



UNIVERSITY OF LEEDS

This is a repository copy of *Applying the Wells-Riley equation to the risk of airborne infection in hospital environments: The importance of stochastic and proximity effects.*

White Rose Research Online URL for this paper:
<http://eprints.whiterose.ac.uk/7702/>

Proceedings Paper:

Noakes, C.J. and Sleight, P.A. (2008) Applying the Wells-Riley equation to the risk of airborne infection in hospital environments: The importance of stochastic and proximity effects. In: *Indoor Air 2008 : The 11th International Conference on Indoor Air Quality and Cl.* Indoor Air 2008, 17-22nd August 2008, Copenhagen, Denmark. , Copenhagen .

Reuse

See Attached

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

Applying the Wells-Riley equation to the risk of airborne infection in hospital environments: The importance of stochastic and proximity effects

Catherine J. Noakes* and P. Andrew Sleight

Pathogen Control Engineering Research Group, School of Civil Engineering, University of Leeds, Leeds, LS2 9JT

*Corresponding email: C.J.Noakes@leeds.ac.uk

SUMMARY

Although the Wells-Riley equation for airborne infection is used to estimate infection risk in a range of environments, researchers generally assume complete air mixing and don't consider either the stochastic effects in a small population or the proximity of susceptible people to an infectious source. This study presents stochastic simulations using the Wells-Riley model to evaluate the infection risk and variability among small populations such as hospital patients. This is linked with a simple multi-zone ventilation model to demonstrate the influence of airflow patterns and proximity to an infectious source on the risk of infection for an individual. The results also highlight that risk assessments made using data derived using complete mixing assumptions may significantly underestimate the real risk for those close to the infectious source.

KEYWORDS

Airborne infection, Ventilation, Wells-Riley, Air mixing

INTRODUCTION

Airborne transmission of infectious diseases has been the subject of significant interest over recent years with increasing evidence that indoor air quality has a significant influence on the health of individuals and plays an important role in the transmission of infection. Pulmonary tuberculosis is an archetypal example of a disease that is transmitted by an airborne route and currently a particular concern as it is once again a world-wide health problem, compounded by the increased susceptibility to infection with *M. tuberculosis* in HIV/AIDS patients and the emergence of multi drug-resistant tuberculosis (MDR-TB) (Tancock 1998). The 2003-03 SARS outbreak was initially thought to be spread through contaminated droplets however the infection of individuals without sufficiently close contact with a known case (Scales et al 2003), and retrospective studies of the building airflow patterns suggested that airborne dispersal may play a significant role (Li et al 2005). Airborne dissemination of pathogens has also been implicated in many hospital-acquired infections including nosocomial outbreaks of *Staphylococcus aureus* (including MRSA) (Kumari et al. 1998), *Acinetobacter* spp (Allen and Green 1987) and viral outbreaks such as norovirus.

Despite the global scale of the problem, relatively little research has been undertaken to quantify the risk of airborne transmission in enclosed spaces, and the majority of previous studies stem from the work of Wells (1955) and Riley et al. (1978), using an analytical expression known as the Wells-Riley equation. Although this has been applied to numerous risk analysis studies, including the evaluation of personal protective equipment (Gammiatoni and Nucci 1997), tuberculosis risk in buildings (Nardell et al. 1991) and the dispersion of *Bacillus anthracis* from envelopes (Fennelly et al. 2004) the model has a number of limitations (Beggs et al 2003). In most cases the analysis assumes that the air is well mixed

leading to a uniform concentration of bioaerosols throughout the space so does not account for the influence of proximity between infective and susceptible people. The model also does not consider the stochastic effects inherent in a small population, resulting in the quantification of the average risk only rather than the expected range.

This study aims to address some of the limitations with the Wells-Riley model by developing a stochastic formulation of the model and combining it with simple zonal-mixing ventilation equations. This enables evaluation of the stochastic effects among small populations such as hospital patients as well as the effect of airflow and proximity to the infectious source. The model is used to investigate the influence of air mixing on the risk of infection in a hypothetical hospital ward housing 18 patients in 6 bedded bays. Monte-Carlo simulations are used to model typical risk profiles for each scenario.

METHODS

Fully Mixed Model

The Wells-Riley model for airborne infection is typically used to predict the number of new cases infected, N_C , over a period of time t (s), in an indoor environment ventilated at a constant rate Q (m^3/s)

$$N_C = S \left(1 - e^{-\frac{Iqp t}{Q}} \right) \quad (1)$$

Here S represents the number of susceptible people in the space, I represents the number of infectious people and p (m^3/s) is the pulmonary ventilation rate of susceptible individuals. q represents a unit of infection termed a ‘quantum’, introduced by Wells (1955) to express the response of susceptible individuals to inhaling infectious droplet nuclei. He postulated that not all inhaled droplet nuclei will result in infection and defined a quantum of infection as the number of infectious droplet nuclei required to infect $1-1/e$ susceptible people. Equation (1) is based on the Poisson law of small chances, which assumes that in a small enough time period only one new infection is likely. This is suitable for most airborne infections where it is easy to define a time period that approximates to this criterion. Although the Wells-Riley model is derived from this probabilistic approach, it is more commonly used in deterministic simulations, with equation (1) used to predict average infection risk in different scenarios. However, treating the model as a deterministic process is only strictly suitable for large populations, and to understand the risks for small numbers such as hospital patients it is necessary to apply the model in a stochastic simulation.

By considering a population of $S(t)$ susceptible people at time t and assuming the number of infectors is constant (i.e. new cases do not become infectious themselves in the timescale of the model), equation (1) can be derived from classical deterministic infection theory [Noakes et al 2006, Renshaw 1991) where the infection rate, λ is equivalent to

$$\lambda = \frac{Iqp}{Q} \quad (2)$$

The equivalent stochastic process can be derived by considering the probability that there are S uninfected susceptibles at time t , $p_S(t) = \text{Pr}(S \text{ susceptibles at time } t)$

In a small time interval, dt , such that the probability of more than one infection is negligible, two outcomes are possible; one new infection with probability $\lambda dt S$ or no new infection with probability $1 - \lambda dt S$. Therefore the process can be expressed as

$$p_S(t + dt) = p_S(t)(1 - \lambda dt S) + p_{S+1}(t)\lambda dt(S + 1), \quad (3)$$

which as dt tends to zero yields the differential equation

$$\frac{dp_S(t)}{dt} = -\lambda S p_S(t) + \lambda(S + 1)p_{S+1}(t) \quad (4)$$

To develop a numerical model to simulate the process described by equations (3) and (4), the technique described by Renshaw (1991) is applied. In this approach the process is considered to consist of a series of infection events where the susceptible population decreases by one in each case. Rather than run the simulation based on a fixed time step considering the event probability at each time, the inter-event times are constructed using a random variable, yielding a more efficient numerical process with less simulation steps. As shown by Renshaw, for a population of S susceptibles, the time T to the next event is an exponentially distributed random variable with

$$\Pr(T \geq t) = \exp(-\lambda S t) \quad (5)$$

This can be used to simulate the time to the next event, t using a random number $0 \leq Y \leq 1$ by the equation

$$t = -\ln(Y)/(\lambda S) \quad (6)$$

With λ defined by equation (2), the result in equation (6) can be easily applied to derive a series of inter-event times corresponding to the new cases of infection amongst the susceptible population in a ventilated indoor environment.

Zonal Model

The fully-mixed model is extended for application to a space divided into multiple zones. The air within each zone is treated as uniformly mixed; however the mixing between the zones is limited, leading to a concentration distribution throughout the space. The development of this model is carried out in two distinct stages; a zonal ventilation model to evaluate the distribution of infectious material followed by the extension of the infection risk model to evaluate the expected rate of new infections in the ward.

Ventilation Model

The influence of air mixing was simulated by treating the infectious quanta as a deterministic variable equivalent to a contaminant concentration in the environment. The model was developed to simulate a typical hospital ward layout as shown in Figure 1 comprising three identical 6-bedded bays that open onto a common corridor. Each bay is divided into two equal zones and the corridor split into three equal zones corresponding to the adjacent ward with ventilation air supplied and extracted from each zone and mixing between adjacent zones.

The concentration of infectious material in the i^{th} zone, C_i , can be approximated by considering the generation, ventilation removal and inter-zonal transfers to give

$$V_i \frac{dC_i}{dt} = q_i I_i - Q_{oi} C_i - \sum_k \beta_{ik} C_i + \sum_k \beta_{ki} C_k \quad (7)$$

Here the term $q_i I_i$ represents the generation rate in the zone, Q_{oi} is the extract ventilation rate in zone i and β_{ik} and β_{ki} represent the volume flow rate of air to and from adjacent zones k

respectively. In this study this is a constant value in both directions across all zonal boundaries, β_o . Under steady state conditions equation (7) is equal to zero for each zone and yields the matrix system (8) that is solved numerically using Gaussian elimination technique.

$$\begin{bmatrix} -(Q_1 + \beta_{12}) & \beta_{21} & 0 & \cdots \\ \beta_{12} & -(Q_2 + \beta_{21} + \beta_{23}) & \beta_{32} & \cdots \\ 0 & \beta_{23} & -(Q_3 + \beta_{32} + \beta_{36}) & \cdots \\ \vdots & \vdots & \vdots & \ddots \end{bmatrix} \begin{bmatrix} C_1 \\ C_2 \\ C_3 \\ \vdots \end{bmatrix} = \begin{bmatrix} q_1 I_1 \\ q_2 I_2 \\ q_3 I_3 \\ \vdots \end{bmatrix} \quad (8)$$

Infection Risk Model

The infection risk model is extended to evaluate the risk in each of the zones within the model. The infection rate described by equation (2) is now zone dependent with the term qI/Q replaced by the zone concentration C_i from the solution of equation (8), giving

$$\lambda_i = C_i p \quad (9)$$

As previously the Poisson assumption is made, such that only one new infection occurs in a small time-step dt and the model is formulated to simulate the inter-event times. However now the new infection may occur in any one of the occupied zones within the model, so it is necessary to examine the relative probability of infection in each zone to determine which zone each infection event occurs in. At each time step the probability that the next infection event will be in zone i is given by

$$\text{Pr}(\text{infection in zone } i) = \frac{\lambda_i S_i}{R(k)} \quad \text{where } R(k) = \sum_{k=1}^9 \lambda_k S_k \quad (10)$$

with the inter-event time now given by

$$t = -\ln(Y) / R(k) \quad (11)$$

Numerical simulation of this process again follows the methodology described by Renshaw:

- (i) calculation of $\frac{\lambda_i S_i}{R(k)}$ for each zone at the current time-step
- (ii) generation of a first random number, $0 \leq Y \leq 1$ to find the inter-event time
- (iii) generation of a second random number $0 \leq X \leq 1$ to establish which zone is infected based on infection in zone 1 if $0 \leq X \leq \lambda_1 S_1 / R(k)$, zone 2 if $\lambda_1 S_1 / R(k) \leq X \leq \lambda_2 S_2 / R(k)$ etc.
- (iv) change S_i to S_{i-1} in infected zone i

Numerical Procedures

Excel and VBA (Microsoft Corporation, USA) were used to determine numerical solutions to both the fully mixed and zonal infection models. In both cases Monte-Carlo techniques were used to run each model up to 1000 times to calculate average behaviour as well as variation due to the stochastic effects through calculating the standard deviation. As the models are defined in terms of inter-event times, which are different in every simulation due to the random number in the event time definition, it was necessary to map each simulation onto a regular time scale in order to be able to find average data across more than one simulation. The simulations were mapped onto a 170 hour time period divided into hourly steps, then plotted every 3 hours to enable the data to be clearly seen.

RESULTS

The models described above were used to investigate the influence of stochastic and proximity effects through the application of the mixing model to a simple ward layout shown in Figure 1. The simulations assumed a full ward occupancy of 18 patients (6 per bay) of which one located in zone 1a was assumed to be infectious and producing quanta at a rate of 30 quanta/hour (Riley et al. 1978, Beggs et al. 2003). All patients were equally susceptible and breathed the ward air at a constant rate of $0.01 \text{ m}^3/\text{min}$ (10 l/min). Ventilation air was assumed to be supplied and extracted to each zone at a constant rate of $3 \text{ m}^3/\text{min}$, with the total ventilation rate of $27 \text{ m}^3/\text{min}$ used in the fully mixed model. The inter-zone mixing parameter β_0 was constant across all zone boundaries with a value of 9 or $27 \text{ m}^3/\text{min}$ depending on the simulation. This value was estimated by considering the inter-zone volume flow rate to be given by the expression $\frac{1}{2}vA$ where v is the average air velocity at the interface and A is the interface area (Beggs and Sleigh 2002). For an open area of 6 m^2 and an average air velocity of 0.05 m/s , this yields a mixing flow rate of $9 \text{ m}^3/\text{min}$.

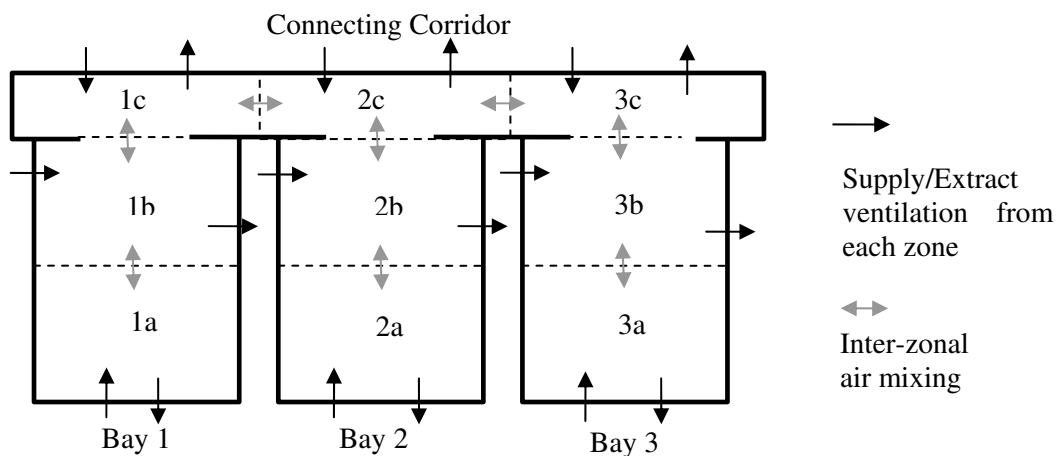
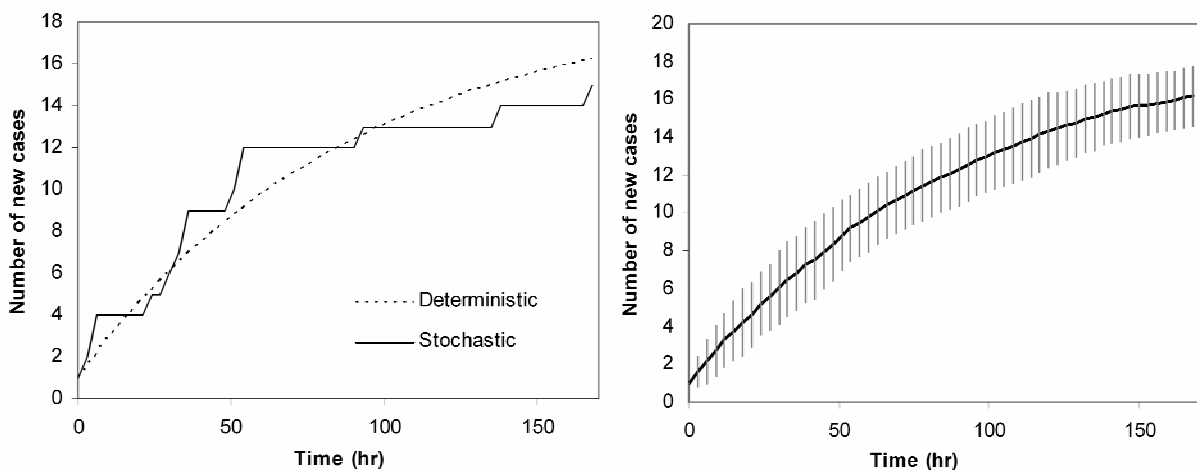


Figure 1. Schematic of the hypothetical ward layout used in the study showing the nine computational zones and the possible air transfers through ventilation and inter-zonal mixing.



(a) Comparison of a single simulation run to show a possible progression predicted by both models.

(b) Average results from a Monte-Carlo simulation with 100 runs. Error bars show 1 standard deviation from average value.

Figure 2. Comparison of disease progression predicted by the fully mixed stochastic model with the average behaviour predicted by equation (1).

The two models are initially used to examine the importance of the stochastic nature of infections and the proximity of the susceptibles to the index case. Figure 2 shows results from the fully mixed stochastic model, compared to the deterministic behaviour described by equation (1). It can be seen from Figure 2 (a) that both models show the same trend, however the progression of an infection predicted by the stochastic model varies considerably about the average line provided by the deterministic model. Figure 2 (b) presents the average results from 100 simulations, with the error bars representing one standard deviation in the data. This highlights the extent of the variability that could be expected in the progression of an infection amongst a small population. Although the fully mixed stochastic average is equivalent to equation (1), using this equation alone to evaluate risk yields only a single value without the likely variability that occurs in reality.

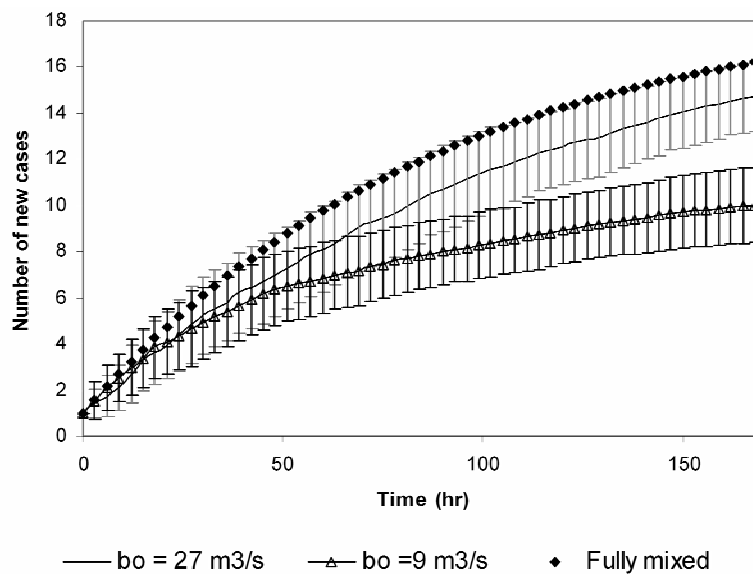


Figure 3. Effect of air mixing on the total rate of infection.

The results in Figures 3 and 4 compare the zonal model with fully mixed results for two different mixing rates, β_o . Figure 3 considers the effect of air mixing on the total number of new cases across the whole ward. With a value of $\beta_o = 9 \text{ m}^3/\text{s}$ the overall infection rate is much slower than fully mixed model, with less than 2/3 of the predicted total number of cases after the 170 hr time period. Increasing the mixing to $\beta_o = 27 \text{ m}^3/\text{s}$ increases the rate at which the infection spreads with now around 85% of the fully mixed model.

Figure 4 presents the infections in each ward, again with the interzonal mixing factor $\beta_o = 9 \text{ m}^3/\text{s}$ and $\beta_o = 27 \text{ m}^3/\text{s}$. It is clear from these results how significant the proximity to an index case is in the risk of a disease spreading. In both cases the patients in the same ward as the index case are rapidly infected, however those in other wards have a much lower risk. With $\beta_o = 9 \text{ m}^3/\text{s}$ the total number of infections in ward 3 are less than 1/3 of ward 1 after 170 hours, with the infection rate becoming more uniform as the mixing increases. This also gives an initial indication how the ventilation can either protect or expose other patients depending on the degree of mixing between zones.

values derived from outbreaks to estimate risk and design control procedures may significantly underestimate the actual risk, particularly for susceptible people in closer proximity to the index case.

CONCLUSIONS

The models presented in this study give some valuable insight into the variability in the risk of infection in a small population as well as the influence of the ventilation system on the cross-transmission of infection. Although the study focuses on theoretical models, the concepts are a potentially powerful addition to a ventilation system design tool by enabling airborne concentrations to be related to actual risk to occupants. The results also demonstrate the importance of proximity to an infectious source in the risk of transmission and highlight how risk assessments and control strategies based on assuming fully mixed conditions could significantly underestimate the infection risk for some individuals.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the support of the Department of Health, Estates & Facilities Division Research and Development Fund in funding this study.

REFERENCES

- Allen K.D., Green H.T. 1987. Hospital outbreak of multi-resistant *Acinetobacter anitratus*: an airborne mode of spread? *Journal of Hospital Infection*, 9, 110 – 119.
- Beggs C.B. et al. 2003. The transmission of tuberculosis in confined spaces: an analytical study of alternative epidemiological models. *International Journal of Tuberculosis and Lung Disease*, 7, 1015-1026.
- Beggs C.B., Sleigh P.A. 2002. A quantitative method for evaluating the germicidal effect of upper room UV fields. *Journal of Aerosol Science*, 33, 1681-1699.
- Fennelly K.P. et al. 2004. Airborne infection with *Bacillus anthracis*- from mills to mail. *Emerging Infectious Diseases*, 10, 996-1001.
- Gammaitoni L., Nucci M.C. 1997. Using a mathematical model to evaluate the efficacy of TB control measures. *Emerging Infectious Diseases*, 3.
- Kumari D.N.P. et al. 1998. Ventilation grilles as a potential source of methicillin-resistant *Staphylococcus aureus* causing an outbreak in an orthopaedic ward at a district general hospital. *Journal of Hospital Infection*, 39, 127-133.
- Li Y. et al. 2005. Role of air distribution in SARS transmission during the largest nosocomial outbreak in Hong Kong. *Indoor Air*, 15(2), 83-95.
- Nardell E.A. et al. 1991. Airborne infection: Theoretical limits of protection achievable by building ventilation. *American Review of Respiratory Disease*, 144, 302 - 306.
- Noakes C.J. et al. 2006. Modelling the Transmission of Airborne Infections in Enclosed Spaces. *Epidemiology and Infection*.
- Renshaw E. 1991. *Modelling Biological Populations in Space and Time*. Ed. Cannings C., Hoppensteadt F.C., Segel L.A. Cambridge University Press.
- Riley E.C., Murphy G., Riley R.L. 1978. Airborne spread of measles in a suburban elementary school. *American Journal of Epidemiology*, 107, 421 – 432.
- Scales D.C. et al. 2003. Illness in intensive care staff after brief exposure to severe acute respiratory syndrome. *Emerging Infectious Diseases*, 9 (10), 1205-1210.
- Tancock N. 21st Century time bomb. *Developments* 1998; First Quarter: 30 – 31.
- Wells W.F. 1995. Airborne contagion and air hygiene. Cambridge, MA: Harvard University Press.