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Risk of indoor airborne infection transmission estimated from carbon dioxide concentration

Abstract The Wells–Riley equation, which is used to model the risk of indoor airborne transmission of infectious diseases such as tuberculosis, is sometimes problematic because it assumes steady-state conditions and requires measurement of outdoor air supply rates, which are frequently difficult to measure and often vary with time. We derive an alternative equation that avoids these problems by determining the fraction of inhaled air that has been exhaled previously by someone in the building (rebreathed fraction) using CO_2 concentration as a marker for exhaled-breath exposure. We also derive a non-steady-state version of the Wells–Riley equation which is especially useful in poorly ventilated environments when outdoor air supply rates can be assumed constant. Finally, we derive the relationship between the average number of secondary cases infected by each primary case in a building and exposure to exhaled breath and demonstrate that there is likely to be an achievable critical rebreathed fraction of indoor air below which airborne propagation of common respiratory infections and influenza will not occur.

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Practical Implications
The likelihood of airborne transmission of infection indoors can be estimated using continuous CO_2 measurements and the risk equation developed in this paper without assuming that the concentration of an infectious agent has reached steady-state and without measuring the outdoor air supply rate or assuming that it remains constant over time.

Introduction

Person-to-person transmission of infectious agents through the recirculated air of modern office buildings is a potential source of significant morbidity (Fisk and Rosenfeld, 1997; Milton et al., 2000) and targeted for research funding by the US National Occupational Research Agenda (National Institute for Occupational Safety and Health, 1998). Accurate mathematical models of airborne infection are needed to aid in designing future epidemiologic studies, for estimating the public health impact of building design parameters, and for estimating risk such as from secondary transmission of biological warfare agents. The Wells–Riley equation (Barnhart et al., 1997; Catanzaro, 1982; Fennelly and Nardell, 1998; Nardell et al., 1991; Nicas, 2000; Riley and Nardell, 1989; Riley et al., 1978), which requires knowledge of the outdoor air supply rate, is commonly used to compute risk of airborne infection. The outdoor air supply rate can be measured directly or estimated based on CO_2 measurements. A key assumption of this equation is that airborne infectious particles are droplet nuclei that remain suspended in air for long periods of time and that their concentration is at a steady-state level throughout the exposure.

Exhaled breath is the vehicle for release of airborne infectious particles. Exhaled breath contains almost 40,000 p.p.m. of CO_2 compared with approximately 350 p.p.m. in outdoor air. Because most buildings do not contain significant internal sources of CO_2, apart from occupants, we may consider CO_2 as a surrogate for exhaled breath. Thus, the fraction of inhaled air that has been exhaled previously by someone in the building (rebreathed fraction) is easily computed. Because

airborne communicable infection can only be acquired by inhaling air that has been previously exhaled and because CO_2 is a marker for exhaled breath, it would be useful to be able to relate infection risk directly to the rebreathed fraction, particularly now that continuous monitoring of CO_2 concentration is relatively inexpensive and convenient. A method to compute infection risk based directly on continuous CO_2 monitoring would also allow elimination of assumptions about steady-state conditions, constant outdoor air supply rates, and the relationship between CO_2 concentration and outdoor air supply rate. In addition, it would remove the necessity of making direct measurements of outdoor air supply rate for the purposes of estimating infection risk. To achieve this goal, we begin by revisiting the Wells–Riley equation.

Wells–Riley equation revisited

For the purpose of estimating the probability of airborne transmission of an infectious agent indoors, Riley et al. (1978) developed what is now called the Wells–Riley equation:

$$P = \frac{D}{S} = 1 - \exp\left(-\frac{Ipqt}{Q}\right) \quad (1)$$

where P is the probability of infection for susceptibles, D is the number of disease cases, S is the number of susceptibles, I is the number of infectors, p is the breathing rate per person (m^3/s), q is the quantum generation rate by an infected person (quanta/s), t is the total exposure time (s), and Q is the outdoor air supply rate (m^3/s).

The key to understanding Equation 1 is the often misunderstood parameter q, the generation rate of infectious quanta by an infected person. Wells (1955) conceived the idea of a quantum (or infectious dose) in an effort to describe the stochastic behavior of airborne infection. The fact that a quantum of infection may be a large number of organisms does not mean that more than one organism ultimately initiates infection and does not support the concept of a multiple hit model as suggested by some authors (Nicas, 1996). Wells (p. 126) pointed out that even when a quantal dose is much more than a single organism; 'infection bears a Poisson relation to this dose… The host responds as though a single organism penetrated to a vulnerable locus where conditions are favorable to its multiplication and induction of infection.' Hence, exposure to one quantum of infection gives an average probability of 63% ($1-e^{-1}$) of becoming infected (essentially an infectious dose 63%, ID_{63}). For some organisms, the probability of any one organism finding and taking advantage of a vulnerable locus is extremely low.

The belief that multiple independently deposited organisms are required to initiate infection is not borne out by biological evidence, nor is it biologically plausible. Thus, q represents the generation rate of infectious doses, not organisms or infectious particles; it is the average infectious source strength of infected individuals.

In order to derive Equation 1, Riley et al. (1978) made two other salient assumptions: (1) a well-mixed airspace, and (2) steady-state conditions. The first assumption implies that an infectious particle has an equal chance of being anywhere within a building's airspace, regardless of when and where the infectious particle was generated. The second assumption implies that the quantum concentration and the outdoor air supply rate remain constant with time. Here, we show that using CO_2 concentration as a biomarker for exhaled breath allows derivation of a mathematical model that does not require the assumption of steady-state conditions. An additional assumption is that elimination of infectious particles caused by loss of viability, filtration, settling, and other mechanisms are small compared with removal by ventilation; the usefulness of the proposed model is, of coarse, dependent on the validity of this assumption as discussed below.

Results

Rebreathed fraction

Of the total CO_2 in indoor air, a portion is of human origin, and assuming no other sources, the remainder enters the room with the outdoor air. Thus, if the airspace is well mixed,

$$C_a V_e = (C - C_o)V \quad (2)$$

where C_a is the volume fraction of CO_2 *added* to exhaled breath during breathing, V is the volume of the shared air space, V_e is the equivalent volume of exhaled breath contained in indoor air (m^3), C is the volume fraction of CO_2 in indoor air, and C_o is the volume fraction of CO_2 in outdoor air.

The volume fraction of CO_2 added to exhaled breath and the rate of breathing remain essentially constant during short-duration exposures to inspired CO_2 concentrations up to approximately 15,000 p.p.m. (Kellogg, 1964; Schaefer et al., 1963). At low levels of oxygen consumption, such as office work, the CO_2 production rate and breathing rate are approximately 0.30 l/min and 8.0 l/min, respectively, giving a C_a of 0.038.

Solving Equation 2 for V_e/V gives

$$f = \frac{V_e}{V} = \frac{C - C_o}{C_a} \quad (3)$$

where f is equivalent to the fraction of indoor air that is exhaled breath, which is also the rebreathed fraction. Thus, if the indoor CO_2 concentration is 700 p.p.m.

above the outdoor level, which according to the American Society of Heating, Refrigeration, and Air-Conditioning Engineers (ASHRAE, 1999a) is the maximum CO_2 concentration providing air quality that will be satisfactory to a majority of people 'with respect to human bioeffluents (body odor)', then an inhaled breath would contain 1.8% exhaled breath. Equation 3 is valid whether or not steady-state conditions have been reached.

For the total exposure period t, the time-weighted average fraction of indoor air that is exhaled breath ($\bar{f}$) can then be computed easily by integrating f over time and dividing by the elapsed time.

Carbon dioxide-based risk equation

As was done for the derivation of the Wells–Riley equation, we assume that the airspace is well mixed; this assumption has been widely used to predict contaminant concentration indoors, although its validity has not been well verified. We also assumed that elimination of infectious particles caused by loss of viability, filtration, gravitational and diffusional deposition on surfaces, and other mechanisms are small compared with removal by ventilation. For further discussion of this assumption, see below.

In addition to the above assumptions, if the quantum generation rate (q), the breathing rate (p), the number of infectors (I), and people in the ventilated space (n) remain constant, then the quantum concentration in the ventilated space (N) is equal to the concentration of quanta in the exhaled breath of infectors (q/p) multiplied by the volume fraction of air in the space that was exhaled by infectors (fI/n):

$$N = \frac{fIq}{np} \tag{4}$$

Thus, for the total exposure period (t), the average quantum concentration ($\bar{N}$) can be obtained directly from the average fraction of indoor air that is exhaled breath ($\bar{f}$):

$$\bar{N} = \frac{\bar{f}Iq}{np} \tag{5}$$

The average number of quanta breathed by a susceptible person ($\bar{\mu}$) can be calculated from the following equation:

$$\bar{\mu} = pt\bar{N} \tag{6}$$

As discussed by Wells (1955), the number of susceptible individuals infected is Poisson distributed. Thus, the probability that a susceptible person remains uninfected is equal to $e^{-\bar{\mu}}$, and its complement is the probability of infection (P):

$$P = 1 - e^{-\bar{\mu}} \tag{7}$$

Substituting $\bar{N}$ from Equation 5 into Equation 6 and placing the resulting expression for $\bar{\mu}$ into Equation 7 gives

$$P = \frac{D}{S} = 1 - \exp\left(-\frac{\bar{f}Iqt}{n}\right) \tag{8}$$

Equation 8 has very general applicability; it is valid for both steady-state and non-steady-state conditions and when the outdoor air supply rate varies with time.

Basic reproductive number in a shared indoor airspace (R_{A0})

The basic reproductive number (R_0) is the number of secondary infections that arise when a single infectious case is introduced into an population where everyone is susceptible. If for a given population and infectious agent, $R_0 > 1$ then that agent can spread in the population. The larger the value of R_0 the more likely is the infection to reproduce rapidly in the form of an epidemic. The reproductive number for an infectious disease in a building environment (R_{A0}) can be derived from Equation 8 where $I = 1$ and $S = n - 1$; thus,

$$R_{A0} = (n-1)\left[1 - \exp\left(-\frac{\bar{f}qt}{n}\right)\right]. \tag{9}$$

In the basic epidemiologic model, R_0 can be expressed as the product of three parameters (Anderson and May, 1991): (1) probability of transmitting infection per contact, (2) duration of infectious period, and (3) number of hosts (the size of the susceptible population). However, as for R_0 in some epidemiologic models (Anderson and May, 1991), Equation 9 shows that R_{A0} is not simply a linear function of the number of building occupants.

The critical rebreathed fraction ($\bar{f}_c$), corresponding to a basic reproduction number of 1, can be derived from Equation 9:

$$\bar{f}_c = \frac{1}{qt}\ln\left(\frac{n-1}{n-2}\right)^n \tag{10}$$

For $n > 30$, the following approximation will give an error of 5% or less:

$$\bar{f}_c \cong 1/qt \tag{11}$$

That is, the critical rebreathed fraction is approximately equal to the reciprocal of the number of quanta that an infector releases into a building. For example, if $q = 4$ quanta/h and $t = 25$ h ($qt = 100$ quanta), then below a rebreathed fraction of 1%, which is equivalent to an indoor CO_2 concentration that is <380 p.p.m. above the outdoor concentration (or approximately 730 p.p.m.), the basic reproductive number would be <1.

Evaluation of assumptions

In the derivation of the model, we assumed that elimination of infectious particles caused by loss of viability, filtration, gravitational and diffusional deposition on surfaces, and other mechanisms are small compared with removal by ventilation. Further discussion of this assumption is warranted in that it may not always be valid.

The validity of the assumption regarding loss of infectiousness may depend on temperature and relative humidity. Much of our interest here is in the infectiousness of airborne viruses. There is little data on this subject. However, what data do exist suggests that loss of infectiousness in indoor air can be a very slow process with half-lives as long as 2–3 days (Harper, 1961; Ijaz et al., 1985).

Measurements of outdoor air supply rates for nonresidential buildings are very limited. According to a recent report that summarized the results of three of the larger surveys, outdoor air supply rates vary from 0.3 to 2.9 air changes per hour with schools tending to have the higher rates (Thatcher et al., 2001). These values need to be compared with the expected removal rate of infectious particles caused by filtration, deposition on surfaces, and loss of viability.

Neglecting the removal of particles having diameters on the order of 0.3 μm is probably justified for ventilation filters. In general, fibrous filters exhibit minimum collection efficiency for particles with a diameter of about 0.3 μm, a size that is too large for diffusion to be effective and too small for impaction or interception to be effective (Hinds, 1999). Deposition on room surfaces caused by diffusion and gravity are also small for particles with a diameter on the order of 0.3 μm. Very little information is available on the size of typical airborne droplet nuclei containing infectious agents. Because pathogenic bacteria are larger than 0.3 μm, droplet nuclei containing bacteria must be >0.3 μm and are generally thought to be in the range of 1–3 μm; nuclei-containing viruses, however, may be considerably smaller.

For particles larger than 0.3 μm, the extent of particle deposition on room surfaces will depend on many factors. The results from deposition studies show a wide degree of variability. According to a recent report that reviewed the results from eight studies (Thatcher et al., 2001), deposition rates can vary from 0.05 to 0.1, 0.1 to 1, and 0.5 to 3 h for 0.3, 1, and 3 μm particles, respectively. Thus, for particles greater than about 1μm, neglecting particle deposition on room surfaces is not likely to be valid unless outdoor air supply rates are very high.

Particle collection efficiency of ventilation filters for particles larger than 0.3 μm will depend on the type of filter used. For example, a filter having a minimum efficiency reporting value (MERV) of 5–8 (which is approximately equivalent to a dust-spot efficiency $<35\%$) is used in 'commercial buildings' according to ASHRAE application guidelines contained in ASHRAE Standard 52.2-1999 (ASHRAE, 1999b). These filters are recommended for controlling particles having diameters >3 μm. A filter having an MERV of 9–12 (approximately equivalent to a 40–75% dust-spot efficiency), which according to the guidelines is used in 'better commercial buildings,' is recommended for controlling particles having diameters from 1–3 μm. (Because ASHRAE Standard 52.2 is based on a potassium chloride aerosol, which has a density of about twice that of microorganisms, these filters will actually be less effective at removing supermicrometer infectious particles for which particle collection is due primarily to inertial forces.) This suggests that for buildings using filters having an MERV >8 and for infectious droplet nuclei larger than 1–2 μm, it may not be valid to assume that the elimination of infectious particles caused by filtration is small compared with removal by ventilation. In any case, to the extent that the above assumptions are not met, the proposed model will be conservative in that it will tend to overestimate the probability of infection or underestimate the quantum generation rate. If an investigator feels that the errors introduced by these assumptions are greater than the errors introduced by inaccurate measurement of ventilation rate and the assumption that ventilation is constant in modern buildings, we provide a derivation of a non-steady-state Wells–Riley equation which would allow filtration and surface deposition to be taken into account (see Appendix II) and still have some of the benefits of not assuming a steadystate.

Application of the carbon dioxide-based risk equation

Equation 1, the steady-state Wells–Riley equation, has been used to describe outbreaks and to compute the rate of infectious quanta generation when the outdoor air supply rate could be determined (Barnhart et al., 1997; Catanzaro, 1982; Fennelly and Nardell, 1998; Nardell et al., 1991; Nicas, 2000; Riley and Nardell, 1989; Riley et al., 1978). When the outdoor air supply rate is small or is not constant, however, Equation 1 is invalid because steady-state cannot be assumed. In such cases, modeling of an outbreak and estimation of the quantum generation rate (q) can be done using Equation 8, with the caveats discussed above, if the average fraction of rebreathed air can be determined. To demonstrate the utility of Equation 8, the carbon dioxide-based risk equation, and to generate parameters for describing the relationship of building environment to R_{A0} we estimate the quantum generation rate of rhinovirus 16 based on experimental data published by Dick et al. (1987). They reported on a series of experiments in which panels of eight subjects

(infectors) infected with rhinovirus 16 and 12 uninfected subjects (susceptibles) were placed in a 92.5-m^3 room from 8 AM to 11 PM with breaks for meals to achieve a 12-h exposure. Half of the susceptibles were restrained to prevent transmission via direct contact and fomites, and additional susceptibles were exposed only to the fomites in a separate room. The experimental room was modified to minimize air exchange with other rooms and the outdoors (Dick et al., 1986; Meschievitz et al., 1984; Clair Dick, 2000, University of Wisconsin, personal communication); ventilation measurements and CO_2 concentrations, however, were not reported. The results from these experiments demonstrated that transmission was not due to direct contact or fomites and that the attack rate attributable to airborne transmission was 61% (a total of 22 infected individuals out of 36 susceptibles). Because efforts were made to limit air exchange, exchange rates below 1/h may have been obtained. However, depending on weather conditions and the stack effect, especially given the large number of occupants in the room and northern climate where the experiments were performed, actual air exchange rates may have been higher, perhaps as high as 3/h. We estimated quantum generation rates for air exchange rates of 0.1, 0.3, 1 and 3/h. These values were determined to illustrate the use of Equation 8 and require independent confirmation. Because infectious viral particles are likely to be small and long lived, and because there was no air filtration, the assumptions made in deriving the carbon dioxide equation are reasonable in this case. To the extent that the infectious viral particles are >1 μm or short lived, the analysis here will be a conservative, underestimate of the quantum generation rate for experimental rhinovirus infection.

As an initial step, we derive hypothetical CO_2 concentration curves that could have been measured had the researchers monitored the experimental room at 10-min intervals (Figure 1a). Subjects left the room for two 1.5-h meal breaks, giving two periods of decline in room CO_2 concentration. During the breaks, infectors and susceptibles were kept separated in a well-ventilated dining area. Using this information, we calculate the rebreathed fraction (f) at 10-min intervals, as shown in Figure 1b. Exposure of susceptibles to exhaled air from infectors is assumed to be zero during the breaks (i.e. $f = 0$). We then calculate the average rebreathed fraction ($\bar{f}$) by averaging f over the experimental test period. The CO_2 concentrations estimated for the lowest air exchange rate make that scenario seem improbable, but the moderate hyperpnea that would have been induced under those conditions would be in the range of uncertainty in our estimates of the breathing rates for the experimental subjects. Thus, we use Equation 8 to estimate quantum generation rates shown in Table 1.

The analysis suggests that q for rhinovirus 16 is in the range of 1–10/h, similar to that observed for pulmonary tuberculosis (Riley and Nardell, 1989), one to two orders of magnitude less than we estimate for influenza (see Appendix I), and more than two orders of magnitude less than the approximately 570/h that characterize an average case of measles (Riley et al., 1978). These results are consistent with the observation that extended exposure times were required to achieve transmission of rhinovirus 16 in other experiments (Meschievitz et al., 1984) and the slow spread of rhinovirus infections compared with the more rapid spread of influenza and the explosive epidemics characteristic of measles.

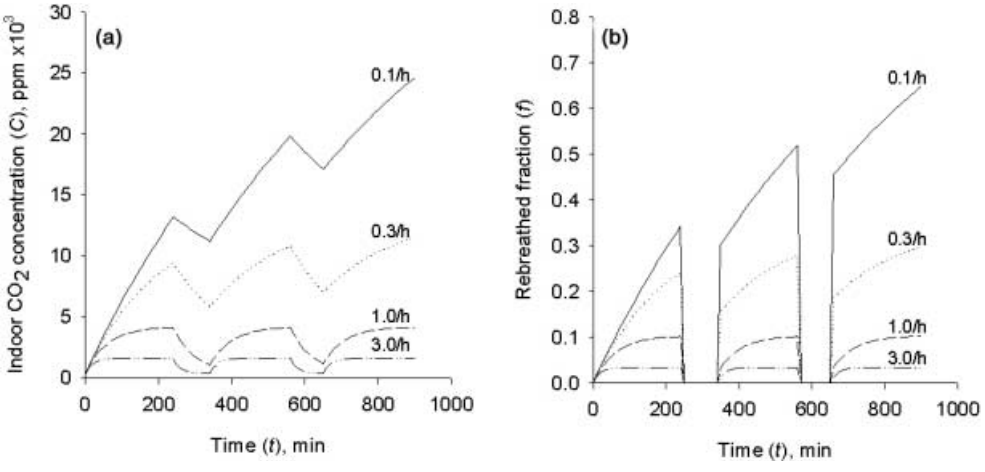

Fig. 1 Estimated CO_2 concentration and rebreathing of air in a 92.5-m^3 experimental room during an experimental exposure. (a) CO_2 concentrations are estimated for a 15-h experiment with outdoor air exchange rates of 0.1, 0.3, 1, and 3/h. The estimates are based on 20 occupants in the room for three 4-h intervals separated by two 1.5-h periods during which there were no occupants. (b) The estimated rebreathing of exhaled air by study subjects based on CO_2 estimates assuming no rebreathing during two 1.5-h breaks.

Table 1 Infectious quanta generation rate (q) for rhinovirus in an experimental room[a]

	Outdoor air exchange rate (1/h)			
	0.1	0.3	1	3
$\bar{f}$[b]	0.30	0.16	0.07	0.03
q (1/h)[c]	0.6	1.2	3.0	7.8

[a] Number of infectors, $I = 8$, and total number of subjects in the experimental room, $n = 20$.
[b] Average fraction of indoor air that is exhaled breath.
[c] Average generation rate of infectious quanta by infected subjects.

Implications for airborne transmission of respiratory infections among school children and office workers

As examples of how Equations 8 and 9 can be employed for risk assessment, we consider several scenarios ranging from highly infectious agents such as measles with high values for q to rhinoviral infections with very low q values. For each scenario, we analyze an area within the school or office that represents an independently ventilated unit – a shared airspace, whether it is a single room or an entire floor of a large building. We assume that one individual develops illness at the start of a school or workday and exposes others for a defined number of hours. Then, knowing the number of occupants in the ventilated area and the average CO_2 over time, we can use Equation 9 to compute R_{A0} for this environment.

The family of curves shown in Figure 2a describes R_{A0} for a hypothetical measles outbreak with a quantum generation rate of 570/h. We assume that the initially infectious individual remains at school for two school days during the infectious period (10 h). R_{A0} increases almost linearly with the size of the population at high CO_2 concentrations. However, R_{A0} does not increase directly with size of the population at low CO_2 concentrations. Rather, R_{A0} levels off for buildings with low CO_2 concentrations. But, even the lowest CO_2 concentration curves show that R_{A0} is much greater than 1. Thus, rapid spread can be predicted even in buildings with very good ventilation – i.e. based on Equation 11, the critical rebreathed fraction is 0.0175%, which is lower than can be realistically achieved.

Figure 2b describes R_{A0} for a hypothetical influenza outbreak characterized by a quantum generation rate of 100/h (see Appendix I for our choice of q) where the initial infector is assumed to remain in the building for 4 h. Again we see the leveling off of R_{A0}, although this time it occurs even at high CO_2 concentrations. At low CO_2 concentrations R_{A0} falls below 1; the critical rebreathed fraction is 0.25% equivalent to a CO_2 concentration of approximately 100 p.p.m. above background. Thus, very high outdoor air supply rates may be effective in limiting the spread of influenza.

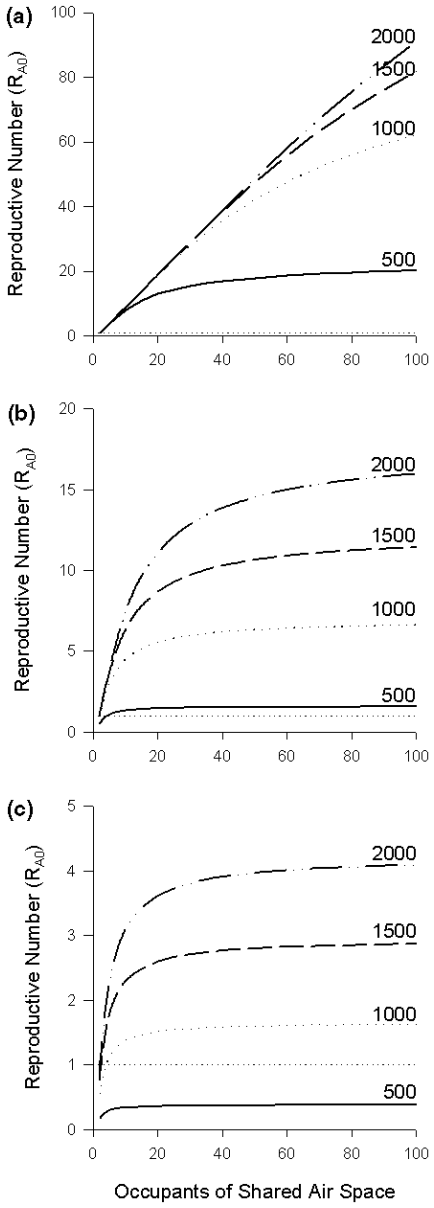

Fig. 2 R_{A0} for (a) measles, (b) influenza, and (c) rhinovirus in a school or office as a function of number of occupants: each curve represents a different mean CO_2 concentration. (a) We assumed $q = 570$ quanta/h, $t = 10$ h, $C_o = 350$ p.p.m., and $C_a = 37{,}500$ p.p.m. (b) We assumed $q = 100$ quanta/h, $t = 4$ h. (c) We assumed $q =$ quanta/h, $t = 24$ h.

In Figure 2c, we show R_{A0} for rhinovirus infections assuming a q of 4/h, the middle of the range that we estimated from the experimental data, and assuming that the infector spends a total of 24 h in the building while infectious. All of the curves are level above 20 occupants, the critical rebreathed fraction is equivalent to approximately 400 p.p.m. above background and even modest outdoor air supply rates would be sufficient to prevent propagation of infection. However, the current ASHRAE standard of 700 p.p.m. above background (ASHRAE, 1999a), a concentration of approximately 1000 p.p.m., would not prevent the

infection from spreading through the building population.

Discussion and conclusions

We have shown that the risk of indoor transmission of infection by the airborne route can be estimated using a CO_2-based risk equation (Equation 8) without assuming that the concentration of an infectious agent has reached steady-state and without measuring the outdoor air supply rate or assuming that it remains constant over time. This equation allows improved accuracy of risk modeling in modern buildings where, by design, ventilation with outdoor air varies with time and often cannot be measured accurately. The equation also allows estimation of risk in buildings and other indoor environments when they are poorly supplied with outdoor air, an important capability when outdoor air supply is reduced out of concern for energy conservation. In Appendix II, a non-steady-state Wells–Riley equation is also developed that can make estimates for buildings with low outdoor air supply rates provided that the rate is known and can be assumed not to vary with time.

Analysis of the basic reproductive rate of infection from Equation 9 for a built environment shows that R_{A0} is independent of population size for certain combinations of strength and duration of infectiousness when outdoor air supply rates are high. This departure from the expected behavior of R_{A0} with increasing population occurs because contact between cases and susceptibles through rebreathing of exhaled air is held constant when CO_2 concentration is constant. For studies of indoor airborne transmission of acute respiratory infections with $q < 100$/h and CO_2 concentrations < 1000 p.p.m., this implies that investigators need not match buildings on size as long as they have more than approximately 25 occupants. The analyses presented also show that increased outdoor air supply can prevent the airborne transmission of some common respiratory infections and influenza, but will have little impact on highly contagious diseases such as measles.

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Appendix I

Quantum generation rate for influenza

Moser et al. (1979) reported that a Boeing 737 with a 56-seat passenger compartment and a forward freight compartment was delayed for 4.5 h by engine trouble. The plane, with 54 people aboard, was without mechanical ventilation during the delay. One passenger became ill with influenza within 15 min after boarding the plane. This index case and 29 other people remained on the plane throughout the delay. Based on the report, the passenger compartment contained approximately 3 m^3 per seat for a total volume of 168 m^3. We assume that there was a small amount of outdoor air exchange facilitated by open doors during part of the interval and movement of passengers in and out of the plane. There is uncertainty about outdoor air exchange rates, and they changed after the doors were opened to cool the plane midway through the delay. This example is, nonetheless, useful to give a rough estimate of the quanta generation rate for a highly contagious case of influenza. We used hypothetical outdoor air exchange rates of 0.1 and 0.5/h. Because of uncertainty about exposure times for 24 of the 54 people aboard, we only compute q using the 29 susceptibles (S) who remained on the airplane throughout the delay, 25 of whom contracted influenza (D). We used a breathing rate (p) of 8 l/min per passenger, and assume that movement of passengers and thermal convection were sufficient to satisfy the requirement for a well-mixed airspace. From the non-steady-state Wells–Riley equation (Appendix II, Equation 17), we calculate q to be 79 and 128 quanta/h at estimated outdoor air exchange rates of 0.1 and 0.5/h, respectively, whereas using the steady-state Wells–Riley equation (Equation 1) gives 15 and 77 quanta/h. Using the steady-state equation underestimates q by a factor of 5 and 1.7 for outdoor air exchanges of 0.1 and 0.5/h, respectively. Independent confirmation of these values for q is needed.

Appendix II

Non-steady-state Wells–Riley equation

If we assume, as for derivation of the Wells–Riley equation, that the airspace is well mixed and that elimination of infectious particles caused by loss of viability, filtration, settling, and other mechanisms are small compared with removal by ventilation, then the accumulation rate of quanta is equal to the quantum generation rate minus the rate of quantum removal by ventilation:

$$V\frac{\mathrm{d}N}{\mathrm{d}\theta} = Iq - NQ \tag{12}$$

where V is the volume of the ventilated space (m^3), N is the quantum concentration (quanta/m^3), and θ is the time elapsed from when the building becomes occupied (s). If filtration or other infectious-particle loss mechanisms are important, Q in Equation 12 can be replaced with the sum of the outdoor air supply rate and the loss rates for these mechanisms. For an initial quantum concentration equal to 0,

$$\int_0^N \frac{\mathrm{d}N}{Iq - NQ} = \frac{1}{V}\int_0^\theta \mathrm{d}\theta \tag{13}$$

If the outdoor air supply rate, the quantum generation rate, and the number of infectors are assumed to be constant, then

$$N = \frac{Iq}{Q}\left[1 - \exp\left(-\frac{Q\theta}{V}\right)\right] \tag{14}$$

where Q/V is the outdoor air exchange rate. The average quantum concentration ($\bar{N}$) over the time period from 0 to θ can then be calculated:

$$\bar{N} = \frac{1}{\theta}\int_0^\theta N\,\mathrm{d}\theta = \frac{Iq}{Q}\left\{1 - \frac{V}{Q\theta}\left[1 - \exp\left(-\frac{Q\theta}{V}\right)\right]\right\} \tag{15}$$

If the exposure occurs over multiple time periods of equal duration (θ), such as 8 h a day at the office each week, then the average quanta concentration calculated from Equation 15 is also valid for the total exposure period (t).

Substituting $\bar{N}$ from Equation 15 into Equation 6 gives

$$\bar{\mu} = \frac{Iqpt}{Q}\left\{1 - \frac{V}{Q\theta}\left[1 - \exp\left(-\frac{Q\theta}{V}\right)\right]\right\} \tag{16}$$

When the total exposure occurs in a single time period, then $t = \theta$.

Substituting $\bar{\mu}$ from Equation 16 into Equation 7 gives the non-steady-state version of the Wells–Riley equation:

$$P = 1 - \exp\left[-\frac{Iqpt}{Q}\left\{1 - \frac{V}{Q\theta}\left[1 - \exp\left(-\frac{Q\theta}{V}\right)\right]\right\}\right] \quad (17)$$

When the number of air changes during an individual exposure period, $Q\theta/V$, is sufficiently large, Equation 17 reduces to the steady-state Wells–Riley equation (Equation 1). For short intervals or poorly ventilated buildings with small $Q\theta/V$, however, Equation 1 can significantly overestimate the probability of infection, or underestimate an infected individual's quantum generation rate. Equation 8 can also be derived from Equation 17.