Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection (2011) 62, 1—13

ELSEVIER

BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

REVIEW

The role of particle size in aerosolised pathogen transmission: A review

Jan Gralton [a,b], Euan Tovey [c], Mary-Louise McLaws [a], William D. Rawlinson [b,d,e,*]

[a] School of Public Health and Community Medicine, The University of New South Wales, Australia
[b] Virology, UNSW and POWH Research Laboratories, Prince of Wales Hospital, Australia
[c] Woolcock Institute of Medical Research, University of Sydney, Australia
[d] School of Medicine, The University of New South Wales, Australia
[e] School of Biotechnology and Biological Sciences, The University of New South Wales, Australia

Accepted 11 November 2010
Available online 19 November 2010

KEYWORDS
Particle;
Aerosol;
Airborne;
Size;
Transmission

Summary Understanding respiratory pathogen transmission is essential for public health measures aimed at reducing pathogen spread. Particle generation and size are key determinant for pathogen carriage, aerosolisation, and transmission. Production of infectious respiratory particles is dependent on the type and frequency of respiratory activity, type and site of infection and pathogen load. Further, relative humidity, particle aggregation and mucus properties influence expelled particle size and subsequent transmission. Review of 26 studies reporting particle sizes generated from breathing, coughing, sneezing and talking showed healthy individuals generate particles between 0.01 and 500 μm, and individuals with infections produce particles between 0.05 and 500 μm. This indicates that expelled particles carrying pathogens do not exclusively disperse by airborne or droplet transmission but avail of both methods simultaneously and current dichotomous infection control precautions should be updated to include measures to contain both modes of aerosolised transmission.

Introduction

Natural human respiratory activities include breathing, talking, sneezing, and coughing.

Several mechanisms of particle generation from these activities have been postulated.[1—9] Early studies propose that normal breathing produces particles through the processes of condensation and high-speed atomization.[1,2] Warm and wet gas in the alveolar region transits from the

* Corresponding author. Virology Research, Department of Microbiology, South Eastern Area Laboratory Service, Prince of Wales Hospital, Randwick, NSW 2031, Australia. Tel.: +61 2 93829113; fax: +61 2 93828533.
E-mail address: w.rawlinson@unsw.edu.au (W.D. Rawlinson).

0163-4453/$36
doi:10.1016/j.jinf.2010.11.010

lungs into the upper airways, where the gas cools to a liquid state[1] and turbulent high-speed airflow expels liquid as particles during exhalation.[2] Further atomization of particles also occurs during talking, sneezing and coughing, due to increased turbulent airflows expelling particles at higher velocities.[3] A later study suggested particle generation during breathing occurs from the re-opening of small airways during inhalation[4]; this mechanism has been supported by recent data examining mechanisms during exhalation[5,6] where particles are formed by the bursting of liquid films that cover the airway openings.[7,8]The vigorous vibration and energetic movement of the vocal chords during speech and coughing have also been suggested to be responsible for the majority of particle generation.[9]

This review examines the role of particle size in the aerosolised spread of infectious disease. Specifically we first detail why particle size is important. We then provide an overview of the literature that has measured particle sizes generated from different respiratory activities. Subsequently, we briefly discuss the different sizing methods and their limitations. This review also highlights some of the extraneous factors, outside the act of particle generation, that further complicates particle sizing and the use of size in infection control precautions. We conclude by identifying remaining gaps in the current knowledge of particle size and their implications.

The importance of particle size

Aerosolised disease transmission can be classified as either droplet or airborne transmission. Droplet transmission is defined as the transmission of diseases by expelled particles that have a propensity to settle quickly to the ground, usually within 1 m of the site of generation, due to their size.[10–12] Thus, infection by droplet transmission is reliant on close proximity between infected and susceptible hosts and direct contact between the droplet carrying the infectious agent and the respiratory tract of a susceptible host. Settled droplets may also facilitate fomite transmission of infection.[13,14] Conversely, airborne transmission is defined as the transmission of infection by expelled particles that are comparatively smaller in size. These particles can remain suspended in the air for prolonged periods and thereby potentially expose a greater number of susceptible individuals to possible infection at a greater distance from the source.[12,15–17] This paradigm between droplet and airborne transmission has been underpinned by early studies by Wells, who described the settling of expelled particles as being a function of size, time and evaporation,[10] and by Hamburger and Robertson, whom described the distance travelled by particles expelled during sneezing and coughing events as a function of time.[18]

The World Health Organisation employ a 5 μm cut-off to delineate between airborne ($\leq$5 μm) and droplet transmission ($>$5 μm).[19,20] While we will use this framework in this review, we will later discuss how this single cut-off delineation fails to acknowledge that the size of particles and the resulting behaviour follows a continuum and may overlap either side of this cut-off. There are also physiological concerns which warrant a better understanding of the role of particle size in disease transmission. Deposition models have concluded that particles $<$10 μm in diameter are more likely to penetrate deeper into the respiratory tract while particles $\geq$10 μm in diameter are more likely to impact onto the surfaces of the upper airways and are less likely to penetrate into the lower pulmonary region.[21–29] Although small particles may also deposit in the upper airways,[26,30,31] the usual behaviour is for small particles to travel with the inhaled air current and avoid impaction within the nasal region; this enables deposition lower in the respiratory tract[23,32] and the establishment of infection in this region.[26] Similar reasoning is also used by Nicas (2005), who used an equilibrium size of 10 μm in diameter in risk calculations of airborne transmission.[29] Based upon the likelihood of deposition in the respiratory tract rather than generated particle size, Weber and Stilianakis, in their review article, suggest a cut-off of 10 μm in diameter to separate particles likely to transmit disease (particles $\leq$10 μm in diameter) from those that are less likely (particles $>$10 μm in diameter).[33] This group also used this cut-off in recent computer models and proposed likely predominant airborne transmission of particles $\leq$10 μm in sustained disease outbreaks and likely predominant droplet transmission in short-term epidemic outbreaks.[34] Other factors, such as infectious dose at different sites, are also implicated in the establishment of infection in the respiratory tract and have been reviewed elsewhere.[35]Compared with upper respiratory tract infections, lower respiratory tract infections are associated with increased severity, morbidity and fatality[36–38] due to the possibility of causing impairment of lung function,[39,40] the initiation of other chronic respiratory illness[41–44] and the effects of comorbid factors.[39,45–47] Better understanding of the site of deposition of infected particles, the relationship between particle size and pathogen load and the critical pathogen load of particles required for the establishment of infection in the different regions of the airways is necessary before particle size can be robustly established as an index of transmissibility for infection control measures.

Particles and the spread of infection

The probability of the spread of infection by aerosolised particles is broadly dictated by 1) the clinical manifestation of disease 2) site of infection 3) the presence of a pathogen and 4) type of pathogen (see Table 1).

Clinical manifestations of disease

The relative contributions of the different respiratory activities for the spread of disease remains contentious due to the numerous factors involved, such as the frequency of different respiratory activities, the number of particles produced per activity, and the pathogen load size distribution of different sized particles. Recently respiratory viruses have been detected in particles during tidal breathing — an activity that is continuous but previously assumed to produce a low number of particles.[48–51] Other studies suggest that vibration of the vocal chords and vocalisation (associated with intermittent activities such as coughing, sneezing and talking) contributes more to particle atomization[9,52,53] and the production of particles that carry microorganisms.[54] Disease propagation may also be associated with the frequency of the different respiratory activity. While sneezing

Table 1 Factors affecting disease transmission via aerosolised modes.

Factors	Effect
Type of respiratory activity	Different activities (for example breathing, coughing, sneezing, talking) produce different numbers and sizes of particles
Frequency of respiratory activity	Frequent activities associated with clinical disease are more likely to spread pathogen
Number of particles generated	Activities that atomize more particles are more likely to spread pathogen
Site of infection	Activities that generate aerosols from the infected region of the respiratory tract are likely to propagate disease
Pathogen load	Sufficient pathogen load must be present in expelled particles to establish infection in a susceptible individual.
Pathogen type	The size of the pathogen may determine the size and infectivity of expelled particles.

may produce more particles containing virus than coughing,[15,22,55,56] Couch et al. (1966) found that coughing is more frequent than sneezing during infection with Coxsackievirus A, — implying that coughing is the more efficient method of transmission for this infection.[57] It can be speculated that since coughing is one of the most common clinical symptoms associated with influenza infections,[58,59] coughing may also drive the aerosolised spread of this infection. While limited cough frequency data is available, evidence from modelling of flow dynamics also lends support to such speculation[60] as does the observations of sneezing counter-indicating an influenza diagnosis.[61]

Site of infection

The site of infection should also be considered in terms of understanding the source of aerosolised particles. As a starting proposition, to ensure expelled particles carry pathogen, the site of infection should be the same or very close to the site of particle generation. As earlier discussed, coughing and speech are reported to produce particles from vibrations of vocal chords.[9] This implies that infection of the larynx is the optimal location for propagation of pathogen by these activities. Particle generation during breathing has recently been associated with opening of the small airways,[4–6] indicating that infection of the lower respiratory tract is important for aerosolised transmission from breathing. If particle generation occurs outside of the site of infection, we speculate that there is a reduced likelihood that particles will contain a sufficient pathogen load to establish secondary infection. If multiple sites are infected, the number of particles carrying pathogen will be increased if simultaneous respiratory events occurs (for example simultaneous coughing and breathing); conversely, dilution of the number of particles carrying pathogen will occur if simultaneous atomization occurs at additional but non-infected sites. An example of this dilution is the observation that the majority of particles produced during sneezing arise from the mouth[2] despite sneezing being a reflex of the irritation of the nasal region and generating particles from the lower respiratory tract with additional secretions from the nasal region.[62–64] The relative proportions of particles that arise from the different areas of the respiratory tract during a respiratory activity and the change in these proportions during simultaneous respiratory activities, in healthy and in infected states, is poorly described in the literature and precludes further discussion of the site of infection and the site of particle generation are in disease spread.

The presence of pathogen

Obviously secondary infection can only result if pathogen is present in expelled particles. Early observations indicated that regardless of the frequency of respiratory activities or the number of particles generated by the different activities, very few particles actually carry pathogens[15] and that efficient disease transmission is more reliant upon pathogen load in particles and the flow of saliva than atomization of particles.[65] Of further significance is the relationship between particle size and infectivity. While it may be that many particles carry pathogen, pathogens may be inactivated due to desiccation and other environmental factors. Computer models have pointed out that aerosolised transmission dynamics are pathogen-specific, due to pathogen-specific peak shedding and inactivation rates[66]and that models need to include an inactivation parameter to account for pathogens that are no longer infectious.[67]

Type of pathogen

A number of fungal, bacterial and viral pathogens is responsible for causing respiratory infections by utilising aerosolised modes of transmission (see Table 2). The size of these pathogens may firstly dictate the size of the particle carrying the pathogen. For example, larger pathogens such as bacteria have been found in larger particles[54,55,68–70] whereas particles produced from virally infected individuals have been much smaller[49,56,71] (see Fig. 1). Secondly, the size of pathogens may dictate the infectivity of particles. Large pathogens, such as bacteria and fungi, may not be able to be carried at high concentration in particles without breaking up into smaller particles soon after expulsion. In light of this, some large sized pathogens may find it difficult to establish an infection if a high concentration of pathogen is required.

Particles in the past

The PubMed database was used to find studies of expelled particle sizes. The following search strings were used: aerosol

Table 2 Common respiratory pathogens transmitted by aerosolised routes of transmission, as reviewed by the CDC, 2007.[20]

Fungal pathogens	Bacterial pathogens	Viral pathogens
Aspergillus spp. (spores)	*Neisseria meningitidis*	Rhinoviruses
	Mycoplasma pneumoniae	Influenza viruses
	Bordetella pertussis	Respiratory Syncytial virus
	Streptococcus spp.	SARS-associated coronavirus
	Staphylococcus aureus	Rubeola virus
	Mycobacterium tuberculosis	Varicella Zoster virus
		Norovirus
		Rotavirus

AND size, particle AND size, bioaerosol AND size. Our search criteria included: i) an open date limit to 2010; ii) must be in English or translated into English and ii) published studies. Retrieved studies were also reviewed for additional references that did not appear in the PubMed search. Due to the limited number of studies available, conference abstracts were also included in this review. Airborne-sized particles were considered to be particles $\leq$5 μm in size and droplet-sized particles were considered to be particles >5 μm in size.

Early studies of particle size utilised methods of impaction upon solid[15,68,69,72,73] and liquid interfaces[15,56,68,74] and high-speed photography[2] (Table 3). The most basic of the described impactors is the microscope slide and the paper strip. These surfaces are held close to the mouth and nose and capture expelled particles during respiratory activities. The surfaces are then examined by microscopy to measure particle size.[15,56,69,75] This type of impaction is inherently biased towards the collection of droplet-sized particles because of the propensity for airborne-sized particles to remain suspended in the air and not impact. More complex solid impactors, such as the sieve sampler used by Eichenwald et al.[68] (and the Andersen sampler used later by Fennelly et al.[70] and Wainwright et al.[54]) utilises the difference in inertial mass that accompanies changes in particle size to differentiate between different particle sizes. The larger particles, with increased inertial mass, impact on the earlier stages of the sampler while small particles, with less inertial mass, are able to avoid impaction and move through to the latter stages of the sampler. This method is normally used to size particles carrying bacterial and fungal pathogens on an agar surface for later cultivation. A liquid impactor, also known as a liquid impinger, operates similarly to a solid impactor in terms of relying upon inertial mass. However, instead of particles impacting onto a solid surface, liquid impingement requires particles to impact into a liquid, which is then cultivated. Often liquid impingers are accompanied by pre-impinger to initially collect the largest particles. However, as noted by Gerone et al.,[56] droplet-sized particles may be difficult to collect for sizing with a sampler or impactor because of rapid settling after expulsion preventing any collection upon an impaction surface. Previous studies have identified that collection efficiency by impaction is impeded by the effects of drying, which reduces particle size beyond the limits of collection[76–82] and particle bounce (particles bouncing off the impaction surface and onto non-collection surfaces).[82] Physical slippage (particles slipping onto the wrong collection surface for sizing) may also reduce the accuracy of particle sizing. Impaction may be also inhibited by a small particle size which will remain aerosolised or bounce off the settling surface[83–87] — this gives rise to a proclivity for the collection of heavier, large particles, rather than airborne-sized particles. The physical nature of impaction may cause particles to also spread, splash or finger and inevitably distort the true particle size if identified by microscopy.[88–94]

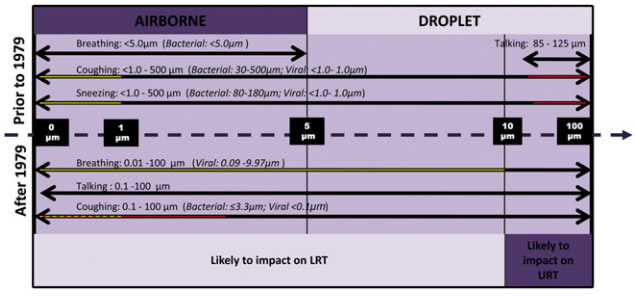

Figure 1 The changing size scale of particle sizes and demarcations of particle size. This schematic indicates the size range of expelled from individuals prior to and after 1979. The black arrow refers to the size range identified from healthy and infected individuals. The red dashed line refers to the size range identified from individuals with known bacterial infections. The yellow dashed line refers to the size range identified from individuals with known viral infections.

Jennison et al. used high-speed photography to resolve and measure particles $\geq$5 μm but was unable to measure smaller particles.[2] Accurate measurement was confounded however by the limited depth of field involved, making particles outside the field of focus appear larger than they are. This study however has importantly contributed to our understanding that different respiratory activities expel different amounts of particles — specifically, while sneezing produces a greater number of particles than coughing, particles from both activities are of a similar size (a sneeze produces 40,000 — 4600 particles with 80% of these particles being smaller than 100 μm compared with coughing which produced up to few hundred particles sized between 20 and >100 μm).

The bias in the methods used in earlier studies weighted the predominant particle size for the four natural respiratory activities towards the production of typical droplet-sized particles rather than airborne-sized particles[2,15,55,69,72,73] with the exception of two studies[56,68] (Table 3): Gerone et al.[56] identified airborne-sized atomization from coughing and sneezing while Eichenwald et al. identified airborne-sized atomization from breathing.[68] Five studies[2,55,56,68,69]

Table 3 Studies that have investigated the size of particles from natural respiratory activities.

Author, Date	Method of sizing (device, where possible)	Infection Status of participants		Predominant particle size range for activity (μm)			
		Healthy	Infected (bacterial/ viral)	Breathing	Coughing	Sneezing	Talking
Heymann et al.,1899[69]	Solid impaction (glass slide with microscopy)	–	Bacterial *Mycobacterium tuberculosis*	–	30–500	–	–
Strauz et al., 1926[72]	Solid impaction (glass slide with microscopy)	–	Unknown infection	–	70–85	–	–
Jennision, 1942[2]	High-speed photography	Healthy	Unknown infection	–	>100[b]	7–100[b]	–
Duguid et al., 1946[15]	Solid impaction (glass slide with microscopy)	Healthy[a]	–	–	100–125 (DN: 8–16)	100–125 (DN: 4–8)	100–125 (DN: 8–16)
Eichenwald et al., 1960[68]	Liquid impaction (impinger) Solid impaction (sieve sampler)	–	Bacterial	<5.0	–	–	–
Buckland et al., 1964[55]	Liquid impaction (impinger)	–	Bacterial Unknown spp.	–	–	80–180	–
Gerone et al., 1966[56]	Solid Impaction Liquid Impaction	–	Viral Unknown spp.	–	<1.0–1.0	<1.0–1.0	–
Loudon et al., 1967[73]	Solid impaction (paper with microscopy)	Healthy[a]	–	–	55.5	–	85
Papineni et al., 1997[95 c]	Optical technology (optical particle counter) Solid impaction (glass slide with transmission electron microscopy)	Healthy	–	OPC: <0.6 SI:>1.0	OPC: <0.6	–	OPC: <0.6
Edwards et al., 2004[100]	Optical technology (optical particle counter)	Healthy	–	0.15–0.19	–	–	–
Fennelly et al., 2004[70]	Solid impaction (Andersen sampler)	–	Bacterial Unknown spp.	–	≤3.3	–	–
Yang et al., 2007[99]	Time-of-flight technology (aerodynamic particle size) Charge separation (scanning mobility particle sizer)	Healthy	–	–	0.62–15.9 (DN 0.58–5.42)	–	–
Fang et al., 2008[101]	Time-of-flight technology (aerodynamic particle sizer)	Healthy	Unknown infection	–	H:<1.0 I: Unknown	–	–
Fabian et al., 2008[49]	Optical technology (optical particle counter)	–	Viral Unknown spp.	0.3–0.5	–	–	–
Hersen et al., 2008[71]	Electrical impaction (electrical low pressure impactor)	Healthy	Viral Unknown spp.	H: 0.09–<0.16 I: 0.09–>9.97	–	–	–
Li et al., 2008[96]	Solid impaction (glass slide with microscopy) Optical technology (dust monitor)	Healthy[a]	–	50–100	50–100	–	50–100
Morawska et al., 2008[9]	Time-of-flight technology (aerodynamic particle sizer)	Healthy	–	0.1–1.0	0.1–1.0	–	0.1–1.0
Chao et al., 2009[98]	Optical technology (interferometric Mie imaging)	Healthy	–	–	4–8	–	4–8

(*continued on next page*)

Table 3 (*continued*).

Author, Date	Method of sizing (device, where possible)	Infection Status of participants		Predominant particle size range for activity (μm)			
		Healthy	Infected (bacterial/ viral)	Breathing	Coughing	Sneezing	Talking
Xie et al., 2009[75]	Solid impaction (glass slide with microscopy) Optical technology (dust monitor)	Healthy	—	—	50—75	—	50—75
Morawska et al., 2009[102]	Time-of-flight technology (aerodynamic particle sizer)	Healthy	—	0.4—1.1	0.4—10.0	—	0.4—4.0
Wainwright et al., 2009[54]	Solid impaction (Andersen sampler)	—	Bacterial Unknown infection	—	≤3.3	—	—
Almstrand et al., 2010[5]	Optical technology (optical particle counter)	Healthy	—	0.3—0.4	—	—	—
Haslbeck et al., 2010[8]	Time-of-flight technology (laser spectrometer)	Healthy	—	0.1—7.0			
Holmgren et al., 2010[7]	Optical technology (optical particle counter) Charge separation (scanning mobility particle sizer)	Healthy	—	OPC: 0.4—4.0 SMPS: 0.01—0.3	—	—	—
Lindsley et al., 2010[97]	Solid impaction (Two-stage aerosol sampler)	—	Viral Influenza spp.	—	<1.0	—	—
Milton et al., 2010[108]	Unknown method	—	Viral Influenza spp.	0.05—5.0	—	—	—
	Expelled particle size range			***0.01—100***	***<0.1—500***	***<1.0—125***	***0.1—125***

Key: DN: Droplet nuclei; H: Healthy; I: Infected; OPC: Optical particle counter; SI: Solid impactor; SMPS: Scanning Mobility Particle Sizer.

[a] Assumed to be healthy individuals but not explicitly described in literature.

[b] No size stratification was made by authors on the basis of diseased state.

[c] Papineni and Rosenthal (1997) measured particles generated from breathing using optical and solid impaction methods — particles from coughing and talking were measured only by optical methods.

demonstrated that a particle size range of <1.0–500 μm was associated with the carriage of microorganisms expelled from breathing, coughing and sneezing. Despite obvious confounding by incomplete capture of all expelled particles and poor resolution of smaller particles, these early studies have consequentially promoted the belief that droplet transmission was the most dominant mode of transmission of infectious aerosols.

Particles in the present

More recently, impaction methods have been used less frequently while the use of charge separation, optical and time-of-flight (TOF) technologies has increased (Table 3). An additional 18 studies have attempted to determine the particle size of expelled aerosols; six studies have used impaction methods[17,54,70,95–97] while fourteen studies have employed optical, charge separation or TOF methods alone or in combination with impaction methods.[5,7–9,17,49,54,75,95,98–102] Of the six studies that used impaction methods,[17,54,70,95–97] two studies determined that the predominant expelled particle size was of droplet-sized particles (range 50–100 μm)[75,96] whereas three studies[54,70,97] complemented the majority of findings from optical, TOF and charge studies[5,7–9,49,71,95,99–102] which described a shift towards a predominant particle size comparable to that of airborne-sized particles (range of 0.01–≤5 μm). An exception to the latter statement is the study by Chao et al. using interferometric Mie imaging (an out-of-focus imaging method which identifies and sizes particles based on the Mie theory of light-scattering properties of spheres[103]) which the investigators acknowledged that the technique is limited in its capacity to detect submicron particles.[98] The sixth impaction study examined impacted particles from breathing using transmission electron microscopy and found the most predominant particle size was >1.0 μm but were unable to define an upper size limit.[95] Interestingly, five studies determined expelled particle size to be either side of the 5 μm delineation for airborne and droplet transmission.[17,71,98,99,102]

The size range found from TOF devices are not unexpected as these devices are more efficient at enumerating particles in the range of 0.7–10 μm and have reduced efficiency for enumerating particles beyond.[104–106] Furthermore, any deviation from a spherical particle shape will affect the acceleration of the particle through the measurement zone, resulting in either under-sizing if particles are non-spherical or over estimating particle size if particles are elongated.[107] Another issue to consider is that the output parameters from different sizing technologies are also different; for examples as detailed in Table 4, impaction and TOF devices measure the aerodynamic diameters of particles whereas devices that measure charge separation measure the mobility diameter. These different output measures confound comparison of particle size.

Despite the inherent weaknesses of TOF technology and interferometric Mie imaging, these recent findings suggest that the burden of infectious disease carriage lies with the airborne-sized particles. Yet, very few published studies, contemporary or otherwise, have attempted to make a clear association between carriage of specific pathogens and particle size.[70,97,108] This is a limited evidence for a definitive understanding of whether pathogen is carried by a certain particle size or if carriage occurs indiscriminate of size or pathogen type. Furthermore, evident in two recent studies,[54,70] as with one of the older studies,[56] is the misconception that one particle is representative of one microorganism. This may not necessarily be the case. Analogous to the cultivation of colonies of microorganisms,[109] one particle may be representative of one microbe or an aggregation of microbes. Furthermore, particles generated in one respiratory event may not all be generated from the same site in the respiratory tract. While this does not afflict the delineation of particle size, it does infer that the establishment of infection may be affected by the factors of particle size, sites of atomization and pathogen load of particles.

Factors that influence particle size

Another point of difference raised by more recent studies that investigated multiple respiratory activities, similar-sized particles were generated by different activities.[75,95,96,98,100,110] Such results may be due to the capabilities of the sizing devices used, however it is prudent to also consider the extraneous or host factors that may drive such similar-sized particles to become vehicles of droplet transmission or vehicles of airborne transmission (Table 5). Further, we now consider the following factors in more detail: 1) relative humidity and evaporation, 2) aggregation and 3) mucus properties.

Evaporation and relative humidity

Wells reported that a water particle of 170 μm diameter generated in dry air (0% water saturation) will fall 2 m in 3 s and will evaporate completely upon settlement to the ground.[10] Under the same conditions, it is also predicted that particles larger than ≥170 μm diameter will fall in the same distance more rapidly while smaller particles will take longer to settle and may remain suspended in the air for a prolonged period, and are likely to completely evaporate. The Wells' evaporation curve is conceptually important for understanding particle fate however the extent and speed of evaporation may be further limited by the presence of hygroscopic salts within expelled particle.[29] Since the first publication of the Well's evaporation curve, other studies have demonstrated it to be incorrect in its details, identifying a comparatively smaller critical particle size (the particle size when the time-of total evaporation equals the total time-of falling 2 m)[17] and longer settling times.[111,112] Also reported by Wells is the effect of relative humidity – where particles are expected to reach equilibrium size slower at higher humidity. Nicas et al. also further comments on the role of relative humidity, indicating that it affects both the rate of evaporation and the equilibrium (final) size of the particle.[29] Relative humidity may also play a role in affecting particle trajectory.[113–115] In particular, increases in vertical and lateral particle movement have previously been associated with decreased relative humidity.[10,17]

Aggregation

Particles may grow after expulsion by aggregation with other particles if released in high concentrations.[116] This

Table 4 Technologies used to measure expelled particles for size.

Technology	Principles of measurement	Output parameter	Examples
Solid impaction	Mechanical impaction onto a solid surface; device may separate particle by an inertial (size) differential caused by size or may require downstream microscopy to determine size	Aerodynamic diameter (Optical diameter, if microscopy is used)	Seive sampler, Andersen sampler, Glass slide (with microscopy)
Liquid impaction	Mechanical impaction into liquid; device separate particles by an inertial (size) differential caused by size	Aerodynamic diameter	Liquid impinger
Electrical impaction	Charges particles to create an inertial differential. Particles impact on different impactor plates according to their charge. Particles on each plate are then enumerated	Aerodynamic diameter	Electrical low pressure impactor
Optical	Relies upon on the light-scattering properties of particles to change with changes in size	Optical diameter	Optical particle counter, Interferonic Mie imaging
High-speed photography	Measurement of particles taken in sharp focus at high speed	Image diameter	High-speed photography
Time-of-flight	Emits a laser beam which particles pass through. Obstruction of the laser beam caused by the particles is detected	Aerodynamic diameter	Aerodynamic particle size
Charge separation	Charges particles and then separates particles according to how fast particles move across an electrical field	Mobility diameter	Scanning mobility particle sizer

would predispose an expelled particle that begins its existence as a vehicle of airborne transmission to then shift to behave as a vehicle of droplet transmission.

Mucus properties

From the 26 studies investigating particle size (Table 3), only thirteen have sized particles from infected individuals. For the purposes of better understanding disease transmission dynamics, particles from healthy individuals may have limited value. In the one study that compared particle sizes from both healthy and infected individuals,[71] it was found that particles from infected individuals were larger than those from healthy individuals. Disease-induced changes, such as increases in mucus composition, quantity and viscosity, have also been observed,[2,117,118] which may suggest that the increase in size is directly related to increases in mucus viscosity. Differences in mucus composition at the mucus—air interface may be accountable for the inter-individual variability observed in studies of different respiratory activities.[70,75,95,119]

Table 5 Factors determining how particles facilitate aerosolised transmission.

Variable	Effect
Relative humidity	Increases in relative humidity slows down evaporation, reducing its effects on particle size[10,113–115]
Aggregation (Particle concentration per expulsion)	Promotes particle aggregation and increases particle size[128]
Pre-exposure to saline in the airways	Increases particle size and reduces particle number[100,129]
Disease state	Induces changes to mucus composition and increases particle size and number[71,129]

Current research gaps

Improved understanding of the behaviour of particles in the transmission of aerosolised disease has the capacity to stimulate the update of current infection control precautions.

Firstly, the relationship between particle size and particle carriage needs to be clearly understood if infection control policies are to utilise a size demarcation, such as 5 μm, to classify modes of transmission. While there is evidence describing the carriage of *Mycobacterium tuberculosis* (about 3.0 μm in size) in particles ≤3.3 μm, few other pathogens have been studied in such detail. Specifically, the size of the particles carrying respiratory viruses, which are 100-fold smaller than a *M. tuberculosis* bacilli, have only been recently determined for influenza.[97,108] Other viruses, such as rhinoviruses, have not been examined and may be carried in particles differently due to differences in shedding and inactivation patterns.[66] Furthermore the effectiveness of these size-based precautions need to be evaluated to ensure they are advocating protectiveness. Without a strong evidence base, the effectiveness of infection control policies based on a size demarcation should remain contentious.

Secondly, improved understanding particle behaviour may illuminate the 'super-spreaders' of respiratory diseases. 'Super-spreaders' are defined as those individuals who infect a large number of contacts.[120,121] 'Super-spreaders' were responsible for infecting large numbers of susceptible individuals during the Severe Acute Respiratory Syndrome outbreak[122–124] and have been identified as possible sources in influenza epidemics.[121] Some healthy individuals make more particles than others when they breathe, cough, sneeze or talk[7,8,70,75,95,119] and that this may be mirrored with a propensity to be a super-spreader and produce an increased number of pathogens to spread infection during illness. Edwards et al. suggest that this effect may be due to the surface properties of the liquids that line the airways.[100] Determining why certain individuals have the proclivity to make more particles than others and what factors contribute to this proclivity is important for limiting disease spread at the level of the individual and needs to be further investigated.

Possibly the most important unanswered question is why some expelled particles during any respiratory activity carry pathogens and why some do not. Evidence from computer models suggest airborne-sized particles are unlikely to carry pathogen[66] — this is in contrast to the limited evidence from particle size measurements suggesting possible airborne carriage of both bacterial and viral pathogens.[54,70,71,97] Further examination of pathogen carriage needs to clarify whether carriage is a function of the particle size, the site of infection, the site of particle generation (which may be different to site of infection), the concentration of the pathogen in the mucus, changes in the nature of the mucus, the virulence of the pathogen itself. Furthermore, are the particles that carry virus similar to those that carry bacteria and fungi? These questions are of paramount significance for understanding the physiological niches pathogens occupy in the human body and during disease transmission. Research efforts needs to be directed towards examining particle ecology and determining the sites of expelled particle generation during different respiratory activities.

Conclusions

We conclude from our review, that:

- Determining the particle size that carries respiratory pathogens has important implications for the use of droplet and airborne infection control measures
- Infectious particles sized less than 10 μm have more serious health implications as they are able to penetrate into the lower respiratory tract to establish infection
- Simultaneous particle generation from different respiratory activities may occur but may not be apparent
- The probability of the propagation of microbial respiratory disease is dependent on the characteristics of clinical disease and the type and presence of a pathogen.
- Evidence has shown particles generated from respiratory activities range from 0.01 up to 500 μm, with a particle size range of 0.05 to 500 μm associated with infection
- Few studies to date have directly associated specific pathogen carriage with a particular size range
- After expulsion, particle size is influenced by host and extraneous factors which may determine how it facilitates aerosolised transmission.

Despite recent evidence[49,101,125,126] suggesting the role of aerosol transmission has been severely underestimated in the past, the lack of strong observational data for the trajectory of individual respiratory pathogens, especially for viruses, expelled from different respiratory activities discourages updating of the current infection control (5 μm — 1 m) paradigm.[127] This may be in light of recent computer models which suggest that while airborne transmission can occur, very few airborne-sized particles can carry pathogen.[66]

Regardless of the complexities and limitations of sizing particles and the contention of size cut-offs, it remains that particles have been observed to occupy a size range between 0.05 and 500 μm. Even using the conservative cut-off of 10 μm, rather than the 5 μm to define between airborne and droplet transmission, this size range indicates that particles do not exclusively disperse by airborne transmission or via droplet transmission but rather avail of both methods simultaneously. This suggestion is further supported by the simultaneous detection of both large and small particles.[2,71,98,99,102] In line with these observations and logic, current dichotomous infection control precautions should be updated to include measures to contain both modes of aerosolised transmission. This may require airborne precautions to be used when at risk of any aerosolised infection, as airborne precautions are considered as a step-up from droplet precautions. Further elucidation of particle size and the dynamics of particles in disease transmission provides the opportunity for increased understanding of the ecological niches of respiratory pathogens and the development of improved measures to counter the spread of communicable respiratory diseases.

Acknowledgement

The authors would like to acknowledge the contribution of Dr Jenna Iwasenko for the provision of German translations of the earlier literature.

References

1. Slonim NB, Chapin JL. *Respiratory Physiology*. Saint Louis: The C.V. Mosby Company; 1967.
2. Jennison MW. Atomizing of mouth and nose secretions into the air as revealed by high-speed photography. *Aerobiology* 1942; **17**:106–28.
3. Ross BB. Physical dynamics of the cough mechanism. *Journal of Applied Physiology* 1955;**8**:264–9.
4. Gebhart J, Anselm A, Heyder J, Stalhofen W. The human lung as aerosol particle Generator. *Journal of Aerosol Medicine* 1988;**1**:196–7.
5. Almstrand A-C, Bake B, Ljungstrom E, Larsson P, Bredberg A, Mirgorodskaya E, et al. Effect of airway opening on production of exhaled particles. *Journal of Applied Physiology* March 1, 2010;**108**(3):584–8.
6. Johnson GR, Morawska L. The mechanism of breath aerosol formation. *Journal of Aerosol Medicine and Pulmonary Drug Delivery* 2009;**22**(3):229–37.
7. Holmgren H, Ljungström E, Almstrand A-C, Bake B, Olin A- C. Size distribution of exhaled particles in the range from 0.01 to 2.0 [mu]m. *Journal of Aerosol Science* 2010;**41**(5):439–46. doi:10.1016/j.jaerosci.2010.02.011.
8. Haslbeck K, Schwarz K, Hohlfeld JM, Seume JR, Koch W. Submicron droplet formation in the human lung. *Journal of Aerosol Science* 2010;**41**(5):429–38. doi:10.1016/j.jaerosci.2010.02.010.
9. Morawska L, Johnson GR, Ristovski ZD, Hargreaves M, Mengersen K, Corbett S, et al. Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *Journal of Aerosol Science* 2008;**40**(1):256–69.
10. Wells WF. On airborne infection: study II. Droplets and droplet nuclei. *American Journal of Hygiene* 1934;**1934**(20):611–8.
11. World Health Organisation Western Pacific Region. Practical guidelines for infection control in health care facilities [Online Guidelines] Manila: WHO; 2005 [updated 1 January 2005; cited 2008 19 November]; Available from, http://www.wpro.who.int/sars/docs/practicalguidelines/dec2004/chapter3.pdf.
12. Garner JS. Guideline for isolation precautions in hospitals. *Infection Control and Hospital Epidemiology* 1996;**17**(1):53–80.
13. Macias AE, de la Torre A, Moreno-Espinosa S, Leal PE, Bourlon MT, Ruiz-Palacios GM. Controlling the novel A (H1N1) influenza virus: don't touch your face! *Journal of Hospital Infection* 2009;**73**:280–91.
14. Booth TimothyÀ F, Kournikakis B, Bastien N, Ho J, Kobasa D, Stadnyk L, et al. Detection of Airborne Severe Acute Respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. *The Journal of Infectious Diseases* 2005;**191**(9):1472–7.
15. Duguid JP. The size and the duration of air-carriage of respiratory droplets and droplet-nuclei. *The Journal of Hygiene* 1946;**44**(6):471–9.
16. Wang B, Zhang A, Sun JL, Liu H, Hu J, Xu LX. Study of SARS transmission via liquid droplets in air. *Journal of Biomechanical Engineering* 2005;**127**(1):32–8.
17. Xie X, Li Y, Chwang ATY, Ho PL, Seto WH. How far droplets can move in indoor environments – revisiting the Wells evaporation-falling curve. *Indoor Air* 2007;**17**:211–25.
18. Hamburger M, Roberston OH. Expulsion of Group A hemolytic streptococci in droplets and droplet nuclei by sneezing, coughing and talking. *American Journal of Medicine* 1946; **1946**(4):690–701.
19. WHO. Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care. WHO/CDS/EPR/20076 [serial on the Internet] 2007 August 18, 2008]: Available from, http://www.who.int/csr/resources/publications/WHO_CDS_EPR_2007_6c.pdf.
20. Siegel JD, Rhinehart E, Jackson M, Chiarello L, Committee HICPA. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. 2007 [cited 2008 December 8]; Available from, http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf.
21. Austin E, Brock J, Wissler E. A model for deposition of stable and unstable aerosols in the human respiratory tract. *American Industrial Hygiene Association Journal* 1979;**40**(12):1055–66.
22. Morrow PE. Physics of airborne particles and their deposition in the lung. *Annals of the New York Academy of Sciences* 1980;**353**:71–80.
23. Stalhofen W, Gebhart J, Heyder J, Scheuch G. Deposition pattern of droplets from medical nebulizers in the human respiratory tract. *Bulletin Europeen de Physiopathologie Respiratoire* 1983;**19**:459–63.
24. Yu CP, Taulbee DB. A theory of predicting respiratory tract deposition of inhaled particles in man. *Inhaled Particles* 1975;**4** (1):35–47.
25. Brain JD, Valberg PA. Deposition of aerosol in the respiratory tract. *American Review of Respiratory Disease* 1979;**120**: 1325–72.
26. Hatch TF. Distribution and deposition of inhaled particles in respiratory tract. *Microbiology and Molecular Biology Reviews* 1961;**25**:237–40.
27. Knight V. Viruses as agents as airborne contagion. *Annals of the New York Academy of Science* 1980;**353**:147–56.
28. Yeh HC, Phalen RF, Raabe OG. Factors influencing the deposition of inhaled particles. *Environmental Health Perspectives* 1976;**15**:147–56.
29. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogens. *Journal of Occupational and Environmental Hygiene* 2005;**2**:143–54.
30. Cheng YS, Yamada Y, Yeh HC, Swift DL. Diffusional deposition of ultrafine aerosols in a human nasal cast. *Journal of Aerosol Science* 1988;**19**(6):741–51.
31. Cheng YS, Yeh HC, Swift DL. Aerosol deposition in human nasal airway for particles 1 nm to 20 μm radiation. *Protection Dosimetry* 1991;**38**(1):41–7.
32. Licht W. The movement of aerosol particles. *Journal of Society of Cosmetic Chemists* 1972;**23**:657–78.
33. Weber TP, Stilianakis NI. Inactivation of infuenza A viruses in the environment and modes of transmission: a critical review. *Journal of Infection* 2008;**57**:361–73.
34. Stilianakis NI, Drossinos Y. Dynamics of infectious disease transmission by inhalable respiratory droplets. *Journal of the Royal Society Interface* 2010;**7**:1355–66.
35. Tellier R. Review of aerosol transmission of influenza A virus. *Emerging Infectious Diseases* 2006;**12**(11):1657–62.
36. Fendrick AM, Monto AS, Nightengale B, Sarnes M. The Economic burden of non-influenza-related viral respiratory tract infection in the United states. *Archives of Internal Medicine* February 24, 2003;**163**(4):487–94.
37. MacFarlane J, Colville A, Guion A, MacFarlane R, Rose DH. Prospective study of aetiology and outcome of adult lower-respiratory-tract infections in the community. *Lancet* 1993;**341**: 511–4.
38. Tupasi TE, Velmonte MA, Sanvictores MEG, Abraham L, De Leon DE, Tan SA, et al. Determinants of morbidity and mortality due to acute respiratory infections: implications for interventions. *Journal of Infectious Diseases* 1988;**157**(4):615–23.
39. Garbino J, Gerbase MW, Wunderli W, Deffernez C, Thomas Y, Rochat T, et al. Lower respiratory viral illnesses: improved diagnosis by molecular methods and clinical impact. *American Journal of Respiratory and Critical Care Medicine* December 1, 2004;**170**(11):1197–203.

40. Mok JY, Simpson H. Outcome of acute lower respiratory tract infection in infants: preliminary report of seven-year follow-up study. *British Medicine Journal (Clin Res Ed)* July 31, 1982;**285**(6338):333–7.
41. Sigurs N, Gustafsson PM, Bjarnason R, Lundberg F, Schmidt S, Sigurbergsson F, et al. Severe respiratory syncytial virus Bronchiolitis in infancy and asthma and allergy at age 13. *AJRCCM* 2004;**171**:137–41.
42. Barker DJP, Godfrey KM, Fall C, Osmond C, Winter PD, Shaheen SO. Relation of birth weight and childhood respiratory infection to adult lung function and death from chronic obstructive airways disease. *BMJ* 1991;**303**:671–5.
43. You D, Becnel D, Wang K, Ripple M, Daly M, Cormier SA. Exposure of neonates to Respiratory Syncytial Virus is critical in determining subsequent airway response in adults. *Respiratory Research* 2006;**7**(1):107.
44. Illi S, von Mutius E, Lau S, Bergmann R, Niggemann B, Sommerfeld C, et al. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. *BMJ* February 17, 2001;**322**(7283):390–5. 2001.
45. Hiatt PW, Grace SC, Kozinetz CA, Raboudi SH, Treece DG, Taber LH, et al. Effects of viral lower respiratory tract infection on lung function in infants with cystic fibrosis. *Pediatrics* March 1, 1999;**103**(3):619–26.
46. Navarro EE, Gonzaga NC, Lucero M, Queipo SC, Schroeder I, Gomez MLO, et al. Clinicopathologic studies of children who die of acute lower respiratory tract infections: mechanisms of death. *Reviews of Infectious Diseases* 1990;**12**(Suppl. 8): s1065–73.
47. Glezen WP, Greenberg SB, Atmar RL, Piedra PA, Couch RB. Impact of respiratory virus infections on Persons with chronic Underlying conditions. *JAMA* 2000;**283**(4):499–505.
48. Stelzer-Braid S, Oliver BG, Blazey AJ, Argent E, Newsome TP, Rawlinson WD, et al. Exhalation of respiratory viruses by breathing, coughing and talking. *Journal of Medical Virology* 2009;**81**:1674–9.
49. Fabian P, McDevitt JJ, DeHaan WH, Fung ROP, Cowling BJ, Chan KH, et al. Influenza virus in human exhaled breath: an observational study. *PLoS ONE* 2008;**3**(7):e2691. 07/16.
50. Fabian P, McDevitt JJ, Lee WM, Houseman EA, Milton DK. An optimized method to detect influenza virus and human rhinovirus from exhaled breath and the airborne environment. *Journal of Environmental Monitoring* 2009;**11**(2):314–7.
51. Huynh KN, Oliver BG, Stelzer S, Rawlinson W, Tovey ER. A new method for sampling and detection of exhaled respiratory virus aerosols. *Clinical Infectious Diseases* 2008;**46**:93–5.
52. Winslow CE, Robinson EA. An investigation of the extent of bacterial pollution of the atmosphere by mouth-Spray. *American Journal of Public Hygiene* 1910;**20**(3):566–9.
53. Koeniger H. Untersuchungen uber die Frage der Tropfcheninfection. *Ztschr F Hyg* 1900;**36**:125.
54. Wainwright CE, France MW, O'Rourke P, Anuj S, Kidd TJ, Nissen MD, et al. Cough-generated aerosols of *Pseudomonas aeruginosa* and other Gram-negative bacteria from patients with cystic fibrosis. *Thorax* 2009;**64**:926–31.
55. Buckland FE, Tyrrell DAJ. Experiments on the spread of Colds: !. Laboratory studies on the Dispersal of nasal Secretion. *Journal of Hygiene* 1964;**62**(3):365–77.
56. Gerone PJ, Couch RB, Keefer GV, Douglas RG, Derrenbacher EB, Knight V. Assessment of experimental and natural viral aerosols. *Bacteriological Reviews* 1966;**30**:576–84.
57. Couch RB, Cate TR, Douglas RGJ, Gerone PJ, Knight V. Effect of route of inoculation on experimental respiratory disease in volunteers and evidence for airborne transmission. *Bacteriological Reviews* 1966;**30**:517–29.
58. Lee C-S, Lee J-H. Dynamics of clinical symptoms in patients with pandemic influenza A (H1N1). *Clinical Microbiology and Infection* 2010;**16**(4):389–90.
59. Monto AS, Gravenstein S, Elliott M, Colopy M, Schweinle J. Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine* 2000;**160**:3243–7.
60. Gupta JK, Lin C-H, Chen Q. Flow dynamics and characterization of cough. *Indoor Air* 2009;**19**:517–25.
61. Call SA, Vollenweider MA, Hornung CA, Simel DL, McKinney WP. Does this patient have influenza? *JAMA* February 23, 2005;**293**(8):987–97.
62. Seijo-Martinez M, Varela-Freijanes Grandes J, Vazquez F. Sneeze related area in the medulla: localisation of the human sneezing centre? *Journal of Neurology and Neurosurgery Psychiatry* 2006;**77**(4):559–61.
63. Hyden D, Arlinger S. On light-induced sneezing. *Eye* 2009;**23** (11):2112–4.
64. Martin RA, Handel SF, Aldama AE. Inability to sneeze as a manifestation of medullary neoplasm. *Neurology* 1991;**41**: 1675–6.
65. Rubbo SD, Benjamin M. Transmission of Haemolytic streptococci. *The Journal of Hygiene* 1953;**51**(2):278–92.
66. Atkinson MP, Wein LM. Quantifying the routes of transmission for pandemic influenza. *Bulletin of Mathematical Biology* 2008;**70**(3):820–67.
67. Li S, Eisenberg JNS, Spicknall IH, Koopman JS. Dynamics and control of infections transmitted from person to person through the environment. *American Journal of Epidemiology* 2009;**170**(2):257–65.
68. Eichenwald HF, Kotsevalov O, Fasso LA. The "Cloud Baby": an example of bacterial-viral interaction. *American Journal of Diseases of Children* 1960;**100**:30–43.
69. Heymann B. Ueber die Ausstreuung infectioser Tropfchen beim Husten der Phthisiker. *Medical Microbiology and Immunology* 1899;**30**(1):139–62 [translated].
70. Fennelly KP, Martyny JW, Fulton KT, Orme IM, Cave DM, Heifets LB. Cough-generated Aerosols of *Mycobacterium tuberculosis*. *American Journal of Respiratory Critical Care Medicine* 2004;**169**:604–9.
71. Hersen G, Moularat S, Robine E, Ghin E, Corbet S, Vabret A. Impact of health on particle size of exhaled respiratory aerosols: case-control study. *Clean* 2008;**36**(7):572–7.
72. Strausz W. Z Hyg. 1926;105:416 [cited by Duguid, 1946].
73. Loudon RG, Roberts RM. Droplet explusion from the respiratory tract. *American Review of Respiratory Disease* 1967;**95** (3):435–42.
74. Downie AW, Meiklejohn M, St. Vincent L, Rao AR, Sundara Babu BV, Kempe CH. The recovery of Smallpox virus from patients and their environment in a Smallpox hospital. *Bulletin of the World Health Organisation* 1965;**33**:615–22.
75. Xie X, Li Y, Sun H, Liu L. Exhaled droplets due to talking and coughing. *Journal of the Royal Society Interface* 2009;**6**: s703–14.
76. Li C-S, Hao M-L, Lin W-H, Chang C-W, Wang C-S. Evaluation of microbial samplers for bacterial microorganisms. *Aerosol Science and Technology* 1999;**30**:100–8.
77. Fabian P, McDevitt JJ, Houseman EA, Milton DK. Airborne influenza virus detection with four aerosol samplers using molecular and infectivity assays: considerations for a new infectious virus aerosol sampler. *Indoor Air* 2009;**19**:433–41.
78. Tseng C-C, Li C-S. Collection efficiencies of aerosol samplers for virus-containing aerosols. *Journal of Aerosol Science* 2005;**36**(5–6):593–607.
79. Stewart SL, Grinshpun SA, Willeke K, Terzieva S, Ulevicius V, Donnelly J. Effect of impact stress on microbial recovery on an agar surface. *Applied and Environmental Microbiology* April 1, 1995;**61**(4):1232–9.
80. Saldanha R, Manno M, Saleh M, Ewaze JO, Scott JA. The influence of sampling duration on recovery of culturable fungi using the Andersen N6 and RCS bioaerosol samplers. *Indoor Air* 2008;**18**:464–72.

81. Hogan CJ, Kettleson EM, Lee M-H, Ramaswami B, Angenent LT, Biswas P. Sampling methodologies and dosage assessment techniques for submicrometre and ultrafine virus aerosol particles. *Journal of Applied Microbiology* 2005;**99**: 1422–34.
82. Grinshpun SA, Willeke K, Ulevicius V, Juozaitis A, Terzieva S, Donnelly J, et al. Effect of impaction, bounce and Reaerosolization on the collection efficiency of impingers. *Aerosol Science and Technology* 1997;**26**(4):326–42.
83. Esmen NA, Ziegler P, Whitfield R. The adhesion of particles upon impaction. *Journal of Aerosol Science* 1978;**9**(6): 547–56. doi:10.1016/0021-8502(78)90020-4.
84. Lai C-Y, Huang S-H, Chang C-P, Lin J-Y. Reducing particle bounce and loading effect for a multi-hole impactor. *Aerosol Science and Technology* 2008;**42**(2):114–22.
85. Chang M, Kim S, Sioutas C. Experimental studies on particle impaction and bounce: effects of substrate design and material. *Atmospheric Environment* 1999;**33**:2313–22.
86. Dzubay TG, Hines LE, Stevens RK. Particle bounce errors in cascade impactors. *Atmospheric Environment* 1976;**10**(3): 229–34. 1976.
87. Yamamoto N, Fujii M, Endo O, Kumagai K, Yanagisawa Y. Broad range observation of particle deposition on greased and non-greased impaction surfaces using a line-sensing optical microscope. *Journal of Aerosol Science* 2002;**33**(12):1667–79.
88. Ukiwe C, Kwok DY. On the maximum spreading diameter of impacting droplets on well-prepared solid surfaces. *Langmuir* 2004 12/18/;**21**(2):666–73.
89. Moita AS, Moreira AL. The deformation of single droplets impacting onto a flat surface. *Journal of Fuels and Lubricants*; 2002:1477–89 [SAE 2002 Transactions].
90. Bhunia Impingement Splattering SK, Disturbance Surface. *Evolution on turbulent liquid jets in Gases*. Cambridge: Massachusetts Institute of Technology; 1993.
91. ILASS America, 19th Annual conference on liquid atomization and spray systems In: Jepsen RA, Yoon SS, Demosthenous B, editors. *Effects of air on splashing during a droplet impact*. Toronto: Canada; 2006.
92. Hawke SR. *Effects of a thin, flexible nozzle on droplet formation and impingement*. Corvallis: Oregon State University; 2006.
93. Park H, Carr WW, Zhu J, Morris JF. Single drop impaction on a solid surface. *AIChE Journal* 2003;**49**(10):2461–71.
94. Sikalo S, Marengo M, Tropea C, Ganic EN. Analysis of impact of droplets on horizontal surfaces. *Experimental Thermal and Fluid Sciences* 2002;**25**:503–10.
95. Papineni RS, Rosenthal FS. The size distribution of droplets in the exhaled breath of healthy human Subjects. *Journal of Aerosol Medicine* 1997;**10**(2):105–16.
96. Li YG, Chwang ATY, Seto WH, Ho PL, Yuen PL. Understanding droplets produced by nebulisers and respiratory activities. *Hong Kong Medical Journal* 2008;**14**(Suppl. 1):s29–32.
97. Lindsley WG. *Environmental and source measurements of airborne influenza. Current research issues – personal protective equipment for healthcare workers to prevent transmission of pandemic influenza and other viral respiratory infections*. Washingon, DC: Institute of Medicine; 2010. June 3.
98. Chao CYH, Wan MP, Morawska L, Johnson GR, Ristovski ZD, Hargreaves M, et al. Characterization of expiration air jets and droplet size distributions immediately at the mouth opening. *Journal of Aerosol Science* 2009;**40**(2):122–33. doi: 10.1016/j.jaerosci.2008.10.003.
99. Yang S, Lee GWM, Chen C-M, Wu C-C, Yu K-P. The size and concentration of droplets generated by coughing in human Subjects. *Journal of Aerosol Medicine* 2007;**20**(4):484–94.
100. Edwards DA, Man JC, Brand P, Katstra JP, Stone HA, Nardell E, et al. Inhaling to mitigate exhaled bioaersols. *PNAS* 2004;**101** (50):17383–8.
101. Fang M, Lau APS, Chan CK, Hung CT, Lee TW. Aerodynamic properties of biohazardous aerosols in hospitals. *Hong Kong Medical Journal* 2008;**14**(1):26–8.
102. Morawska L, Johnson GR, Ristovski Z, Hargreaves M, Mengersen K, Chao C, et al., editors. Droplets expelled during human expiratory activities and their origins. Paper-1023. In: 11th International conference on indoor air quality and climate paper, Copenhagen, Denmark; 2009.
103. Glover AR, Skippon SM, Boyle RD. Interferometric laser imaging for droplet sizing: a method for droplet-size measurement in sparse spray systems. *Applied Optics* 1995;**34**(36):8409–21.
104. Kinney PD, Pui DYH. Inlet efficiency study for the TSI aerodynamic particle sizer. *Particle and Particle Systems Characterization* 1995;**12**:188–93.
105. Armendariz A, Leith D. Concentration measurement and counting efficiency for the aerodynamic particle sizer 3320. *Aerosol Science* 2002;**33**:133–48.
106. Peters TM, Leith D. Concentration measurement and counting efficiency of the aerodynamic particle sizer 3321. *Aerosol Science* 2003;**34**:627–34.
107. Marshall IA, Mitchell JP. The behaviour of spheroidal particles in time-of-flight aerodynamic particle sizers. *Journal of Aerosol Science* 1992;**23**(Suppl. 1):s297–300.
108. Milton DK, Fabian P, Angel M, Perez DR, McDevitt JJ. Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks swine origin H1N1: the first pandemic of the 21st Century; April 18–20, 2010; [Atlanta, Georgia].
109. Prescott LM, Harley JP, Klein DA. *Microbial growth. Microbiology*. 5th ed. New York: McGraw-Hill; 2002. pp. 118.
110. Morawska L. Droplet fate in indoor environments, or can we prevent the spread of infection? *Indoor Air* 2006;**16**(5):335–47.
111. Wan MP, Chao CYH. Transport characteristics of expiratory droplets and droplet nuclei in indoor environments with different Ventilation airflow patterns. *Journal of Biomedical Engineering* 2007;**129**:341–53.
112. Nichol K, Bigelow P, O'Brien-Pallas L, McGeer A, Manno M, Holness DL. The individual, environmental, and organizational factors that influence nurses' use of facial protection to prevent occupational transmission of communicable respiratory illness in acute care hospitals. *American Journal of Infection Control* 2008;**36**(7):481–7.
113. Schaffer FL, Soergel ME, Straube DC. Survival of airborne influenza virus: effects of propagating host, relative humidity and composition of spray Fluids. *Archives of Virology* 1976;**51**:263–73.
114. Lowen AC, Mubareka S, Steel J, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. *PLoS Pathogens* 2007;**3**(10):e151.
115. Hemmes JH, Winkler KC, Kool SM. Virus Survival as a Seasonal factor in influenza and Poliomyelitis. *Nature* 1960;**188**:430–1.
116. Verreault D, Moineau S, Duchaine C. Methods for sampling of airborne viruses. *Microbiology and Molecular Biology Reviews* September 1, 2008;**72**(3):413–44.
117. Kozlova I, Vanthanouvong V, Marie J, Roomans GM. Composition of airway surface liquid determined by X-ray microanalysis. *Upsala Journal of Medical Sciences* 2006;**111**(1):137–53.
118. Vanthanouvong V, Kozlova I, Johannesson M, Nääs E, Nordvall SL, Dragomir A, et al. Composition of nasal airway surface liquid in cystic fibrosis and other airway diseases determined by X-ray microanalysis. *Microscopy Research and Technique* 2006;**69**(4):271–6.
119. Fairchild CI, Stampfer JF. Particle concentration in exhaled breath. *American Industrial Hygiene Association Journal* 1987;**48**(11):948–9.
120. Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddard LJ, Hedley AJ, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health Intervention. *Science* 2003;**300**:1961–6.

121. Glass LM, Glass RJ. Social contact networks for the spread of pandemic influenza in children and teenagers. *BMC Public Health* 2008;**8**(61).
122. Small M, Tse CK, Walker DM. Super-spreaders and the rate of transmission of the SARS virus. *Physica D* 2006;**215**:146—58.
123. Wang SH, Li YM, Sun BC, Zhang SW, Zhao WH, Wei MT, et al. The SARS outbreak in a general hospital in Tianjin, China — the case of super-spreader. *Epidemiology and Infection* 2006;**134**:786—91.
124. Abdullah ASM, Tomlinson B, Cockram CS, Neil Thomas G. Lessons from the Severe acute respiratory Syndrome outbreak in Hong Kong. *Emerging Infectious Diseases* 2003;**9**(9):1042—5.
125. Lindsley WG, Blanchere FM, Davis KA, Pearce TA, Fisher MA, Khakoo R, et al. Distribution of airborne influenza virus and respiratory syncytial virus in an urgent care medical Clinic. *Clinical Infectious Diseases* 2010;**50**(5):693—8.
126. Blachere FM, Lindsley WG, Pearce TA, Anderson SE, Fisher M, Khakoo R, et al. Measurement of airborne influenza virus in a hospital emergency department. *Clinical Infectious Diseases* 2009;**48**(4):438—40.
127. Roy CJ, Milton DK. Airborne transmission of communicable infection — the elusive pathway. *New England Journal of Medicine* 2004;**350**(17):1710—2.
128. Fiegel J, Clarke R, Edwards DA. Airborne infectious disease and the suppression of pulmonary bioaerosols. *Drug Discovery Today* 2006;**11**(1—2):51—7.
129. Zayas G, Dimitry J, Zayas A, O'Brien D, King M. A new paradigm in respiratory hygiene: increasing the cohesivity of airway secretions to improve cough interaction and reduce aerosol dispersion. *BMC Pulmonary Medicine* 2005;**5**(11): 1—12.