulizers, tracheostomies, bronchoscopies,<sup>113–116</sup> and, in the Amoy Gardens outbreak, a defective sewage system.<sup>4,5</sup>

### Mechanics of aerosol transmission of infectious agents

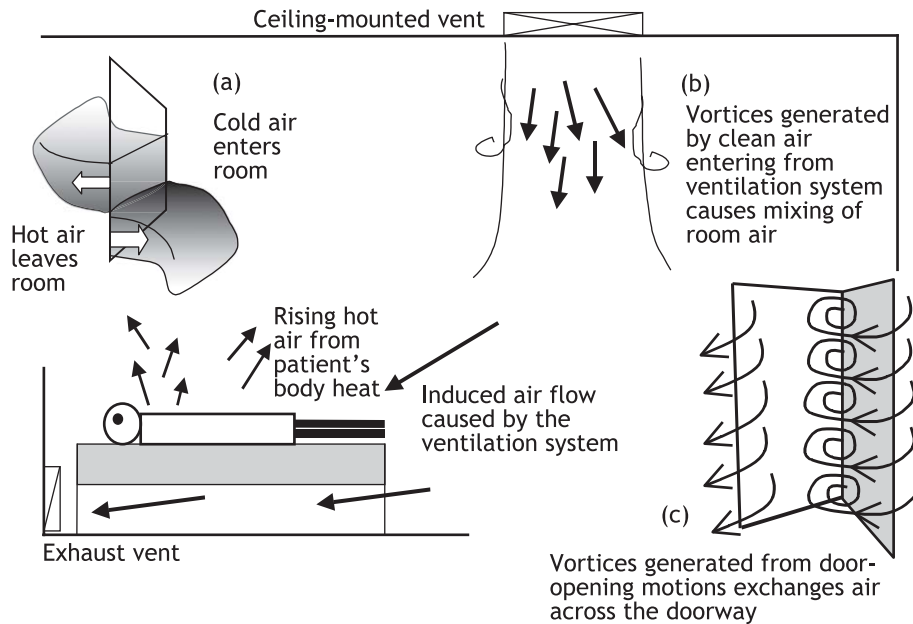
Once infectious droplets are released, the main factors that determine how they move are their size and the airflow patterns that carry them

around (Figure 3). The droplet size changes with time, depending on the environmental conditions. Humidity in the air alters the rate of droplet evaporation and therefore its size. Droplets in dry air evaporate quickly, reduce in size and fall to the ground more slowly.<sup>57</sup> The changing size of a droplet affects how it will respond to airflow patterns and how quickly it will settle. Movement in air is determined by Stokes' settling law, which governs how quickly a sphere falls under the opposing forces of gravity downwards and air friction upwards (Figure 3).<sup>92</sup> Knight estimated the times taken for particles of various diameters to fall 3 m (corresponding to the height of a room).<sup>10</sup> Particles of diameters 1–3  $\mu\text{m}$  remained suspended almost indefinitely, 10  $\mu\text{m}$  took 17 min, 20  $\mu\text{m}$  took 4 min, and 100  $\mu\text{m}$  took 10 s to fall to the floor. 'Naked' viruses, bacteria and fungal spores (i.e. without associated water, mucus or pus droplets) range in approximate size from 0.02 to 0.3  $\mu\text{m}$ , from 5 to 100  $\mu\text{m}$  and from 1 to 10  $\mu\text{m}$ , respectively. Infectious agents from patients can be expelled as individual or clusters of 'naked' organisms, or disseminated on skin cells, mucus or saliva.<sup>107</sup> The amount of solid matter in a droplet ultimately determines its minimal size limit.

Temperature differences can set up large exchange flows between rooms, in a similar way to leaving a front door open on a cold day (Figure 4). Opening a hinged door leads to a sweeping action, which can also move a considerable volume of infectious air across the open doorway (Figure 4). A typical hinged door (about 1 m wide) opening relatively slowly from closed to 45° sweeps out one-eighth of a circle of circumference (C)  $2\pi = 6.3 \text{ m}$  ( $C = 2\pi r$ ).



**Figure 3** Droplet suspension. Illustration of the mechanics of suspension of droplet nuclei produced by an infected patient due to the effects of air friction and gravity.



**Figure 4** Droplet transport. The dispersion of the droplet nuclei is affected by the air flows from an open window, the ventilation system and door opening. (a) The air flow from an open window is affected by temperature differences between the inside and outside. In this figure, inside the room is warm and outside is cold. (b) The ceiling-mounted ventilation vent injects clean air into the room, which is removed by the exhaust vent near the patient's head, diluting the total amount of contaminated air. This also generates a downward flow pattern. (c) The action of opening a door generates a large vortex that sweeps clean air into the room and ejects contaminated air. When there are temperature differences between inside and outside, this also leads to a buoyancy exchange flow indicated in (a).

Therefore, the door edge travels about  $6.3/8 =$  about 0.8 m in about 2 s, generating an air flow with speed of approximately  $0.8/2 = 0.4$  m/s. In practice, doors may be opened faster and wider than this. As the door opens, air inside the room is dragged (or 'entrained') into the region swept by the door, leading to a large exchange of air across the doorway.<sup>117,118</sup> At least one case report has described a secondary case of chickenpox arising from infectious air being transported out of an isolation room containing a patient with severe chickenpox via the opening of a hinged door.<sup>88</sup> Closing a door does not seem to lead to any significant air exchange between rooms. Such problems with hinged doors may be reduced by the use of sliding doors.

The effect of movement of people on air flow produces a similar effect to door opening, but is more complex and difficult to calculate. The velocity of the layer of air closest to the body is comparable to a person's walking speed. As a person moves at speed  $U$ , there is a volume flux,  $F$ , of air volume of approximately  $F = CAU/2$ , where  $C$  is the drag coefficient for a body (approximately equal to 1 in this example),  $A$  is the cross-sectional area of the body (for a person about 1.7 m tall, 0.3 m wide and 0.15 m deep,  $A = 1.7 \times 0.3 = 0.51$  m<sup>2</sup>) and  $U$  is velocity. In addition, there is a wake bubble of volume  $\varepsilon V$ , where

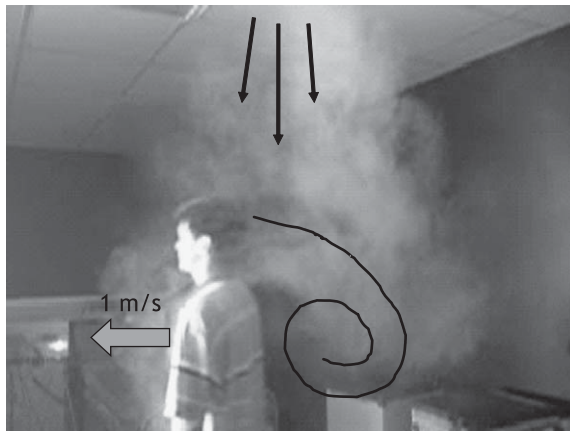
$V$  is the volume of the body. In this example,  $V = 1.7 \times 0.3 \times 0.15 = 0.0765$  m<sup>3</sup> (i.e. a person of 76.5 kg, since  $1 \text{ m}^3 = 100 \times 100 \times 100 \text{ cm}^3 = 1000$  L water, assuming human body density has an average density equal to that of water) and  $\varepsilon = 1-3$ .<sup>119</sup> For a person walking at speed  $U = 1$  m/s, this corresponds to  $F = 1 \times 0.51 \times 1/2 = 0.255$  m<sup>3</sup> = 255 L/s, with an attached wake of  $\varepsilon V = 0.0765 - 0.2295$  m<sup>3</sup> = 76-230 L/s. Thus, movement of people in a room plays a significant part in disturbing the flow and also in transporting infected air from one place to another (Figure 5).

Thus, room air flow is governed by a combination of air movements caused by differences in temperature/humidity and moving bodies/equipment. These complex air movements make the route and suspension time of an infectious particle very difficult to determine once it has left the infectious host. The infectivity of the droplet nuclei will also change with time, as the infectious organism will also be affected by the air temperature and humidity.

### Environmental survival of infectious agents

To transmit from the respiratory tract of one person to another, the organisms in such droplets must





**Figure 5** A snapshot of the movement of one person in the corridor of a full-scale test room for a six-bed general hospital ward. The ward was ventilated by a downward supply system with exhaust at floor level. At the time of the experiment, the supply air stream was marked by smoke. A person walking forward at about 1 m/s would push a front layer of air creating a volume flux,  $F$ , of about 255 L/s, with an attached wake of 76–230 L behind (see main text for calculations). This introduces a significant mixing air flow into the room.

remain airborne for a sufficient amount of time and must remain viable in a sufficient quantity to be inhaled by a susceptible host. Many environmental factors affect the viability of an infectious agent, e.g. temperature, humidity and air flows that might lead to dehydration,<sup>120</sup> ultraviolet (UV) radiation,<sup>121–123</sup> chemical hazards such as exhaust fumes from road transport or air pollution,<sup>120</sup> and possibly cigarette smoke and air fresheners inside houses. Some organisms resist environmental degradation better than others. *M. tuberculosis* is a hardy organism with a thick cell wall, and can survive for long periods in the environment.<sup>111</sup>

Measles and VZV are both lipid enveloped and are sensitive to changes in temperature, relative humidity (RH) and UV radiation.<sup>124</sup> Viruses without a lipid envelope generally survive longer at high RH (>50%), e.g. poliovirus,<sup>6,120</sup> but lipid-enveloped viruses survive longer in low RH (<50%), e.g. influenza,<sup>6,110</sup> Lassa fever virus<sup>125</sup> and human coronavirus (hCoV) 229E.<sup>126</sup> Data on hCoV 229E from Ijaz *et al.* showed that, when airborne, this virus had a survival half-life of about 3 h at an RH of 80%, 67 h at an RH of 50% and 27 h at an RH of 30%, at 20 °C, suggesting that high RH above 80% is most detrimental to survival of this coronavirus.<sup>126</sup> Influenza has been shown to survive for 24–48 h on hard, non-porous surfaces such as stainless steel and plastic, but for less than 8–12 h on cloth, paper and tissues.<sup>127</sup> In addition, influenza virus survived for up to 5 min on hands, and could be

transferred to hands from these non-porous surfaces for 24 h and from tissues for 15 min.<sup>127</sup> More recently, it has been shown that SARS-CoV can survive in alkaline diarrhoea stools for up to four days, and remain infectious in respiratory specimens for more than seven days at room temperature.<sup>128</sup> Similarities with other viruses of nosocomial importance, i.e. other RNA, lipid-enveloped, respiratory viruses such as influenza, suggest that such organisms can survive for long enough in aerosols to cause disease, especially when associated with biological fluids such as mucus, faeces and blood. This sensitivity to environmental conditions may also partially explain the seasonality of some viral infections.

The situation is more complex in airborne bacteria. Gram-negative bacteria such as *Escherichia coli* and *Klebsiella pneumoniae* tend to behave like enveloped viruses, i.e. are less stable at high RH.<sup>120</sup> In contrast, a study on another airborne Gram-negative bacterium, *Salmonella seftenberg*, found the opposite, i.e. that survival or 'tenacity' was highest at high RH.<sup>129</sup> Cox suggested that a temperature of 10 °C offers optimal survival to most infectious pathogens.<sup>120</sup> Hence, it is difficult to predict the survivability of infectious organisms from their structural characteristics alone.

## Infectious doses of aerosol-transmitted agents

The infectious dose of a pathogen is the number of organisms required to cause infection. Theoretically, a single organism in a favourable environment may replicate sufficiently to cause disease. Guidelines for commissioning operating theatres recommend that the bioload in an empty theatre should not exceed 35 bacteria-carrying particles (e.g. skin scales)/m<sup>3</sup> air.<sup>130,131</sup> During an operation, the bioload in the same theatre should not exceed 180 colony-forming units per cubic metre (CFU/m<sup>3</sup>, where 1 CFU represents the progeny from one viable bacterium).<sup>132</sup> Such guidelines are developed in an attempt to minimize the risks of surgical nosocomial transmission.

Data from research performed on biological warfare agents suggest that both bacteria and viruses can produce disease with as few as 1–100 organisms (e.g. brucellosis 10–100, Q fever 1–10, tularaemia 10–50, smallpox 10–100, viral haemorrhagic fevers 1–10 organisms).<sup>132</sup> *M. tuberculosis* may need only a single organism to cause disease, and as many as 3000 organisms can be produced by a cough or talking for 5 min, with sneezing producing many more.<sup>111</sup> For many common agents, the

infectious dose almost certainly varies between individual pathogens and their hosts, e.g. immunocompromised hosts may not only be more susceptible to infection with a lower infectious dose, but may also be a more infectious source, as the pathogen is poorly controlled by the defective immune system. This may allow higher pathogen loads to be disseminated into the surrounding environment in some cases, possibly leading to super-spreading events, such as described in some SARS outbreaks.<sup>1–5</sup> Knowledge of the infectious dose of airborne pathogens may allow an estimate of the number of air changes required in an indoor environment to reduce the concentration of such pathogens below the level that can cause disease.

## Methods of control of infectious aerosols

Li *et al.* reviewed the evidence for the effects of ventilation on the transmission of infectious diseases.<sup>66</sup> They concluded that there was good evidence (as demonstrated by the contemporary technology available at the time of the studies) for aerosol transmission influenced by ventilation factors in outbreaks involving measles,<sup>133</sup> chickenpox,<sup>134</sup> the pneumococcus (*Streptococcus pneumoniae*),<sup>135</sup> SARS-CoV,<sup>1–5</sup> tuberculosis,<sup>136,137</sup> influenza<sup>138,139</sup> and smallpox.<sup>140</sup> Therefore, from this and other studies reviewed here, it should be possible to reduce the risk of aerosol transmission by altering ventilation parameters in healthcare environments.

For short-range aerosol transmission exposures, personal protective equipment (PPE; i.e. gowns, gloves and facemasks) is recommended in addition to the usual contact-transmission prevention precautions (i.e. handwashing, avoiding touching mucous membranes of the eyes, nose and mouth) to protect susceptible healthcare workers. Seto *et al.* performed a study on the effectiveness of masks in reducing infection during the SARS outbreak, and found that surgical masks were effective in reducing infection from SARS to a certain extent.<sup>141</sup> However, with more infectious diseases such as TB, measles or chickenpox, a surgical mask alone may be insufficient aerosol protection, and masks with built-in filters, i.e. filtered face piece masks, may be required. Droplet nuclei produced during respiration, talking, coughing and sneezing from such patients are very small, less than 5 µm in diameter, and behave similarly to smoke particles in air.<sup>142</sup> Where susceptible hosts are widely separated in an indoor space, the potential for airborne transmission depends partially on the ventilation

system present. In the community, some studies during the SARS outbreak in Hong Kong suggested that the use of facemasks and covering the mouth when sneezing may have contributed to an overall reduction in the incidence of viral respiratory infections at this time.<sup>143,144</sup>

For the control of long-range aerosol transmission, the architecture of the healthcare facilities requires consideration. Hospital rooms are connected by doorways, corridors, stairwells and lift shafts. Small pressure differences, induced by natural forces such as thermal buoyancy due to air temperature differences, the wind or mechanical fans, can generate air flows that move air from one room to another. These air flows are very sensitive to doors or windows being kept open, e.g. although opening a window can enhance natural ventilation, this can change the air pressure in neighbouring rooms and corridors, reducing, or even reversing, airflow directions (Figure 4). This highlights the importance of keeping isolation room windows and doors closed.

The use of air filtration aims to reduce airborne concentrations to well below their infectious dose. Besides simply increasing the number of air changes per hour, there are other ways in which manipulation of air flows can be used to reduce the spread of airborne infection in an indoor environment such as a hospital. One main difficulty in designing ventilation systems for removing airborne pathogens is due to the fact that air flow is generally turbulent. In a hospital environment, if a ventilation system can ensure that the inhaled air for each individual mainly consists of fresh outdoor air, the system would be considered effective as the purpose of ventilation is to protect individuals from inhaling hazardous, infectious air.<sup>145</sup> This principle can be broken down into three approaches, as follows.

- Mixing of the contaminated air with uncontaminated air in the room, reducing the peak concentrations of droplet nuclei in the contaminated air. Over time, the average concentration of the droplet nuclei in the room will increase, unless the air is filtered.
- Diluting contaminated air using ‘fresh’ (uninfected) air. Current recommendations of ventilation flow rate in various different guidelines for hospital ventilation and isolation room designs are based on the principle of dilution.<sup>146</sup> A ventilation flow rate of at least 12 air changes (of a room)/h is suggested for new isolation rooms (constructed since 2001). Existing isolation rooms (constructed before 2001) may still use six air changes/h.<sup>89,147</sup>
- Controlling the air flow so that it moves from healthcare workers to patient. This requires

putting patients and exhaust vents in close proximity.

Practically, there are at least two commonly used air distribution systems in general hospital wards. These are the mixing ventilation and displacement ventilation systems (Figure 6).

### Mixing ventilation

The idea is to create a uniform low concentration of infected air in the room air that is subsequently

extracted. The air is supplied along the ceiling or directed upwards along the window or wall surface, as shown in Figure 6(a).

### Displacement ventilation

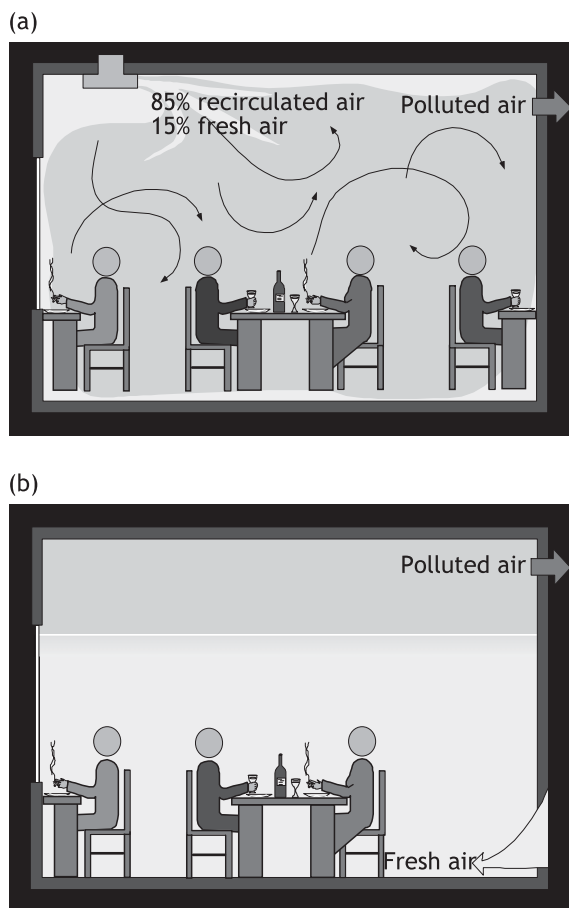
This refers to 'fresh' air sweeping in one direction across a room, carrying the pollutants with it and exhausting the polluted air. The flow is driven by large temperature differences in the room.<sup>145,148</sup>

The vertical downward displacement ventilation system would be the ideal ventilation system for operating theatres, but there is a need for further study in the effectiveness of removing large particles with the upward vertical displacement system shown in Figure 6(b). However, a recent study demonstrated that the exhaled air plumes from a patient lying on his/her side on a bed could be spread over long distances, assisted by differences in air temperature and density, on a ward using displacement ventilation.<sup>149</sup> This suggests that displacement ventilation should be used with caution in hospital wards, where such a risk of aerosol transmission is present.

In practice, ventilation usually consists of a combination of mixing and displacement ventilation. The fresh air stream mixes with convection currents, such as the heat plumes that arise above people and equipment. To remove infectious particles, existing guidelines recommend that the air flow should follow a path from the ceiling supply vents to the healthcare workers, then to the patients, then finally to the exhaust vents that are generally located at a lower level, near the floor.<sup>147</sup>

Ventilation and air flows also affect the thermal comfort of both healthcare workers and patients. The air speed in the occupied zone of a room is designed to be below 0.2 m/s for reasons of comfort.<sup>150</sup> Due to differences in metabolic rate and clothing, the cooling or heating requirements of healthcare workers and patients can be different. Thermal discomfort such as sweating may also discourage the proper use of PPE by HCWs and thus limit its effectiveness.<sup>141</sup>

To reduce the spread of airborne contamination between rooms, it is common to fit ventilation systems with the capability to produce negative pressures, so that the direction of flow around closed leaky windows and doors can be controlled. For instance, in a negative pressure room, the supply flow rate to the room is less than the exhaust flow rate. Such 'negative pressure' isolation rooms are generally separately air-conditioned and temperature controlled, but there is likely to be a temperature difference between adjacent rooms. Current guidelines recommend a minimum negative pressure of 2.5 Pa (0.01 inch water gauge) in



**Figure 6** Illustration of the two commonly used air distribution methods in rooms. (a) Mixing ventilation: the cool air is supplied at ceiling level at high velocity and returned at either ceiling or floor level. The air in the room is generally fully mixed due to the strong mixing created by the overall air recirculation in the room, governed by the strong supply momentum. (b) Displacement ventilation: the cool air is supplied at floor level at low velocity and returned at ceiling level. The air in the room is divided into two parts: the upper part with 'polluted' air and the lower part with 'clean' air. Both parts of figure reproduced with the kind permission of CSIRO Australia. © CSIRO.

relation to corridors, although other guidelines recommend a negative pressure of 5–10 Pa.<sup>147,151–154</sup> In practice, however, the negative pressure will fluctuate with time, depending on the control method and environmental factors. These systems need to be regularly maintained because it is commonly found that some air-supply vents do not supply the air at their specified rate, vents may be blocked and fail to deliver any air, and/or negative pressure rooms are being operated in a positive pressure mode.

Most recently, a study using computational fluid dynamical modelling confirmed that the air exchange rate and airflow patterns are important factors in the control of airborne virus diffusion.<sup>155</sup> Also, despite the recommendations for ceiling to floor level ventilation air flows, this study suggested that this arrangement results in an ‘up-draft effect and poor infection control efficiency’.<sup>147,155</sup> There is an obvious need for further work to determine the optimal methods of ventilation control to reduce the risk of aerosol transmission in healthcare premises.

## Conclusions

- Droplets generated by talking, laughing, coughing and sneezing potentially lead to the generation of an infectious aerosol.
- The survival of such aerosolized pathogens depends upon environmental conditions, such as temperature and RH, both of which can vary with the season and the indoor building environment.
- Such aerosols can be transmitted over short and long distances. Short-range transmission occurs over a distance of <1 m between individuals and is mediated mainly by the interaction of breathing zones of individuals. Long-range transmission occurs between distant locations and is primarily governed by air flows driven by pressure differences generated by ventilation systems, open windows and doors, movement of people or temperature differences.
- Agents able to transmit infection over long distances can almost always transmit infection over short ranges and through direct contact. In addition, large droplets may become small droplets then droplet nuclei via the process of evaporation. This may explain why some infectious agents, normally only associated with short-range transmission, may occasionally cause outbreaks over greater distances.
- Whether an individual acquires an infection depends on the final inhaled pathogen dose and the host’s immune response.

- The airborne transmission of diseases may be restricted in three ways:
  - control the source of infection by quarantine and the use of isolation facilities;
  - control airborne transmission routes by the use of negative pressure ventilation systems, sliding doors instead of hinged doors, and improving seals around doors and windows; and
  - protect exposed susceptible individuals from both aerosol and contact transmission of infection by the use of PPE.

## Search strategy and selection criteria

Data for this review were identified by searches of Medline, references from relevant articles and books, and the authors’ own extensive archives. Search terms included: ‘aerosol transmission’, ‘airborne transmission’, ‘environmental survival’, ‘aerosol suspension’, ‘airborne suspension’, ‘aerosol dispersal’, ‘airborne dispersal’, ‘aerosol dispersion’, ‘airborne dispersion’, ‘infectious dose’, ‘nosocomial airborne infection’, ‘nosocomial airborne transmission’, ‘nosocomial aerosol infection’ and ‘nosocomial aerosol transmission’.

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