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An Integrated Model of Infection Risk in a Health-Care Environment

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Certain respiratory tract infections can be transmitted by hand-to-mucous-membrane contact, inhalation, and/or direct respiratory droplet spray. In a room occupied by a patient with such a transmissible infection, pathogens present on textile and nontextile surfaces, and pathogens present in the air, provide sources of exposure for an attending health-care worker (HCW); in addition, close contact with the patient when the latter coughs allows for droplet spray exposure. We present an integrated model of pertinent source-environment-receptor pathways, and represent physical elements in these pathways as "states" in a discrete-time Markov chain model. We estimate the rates of transfer at various steps in the pathways, and their relationship to the probability that a pathogen in one state has moved to another state by the end of a specified time interval. Given initial pathogen loads on textile and nontextile surfaces and in room air, we use the model to estimate the expected pathogen dose to a HCW's mucous membranes and respiratory tract. In turn, using a nonthreshold infectious dose model, we relate the expected dose to infection risk. The system is illustrated with a hypothetical but plausible scenario involving a viral pathogen emitted via coughing. We also use the model to show that a biocidal finish on textile surfaces has the potential to substantially reduce infection risk via the hand-to-mucous-membrane exposure pathway.

KEY WORDS: Biocidal coating; microbial risk assessment; transmission routes

1. INTRODUCTION

Given concerns about emerging infectious diseases (e.g., pandemic avian flu) and bioterrorism (e.g., smallpox), a risk scenario of current interest involves a health-care worker (HCW) attending a patient with a transmissible respiratory tract disease. The exposure routes of concern for a HCW are (1) hand contact with mucous membranes of the eyes, nose, and/or mouth, (2) inhalation, and (3) respiratory droplet spray (the direct projection of droplets onto mucous membranes). For some respiratory tract pathogens such as influenza virus[1] and rhinovirus,[2] all three exposure routes are involved, whereas for other pathogens, only one or two exposure routes may pertain. For example, person-to-person transmission of *M. tuberculosis* is through inhalation only.[3] Our purpose is to present an integrated model of the different source-environment-receptor pathways, to quantify the rates of pathogen transfer at various steps in the pathways, and ultimately to estimate the pathogen dose and infection risk to a HCW. Many of the model inputs are admittedly uncertain, yet the model permits examining the relative efficacy of different exposure control strategies. A strategy that we assess is the use of a biocidal coating on textile surfaces.

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2. A MARKOV CHAIN MODEL

Infection risk depends, in part, on the dose of viable pathogens delivered to the appropriate receptor tissue(s). The dose due to hand contact with mucous membranes depends on the number of viable pathogens on room surfaces, the frequency of hand contact with contaminated surfaces and with the mucous membranes, and the efficiency of pathogen transfer to and from the hands on contact. The dose due to inhalation depends on the airborne concentration of viable pathogens, the breathing rate, and the fraction of inhaled organisms that deposit in the respiratory tract. In turn, the numbers of viable pathogens on room surfaces and in room air depend on the numbers of pathogens emitted from the patient in events such as coughing and body fluid discharges (and in some cases shedding of scabs), and on the rate of exhaust ventilation and the rate of decline in pathogen viability due to environmental stresses (e.g., ultraviolet radiation, desiccation). Pathogens that have been emitted into room air can settle onto room surfaces, and pathogens that have been introduced onto room surfaces can be resuspended into room air. Pathogens transferred to the hands due to hand-to-surface contact can be redeposited onto room surfaces during subsequent hand-to-surface contacts. The model we present tracks these exchanges between room air, room surfaces, and the hands, and estimates a dose to the mucous membranes and the respiratory tract.

2.1. System Description

We represent physical elements in the source-environment-receptor pathways as "states" in a discrete-time Markov chain model. Fig. 1 is a diagram of the states and pathways, and assumes a quiescent bedridden patient who does not move around

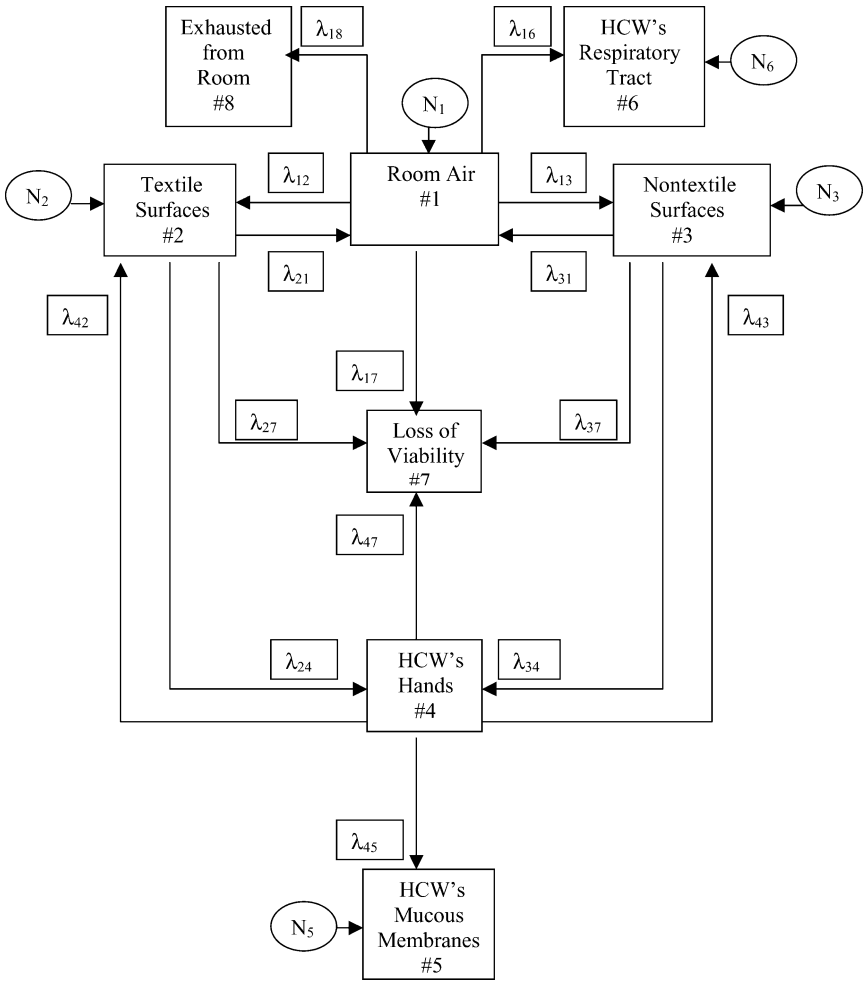

Fig. 1. A diagram of the connections between the eight states in the Markov chain model. A directional arrow from state i to state j signifies that a pathogerz can move from state i to state j in time step Δt. The first-order rate of movement from state i to state j is denoted λ_{ij}.

the room. Room air is designated State 1, textile surfaces are designated State 2, and nontextile surfaces are designated State 3. Pathogens can exchange between States 1 and 2, and between States 1 and 3, due to particle settling and resuspension. The HCW's hands are State 4, and pathogens can be transferred between States 4 and 2, and between States 4 and 3, via hand contact with surfaces. The HCW's mucous membranes are State 5, and the HCW's respiratory tract is State 6. It is assumed that once a pathogen is transferred to a mucous membrane or deposits in the respiratory tract, the pathogen cannot leave. Therefore, States 5 and 6 are "absorbing" states. Loss of pathogen viability is State 7, and pathogens can move to State 7 from States 1 to 4 but not in the opposite direction; therefore, State 7 is an absorbing state. Finally, a pathogen can leave the room in the exiting air flow. Being exhausted from the room is State 8, and is also an absorbing state. States connected by arrows in Fig. 1 are said to directly communicate in one time step, although if there is only one arrow, the communication is in one direction only.

Numbers of pathogens can be introduced into air (N_1), onto textile surfaces (N_2), and onto nontextile surfaces (N_3); we term these quantities initial pathogen loads. We define N_1 as those pathogens carried in respirable particles with an aerodynamic diameter (d_a) < 10 μm; these pathogens remain suspended in air for a duration sufficient to permit dispersion throughout room air. In contrast, N_6 denotes the number of pathogens carried in particles with $10\ \mu\text{m} < d_a < 100\ \mu\text{m}$, which are inspired if the HCW is facing the patient at close range during an expiratory event such as a cough. Particles in this size range tend to settle rapidly onto nearby surfaces and do not disperse throughout room air. The quantity N_5 denotes the number of pathogens in particles with $d_a > 144$ μm that are sprayed directly onto mucous membranes if the HCW is facing the patient at close range during an expiratory event; however, only a small fraction of particles with $d_a > 144$ μm would contact the mucous membranes, and the great majority would become part of loads N_2 and N_3. The basis for the 144-μm cutpoint will be explained subsequently.

Due to the relative infrequency of close contact exposures involving droplet spray and inhalation of pathogens carried on inspirable particles, infection risk due to these events is analyzed outside the Markov chain approach to be described. Instead, we use the Markov chain to estimate the pathogen doses and associated infection risks to the HCW via hand-to-surface-to-mucous membrane transfers and via inhalation of respirable pathogens, and then combine the different risks to estimate an overall risk of infection.

2.2. The Markov Matrix

Consider a pathogen in state i. In the next time step Δt, the pathogen has some probability of remaining in state i, denoted p_{ii}, and has some probability of moving to another state j, denoted p_{ij}. The sum of the p_{ij} (for $j = 1, 2, \ldots, 8$) equals one. For example, in Δt, a pathogen in State 2 (on a textile surface) can remain in State 2 with probability p_{22}, can move to State 1 with probability p_{21} due to resuspension into room air, can move to State 4 with probability p_{24} due to hand-to-surface contact, or can become nonviable with probability p_{27}. Because State 2 does not directly communicate with States 3, 5, 6, or 8, the probabilities p_{23}, p_{25}, p_{26}, and p_{28} are all zero. Because the eight states represent all possible locations of the pathogen: $p_{21} + p_{22} + p_{23} + p_{24} + p_{25} + p_{26} + p_{27} + p_{28} = 1$.

The p_{ij} are entered into an 8×8 array termed a Markov matrix, denoted **P**, in which each row represents a state in the system. Fig. 2 is the **P** matrix for the system shown in Fig. 1. For absorbing States 5–8, the probability of remaining in the absorbing state is one, or $p_{ii} = 1$ for $i = 5, 6, 7, 8$. The **P** matrix concisely describes the system, and affords mathematical simplicity in the following manner. Consider that at time zero a pathogen is introduced into state i, and that $n \times \Delta t$ time steps elapse. The probability that the pathogen is in state j at time $n \times \Delta t$ is the entry

$$\begin{bmatrix} p_{11} & p_{12} & p_{13} & 0 & 0 & p_{16} & p_{17} & p_{18} \\ p_{21} & p_{22} & 0 & p_{24} & 0 & 0 & p_{27} & 0 \\ p_{31} & 0 & p_{33} & p_{34} & 0 & 0 & p_{37} & 0 \\ 0 & p_{42} & p_{43} & p_{44} & p_{45} & 0 & p_{47} & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

Fig. 2. The single-step transition probability matrix **P** for the model system. Each row and column represents a state in the system as numbered in Fig. 1. An entry p_{ij} is the probability that, in one time step, a microbe in state i moves to state j. A zero entry signifies that a microbe cannot move between the two states in one time step. In a given row of **P**, the probability entries sum to one.

in the ith row and jth column of **P** multiplied by itself n times. The latter matrix is designated $\mathbf{P^{(n)}}$, where the superscript (n) indicates n multiplications, and the ith row and jth column entry is designated $p_{ij}^{(n)}$.

Thus, once the probabilities in **P** are assigned, matrix multiplication permits estimating the dose to mucous membranes and the respiratory tract by a given time $n \times \Delta t$ and for given starting values of N_1, N_2, and N_3. Let $\mathrm{E}[D_5]$ denote the expected dose of viable pathogens to the mucous membranes (State 5), and $\mathrm{E}[D_6]$ denote the expected dose of viable pathogens to the respiratory tract (State 6). These doses are quantified as follows:

$$\mathrm{E}[D_5] = N_1 \times p_{15}^{(n)} + N_2 \times p_{25}^{(n)} + N_3 \times p_{35}^{(n)} \quad (1)$$

$$\mathrm{E}[D_6] = N_1 \times p_{16}^{(n)} + N_2 \times p_{26}^{(n)} + N_3 \times p_{36}^{(n)}. \quad (2)$$

2.3. Rates and Probabilities

The probabilities in **P** are related to the λ_{ij} depicted in Fig. 1. The λ_{ij} are first-order (exponential) rate constants with the inverse unit of time, usually minute^{-1}; the subscript ij signifies a transition from state i to state j. If the time step Δt is small, say, 10^{-3} minutes, the product $\lambda_{ij} \times \Delta t$ is approximately equal to the probability that a pathogen in state i will move to state j in Δt. The overall rate at which a pathogen can leave state i is the sum of the rate constants for removal from that state, denoted λ_i. In turn, the probability that the pathogen will *not* leave state i in Δt, or p_{ii}, is the exponential survival probability:

$$p_{ii} = \exp(-\lambda_{i.} \times \Delta t). \quad (3)$$

Given that the pathogen does leave state i, the conditional probability that it moves to state j (where $j \neq i$) is the rate λ_{ij} divided by the total rate λ_i. Finally, the unconditional probability that a pathogen in state i will move to state j in Δt is the product of the probability that it leaves state i, equal to $1 - p_{ii}$, and the conditional probability that it moves to state j given that it leaves state i, equal to $\lambda_{ij} \div \lambda_i$:

$$p_{ij} = \frac{\lambda_{ij}}{\lambda_{i.}} \times [1 - p_{ii}], \quad (4)$$

where $\lambda_{i.} > 0$. If $\lambda_{i.} = 0$, state i is an absorbing state and $p_{ij} = 0$ for $i \neq j$.

To illustrate, consider State 2 (textile surfaces). A pathogen can be resuspended into air with rate λ_{21}, it can be transferred to the hands with rate λ_{24}, and it can lose viability with rate λ_{27}. The overall removal rate is $\lambda_2 = \lambda_{21} + \lambda_{24} + \lambda_{27}$, and the probability that the pathogen does not leave State 2 in Δt is $p_{22} = \exp(-\lambda_2 \times \Delta t)$. The probability that a pathogen in State 2 moves to State 4 in Δt is $p_{24} = (\lambda_{24} \div \lambda_{2.}) \times [1 - \exp(-\lambda_{2.} \times \Delta t)]$.

Because the transfer of pathogens between states is governed by first-order rates, the system can also be described by coupled linear differential equations for which there are analytical solutions. Although the Markov chain and differential equation approaches provide essentially the same results, the former is more concise mathematically and its output has an explicitly probabilistic interpretation.

3. THE DOSE-INFECTION RESPONSE MODEL

We use a nonthreshold model that assumes that a single organism can infect the host with a probability denoted α. Where D is the number of organisms deposited on the appropriate target tissue, and two or more organisms exert independent probabilities of infection, the risk of infection R is[4]

$$R = 1 - (1 - \alpha)^D. \quad (5)$$

The model can account for variable host susceptibility by treating α as variable across individuals,[4] but for simplicity we do not account for interhost variability. Note that the infectious disease literature typically quantifies pathogen infectivity by the infectious dose 50 value (ID_{50}) rather than by the parameter α. The ID_{50} may be described as the expected dose that imparts a 50% chance of infecting a random individual who receives it. The ID_{50} and α are related by the expression $\mathrm{ID}_{50} = \ln(2) \div \alpha$.

In contrast, a threshold model assumes that if the host receives some threshold number (or greater) of organisms, infection is certain to occur, whereas if the host receives fewer than that number, infection is certain not to occur. Variable susceptibility to infection is reflected by interhost variability in the threshold dose value, and the ID_{50} is that deposited dose that infects 50% of the population with certainty. In general, the available published data for most pathogens are too sparse to permit distinguishing between the nonthreshold and threshold frameworks. The former is used here because it is consistent with observed dose-infection response data for a variety of organisms.[4]

Equation (5) requires an integer dose, but the expected dose $\mathrm{E}[D]$ is typically not an integer value. To consider integer doses only, we treat $\mathrm{E}[D]$ as the mean of a Poisson random variable. The unconditional risk

value, E[R], is found by summing R across different integer doses $D = d$ weighted by the probability that $D = d$:

$$\mathrm{E}[R] = 1 - \sum_{d=0}^{\infty} (1-\alpha)^d \frac{(\mathrm{E}[D])^d \exp(-\mathrm{E}[D])}{d!}$$
$$= 1 - \exp(-\mathrm{E}[D] \times \alpha). \quad (6)$$

4. A HYPOTHETICAL EXAMPLE FOR PATHOGENS EMITTED IN COUGHS

We illustrate the framework using a hypothetical viral agent that causes respiratory tract disease and that can infect via all three exposure routes discussed previously. A specific pathogen is not used because we could not identify the complete set of input factor values for any single agent; however, where available, we use published values for factors that should not be agent-specific. For simplicity, we first illustrate the framework without accounting for exposure to droplet spray and inspirable pathogens. Infection risk via the latter two routes will be estimated subsequently. We consider the emission of pathogens in respiratory fluid due to coughing by the patient, and begin by estimating the initial pathogen loads N_1, N_2, and N_3 at the time a HCW enters the patient room.

4.1. Pathogen Loads

The pathogen emission rate is modeled as the product of the volume of respiratory fluid emitted per cough V_F (mL), the rate of coughing E (hour^{-1}), and the concentration of viable pathogens in the fluid C_F(mL^{-1}). Based on the data of the size distribution and numbers of particles emitted in coughs,[5] the respiratory fluid volume per cough is estimated to be $V_F = 0.044$ mL, on average.[6] Based on the observations of cough frequency for a series of 48 pneumonia patients, approximately 60% of patients coughed more than 12 times per hour;[7] therefore, we consider $E = 12$ hour^{-1}. Sparse information is available on the concentrations of different pathogens in respiratory fluid, and their concentrations likely vary across time as well as across pathogens and patients. We assume a reasonable value $C_F = 1.0 \times 10^6$ mL^{-1}. Note that among seven human subjects infected with influenza A virus, peak virus concentrations in nasal washes ranged from 6×10^2 to 2×10^7 tissue culture infectious dose 50 (TCID$_{50}$) units per mL.[8] The TCID$_{50}$ is an operational unit designating an unknown number of virus particles observed to infect 50% of replicate cell cultures each receiving the same volume of virus inoculum. It is likely that a TCID$_{50}$ unit corresponds to more than one virus particle. Given $C_F = 1.0 \times 10^6$ mL^{-1}, the posited overall rate of pathogen emission is

$$(0.044 \text{ mL cough}^{-1}) \times (12 \text{ cough hour}^{-1}) \times (1.0 \times 106 \text{ mL}^{-1}) = 5.3 \times 10^5 \text{ hour}^{-1}.$$

More than 99% of the pathogens emitted in a cough are carried by particles with $d_a > 100\ \mu$m,[6] and these particles tend to rapidly settle close to the point of emission, in this case, onto bed linens. Relatively few pathogens in large particles travel beyond the patient bed and settle onto nearby nontextile surfaces (e.g., surfaces on a bedside table and chair). Further, only about 10^{-4}% of emitted pathogens are associated with respirable particles ($d_a < 10\ \mu$m) that disperse in room air and settle slowly onto room surfaces. Therefore, we apportion the initial locations of pathogens emitted in coughs as follows: 90% on textile (bed linen) surfaces, 10% on nontextile surfaces near the bed, and 10^{-4}% in room air. We note that 10^{-4}% of the estimated 5.3×10^5 hour^{-1} pathogen emission rate signifies that only 0.5 pathogens per hour, on average, are emitted in respirable particles.

We assume that prior to HCW entry into the room, the number of viable pathogens in each of States 1–3 is at its respective steady-state value, which is the rate of introduction of viable pathogens into the compartment divided by the first-order rate of loss from the compartment. Absent a HCW in the room and given a quiescent patient, we assume that the only loss pathway for pathogens on textile and nontextile surfaces is due to environmental stress with the respective rates λ_{27} and λ_{37}. Assume that pathogens on surfaces lose viability with $\lambda_{27} = \lambda_{37} = 0.69$ hour^{-1}, which signifies a pathogen half-life of one hour on both textile and nontextile surfaces. It follows that the initial N_2 value is $[0.90 \times (5.3 \times 10^5 \text{ hour}^{-1})] \div (0.69 \text{ hour}^{-1}) = 6.9 \times 10^5$, and the initial N_3 value is $[0.10 \times (5.3 \times 10^5 \text{ hour}^{-1})] \div (0.69 \text{ hour}^{-1}) = 7.6 \times 10^4$. We note that graphically displayed data for influenza A and B viruses suggest that viability loss rates on cotton surfaces are in the approximate range of 0.3–0.8 hour^{-1}, although the viability loss rates on plastic and stainless steel surfaces are in the approximate range of 0.1–0.2 hour^{-1}.[9]

For airborne pathogens, assume that $\lambda_{17} = 0.69$ hour^{-1}, and that the room is subject to six air

changes per hour such that $\lambda_{18} = 6$ hour^{-1}. Consider that 5 μm is a representative respirable particle size; given a particle density of 1 g cm^{-3}, the overall settling rate from room air is 0.93 hour^{-1}.[10] Assume that textile surfaces (bed linens) and bedside nontextile surfaces (excluding the floor) each represent 5% of the room surface area onto which pathogens can settle, such that $\lambda_{12} = \lambda_{13} = 0.05 \times 0.93$ hour^{-1} $= 0.047$ hour^{-1}. The overall pathogen removal rate from room air is $\lambda_{1.} = \lambda_{12} + \lambda_{13} + \lambda_{17} + \lambda_{18} = 6.8$ hour^{-1}. Inhalation and deposition in the patient's respiratory tract is also a removal mechanism, but for a quiescent patient this loss rate is about 0.1 hour^{-1} and is negligible compared to λ_1. Given a respirable pathogen emission rate of 0.5 hour^{-1}, the initial N_1 value is (0.5 hour^{-1}) $\div$ (6.8 hour^{-1}) $= 7.4 \times 10^{-2}$.

4.2. Rates of Transfer to the Hands, Mucous Membranes, and Respiratory Tract

Assume that N_2 pathogens settle onto 10^4 cm^2 (1 m^2) of bed linen surface area, and that when a HCW enters the room to attend the patient at bedside, the HCW touches the bed linens once a minute with the fingertips of one hand. We estimate that 10 cm^2 is the surface area of the fingertips that would touch the linens (2 cm^2 per fingertip). The transfer efficiency of bacteria from a textile surface to a fingertip during one touch is approximately 0.1%.[11] Assuming a uniform distribution of pathogens on the bed linens, we estimate the transfer rate from textile surfaces to the hands as follows:

$$\lambda_{24} = \frac{10\,\text{cm}^2\ \text{touch}^{-1}}{10,000\,\text{cm}^2} \times 1\ \text{touch minute}^{-1} \times 0.001$$
$$= 1\ \times 10^{-6}\ \text{minute}^{-1}.$$

Absent experimental data on the transfer efficiency from the fingertips to a textile surface, we assume that $\lambda_{42} = \lambda_{24}$.

Assume that N_3 pathogens settle onto 10^4 cm^2 of nontextile surface area (e.g., onto the surfaces of a bedside table and chair). We assume that the attending HCW has less cause, or a lesser tendency, to touch nontextile room surfaces than bed linens, so we posit that the rate of touching these surfaces is once every five minutes, and that 10 cm^2 of the surface area of the fingertips makes contact per touch. The transfer efficiency of viral particles from a nonporous surface to a fingertip during one touch is approximately 0.5%.[12,13] Assuming a uniform distribution of pathogens on nontextile surfaces, we estimate the transfer rate from nontextile surfaces to the hands as follows:

$$\lambda_{34} = \frac{10\,\text{cm}^2\ \text{touch}^{-1}}{10,000\,\text{cm}^2} \times 0.2\ \text{touch minute}^{-1}$$
$$\times\ 0.005 = 1 \times\ 10^{-6}\ \text{minute}^{-1}.$$

Absent experimental data on the transfer efficiency from the fingertips to a nontextile surface, we assume that $\lambda_{43} = \lambda_{34}$.

The rate of contact of the hands with mucous membranes of the eyes, nose, and mouth will vary widely among HCWs. In a study not involving HCWs, the combined frequency of finger contact with nasal membranes and the eyes was about 5 touches per hour (0.083 minute^{-1}).[14] We assume that a touch involves only one fingertip on the same hand that touched the linen, so only 0.2 of the contaminated fingertip surface area contacts the mucous membranes per touch. The transfer efficiency of virus and bacteria from a fingertip to the lips during one touch is approximately 35%.[15] Therefore, we estimate the rate of transfer from the hands to the HCW's mucous membranes as follows:

$$\lambda_{45} = 0.2\ \text{touch}^{-1} \times 0.083\ \text{touch minute}^{-1} \times 0.35$$
$$= 5.8 \times 10^{-3}\ \text{minute}^{-1}.$$

We assume that the loss rate of pathogen viability on the HCW's hands is $\lambda_{47} = 0.69$ hour^{-1}, which is the same value as for the surface and air compartments.

We assume the breathing rate for an adult worker is 1.2 m^3 hour^{-1} (or 0.020 m^3 minute^{-1}),[16] and we assume a room volume of 80 m^3. Given that we treat a 5-μm diameter as representative of respirable particles, the deposition fraction in the respiratory tract (both upper and lower) for this particle size is about 90%.[10] Therefore, we estimate the rate of transfer from room air to the HCW's respiratory tract as follows:

$$\lambda_{16} = \frac{0.020\ \text{m}^3\ \text{minute}^{-1}}{80\ \text{m}^3} \times 0.90$$
$$= 2.3 \times 10^{-4}\ \text{minute}^{-1}.$$

We also assume no resuspension into room air of pathogens on textile and nontextile surfaces, or $\lambda_{21} = \lambda_{31} = 0$, because the HCW is not actively disturbing these surfaces, for example, by shaking or removing bed linens. Because the pathogens in the initial loads N_2 and N_3 are associated with aqueous particles containing salts and protein,[6] it is likely that the dried particle residues would tend to adhere to surfaces and

State 1: $\lambda_{14} = \lambda_{15} = 0$, $\lambda_{12} = \lambda_{13} = 7.8 \times 10^{-4}$ min^{-1}, $\lambda_{16} = 2.3 \times 10^{-4}$ min^{-1}
$\lambda_{17} = 1.16 \times 10^{-2}$ min^{-1}, $\lambda_{18} = 0.1$ min^{-1}

State 2: $\lambda_{21} = \lambda_{23} = \lambda_{25} = \lambda_{26} = \lambda_{28} = 0$, $\lambda_{24} = 10^{-1}$ min^{-1}, $\lambda_{27} = 1.16 \times 10^{-2}$ min^{-1}

State 3: $\lambda_{31} = \lambda_{32} = \lambda_{35} = \lambda_{36} = \lambda_{38} = 0$, $\lambda_{34} = 10^{-1}$ min^{-1}, $\lambda_{37} = 1.16 \times 10^{-2}$ min^{-1}

State 4: $\lambda_{41} = \lambda_{46} = \lambda_{48} = 0$, $\lambda_{42} = \lambda_{43} = 10^{-1}$ min^{-1}, $\lambda_{45} = 5.8 \times 10^{-3}$ min^{-1},
$\lambda_{47} = 1.16 \times 10^{-2}$ min^{-1}

State 5: $\lambda_{51} = \lambda_{52} = \lambda_{53} = \lambda_{54} = \lambda_{56} = \lambda_{57} = \lambda_{58} = 0$

State 6: $\lambda_{61} = \lambda_{62} = \lambda_{63} = \lambda_{64} = \lambda_{65} = \lambda_{67} = \lambda_{68} = 0$

State 7: $\lambda_{71} = \lambda_{72} = \lambda_{73} = \lambda_{74} = \lambda_{75} = \lambda_{76} = \lambda_{78} = 0$

State 8: $\lambda_{81} = \lambda_{82} = \lambda_{83} = \lambda_{84} = \lambda_{85} = \lambda_{86} = \lambda_{87} = 0$

Initial Pathogen Loads: $N_1 = 7.4 \times 10^{-2}$, $N_2 = 6.9 \times 10^{5}$, $N_3 = 7.6 \times 10^{4}$

Fig. 3. Model inputs for the hypothetical scenario involving a HCW visit to a patient room.

require more than casual contact to be dislodged and resuspended.

4.3. The Expected Doses and Infection Risk

At this point, most of the system parameters shown in Fig. 1 are specified, and are summarized in Fig. 3. We assume that the HCW spends 15 minutes at the patient's bedside, in which case there are $n =$ 15,000 time steps given $\Delta t = 0.001$ minute. Based on Equations (1) and (2), the expected doses E[D_5] and E[D_6] are, respectively, 0.43 and 1.2×10^{-4}. The α value depends on the specific pathogen, but for purposes of illustration we use $\alpha = 0.069$, which corresponds to an ID_{50} of 10 organisms. For comparison, $\alpha \approx 0.1$ for the smallpox virus, such that the ID_{50} is approximately seven virus particles.[17] Therefore, infection risk due to hand contact with mucous membranes is $1 - \exp(-0.43 \times 0.069) = 0.029$, and due to inhaling respirable pathogens is $1 - \exp(-1.2 \times 10^{-4} \times 0.069) = 8.3 \times 10^{-6}$. In our risk calculation for the hypothetical viral pathogen, we used the same value of the infectivity parameter α for deposition on mucous membranes and all sites in the respiratory tract. However, for a specific pathogen, the value of α might vary depending on the contact site. For example, the number of influenza A virus required to produce infection via nasal drops in human subjects was observed to be one to two orders of magnitude greater than the number required to infect when delivered via a small particle aerosol (aerodynamic diameters of 1–3 μm).[18,19]

5. CLOSE CONTACT EXPOSURE EVENTS

5.1. Respiratory Droplet Spray

The droplet spray mode of transmission is emphasized in the infection control literature,[20] but we could locate no studies that quantitatively estimated infection risk by this route. A first-pass risk assessment involving coughing is made as follows, although we stress that the extent of mucous membrane contact with droplets emitted by coughs and other expiratory events requires direct experimental investigation. Consider that a HCW is facing the patient at arm's length, which we take to be 0.6 m (2 feet). A cough emits particles with an initial peak velocity of 12.5 m second^{-1}.[21] Table I shows the average number of particles in different equilibrium diameter (d_{eq}) ranges emitted per cough.[5] Based on a previous analysis,[6] we assume that initial particle diameters (Columns 1 and 2) are twice the d_{eq} values, that an emitted aqueous cough particle instantaneously decreases in size to its d_{eq} value due to water loss, and that the d_{eq} value equals the particle's aerodynamic diameter.

We assume that particles with a theoretical stopping distance $\geq$0.6 m reach the HCW's face. The stopping distance (m) is approximately equal to the particle's initial velocity (m/second) multiplied by its terminal settling velocity (m/second) and divided by

Table I. Characteristics of the Respiratory Particles Emitted in the Average Cough

Column Number							
1	2	3	4	5	6	7	8
$d_{0,\min}$ μm	$d_{0,\max}$ μm	$d_{\mathrm{eq},\min}$ μm	$d_{\mathrm{eq},\max}$ μm	$\overline{v}_0$ cm^3	Mean Number of Particles	No. Pathogens per Particle[a]	Droplet Infection Risk
2	5.8	1	2.9	3.8×10^{-11}	121	3.8×10^{-5}	NA[b]
5.8	11.6	2.9	5.8	3.8×10^{-10}	100	3.8×10^{-4}	NA
11.6	17.4	5.8	8.7	1.7×10^{-9}	6.2	1.7×10^{-3}	NA
17.4	22.4	8.7	11.2	4.2×10^{-9}	3.3	4.2×10^{-3}	NA
22.4	52	11.2	26	3.1×10^{-8}	18	3.1×10^{-2}	NA
52	112	26	56	3.2×10^{-7}	64	3.2×10^{-1}	NA
112	170	56	85	1.5×10^{-6}	58	$1.5 \times 10^{\circ}$	NA
170	228	85	114	4.2×10^{-6}	31	$4.2 \times 10^{\circ}$	NA
228	288	114	144	9.1×10^{-6}	20	$9.1 \times 10^{\circ}$	NA
288	346	144	173	1.7×10^{-5}	12	1.7×10^{1}	0.020
346	406	173	203	2.8×10^{-5}	5.3	2.8×10^{1}	0.012
406	464	203	232	4.3×10^{-5}	4.3	4.3×10^{1}	0.0010
464	524	232	262	6.3×10^{-5}	3.5	6.3×10^{1}	0.0089
524	582	262	291	8.9×10^{-5}	2.7	8.8×10^{1}	0.0065
582	700	291	350	1.4×10^{-4}	5.0	1.4×10^{2}	0.013
700	878	350	439	2.6×10^{-4}	0.50	2.6×10^{2}	0.0013
878	1,172	439	586	5.8×10^{-4}	5.0	5.8×10^{2}	0.012
1,172	1,468	586	734	1.2×10^{-3}	1.8	1.2×10^{3}	0.0046
1,468	1,762	734	881	2.2×10^{-3}	1.3	2.2×10^{3}	0.0035
1,762	2,058	881	1,029	3.7×10^{-3}	0.33	3.7×10^{3}	0.0008
2,058	2,352	1,029	1,176	5.6×10^{-3}	0.67	5.6×10^{3}	0.0015
2,352	2,942	1,176	1,471	9.8×10^{-3}	1.7	9.8×10^{3}	0.0043
2,942	3,532	1,471	1,766[c]	1.8×10^{-2}	0.67	1.8×10^{4}	0.0017

[a]Expected number of pathogens per particle with volume $= \overline{v}_0$ given $C_{\mathrm{F}} = 1 \times 10^6$ mL^{-1}.
[b]NA = not applicable.
[c]The reported diameter for this range was >1,471 μm. To assign an expected number of pathogens per particle, we specified an upper range limit of 1,491 μm + 295 μm = 1,766 μm because the preceding diameter range spanned 295 μm.

gravitational acceleration (9.81 m second^{-2}). In turn, cough particles with $d_{\mathrm{a}} > 150$ μm and terminal settling velocities >0.47 m second^{-1} have theoretical stopping distances >0.6 m. With reference to Table I, we assume that particles with $d_{\mathrm{eq}} > 144$ μm are able to travel 0.6 m to the HCW's face within one second, and that particles with $d_{\mathrm{eq}} < 144$ μm lose their momentum at some point between the patient and the HCW.

We assume that cough particles conically spread over a 60° angle (as measured in a plane) as they move away from the patient, such that at the HCW's position a given particle can be anywhere in a conceptual circle of diameter 0.70 m with surface area 0.38 m^2. Based on measurements made by the authors, the projected surface area of the mucous membranes of the eyes, nose, and lips is 10–20 cm^2; we use the value 15 cm^2. If a particle with $d_{\mathrm{eq}} > 144$ μm strikes a circle with area 0.38 m^2 at a random position, the probability that it strikes a mucous membrane positioned in that same circle is (15 cm^2) $\div$ (3.8×10^3 cm^2) = 3.9×10^{-3}.

The risk of infection by droplet spray is a combination of the probabilities that one or more particles from the different diameter ranges contact a mucous membrane and causes infection. Given contact, cough particles with different diameters can impart far different risks due to the variable number of pathogens they carry. The Appendix outlines the computation of infection risk due to the droplet spray in one cough given the following circumstances: (1) the HCW faces the patient at 0.6 m distance; (2) the cough particles conform to the characteristics in Table I; (3) $C_{\mathrm{F}} = 1 \times 10^6$ mL^{-1}; and (4) $\alpha = 0.069$. The estimated infection risk per cough due to droplet spray is 0.14.

However, this risk is conditioned on the HCW facing the patient at close range at the moment the latter coughs. Therefore, estimating the unconditional infection risk involves considering the proportion of coughs during which the HCW faces the patient at

arm's length, and the number of coughs while the HCW is in the room. If a HCW is at close range for, say, 5% of the 15-minute period, the probability that the HCW is at close range when the patient coughs is 0.05, and the unconditional infection risk per cough due to droplet spray is $0.14 \times 0.05 = 0.007$. We previously assumed that for a pneumonia patient, cough frequency was 12 hour^{-1}. If a HCW spends 15 minutes with the patient, it is expected that the HCW is present during three coughs. Given $C_F = 1 \times 10^6$ mL^{-1} and $\alpha = 0.069$, the HCW's infection risk due to droplet spray is $1 - (1 - 0.007)^3 = 0.021$.

5.2. Inspirable Pathogens

Proximity to the patient during coughing also exposes the HCW to inspirable pathogens. An estimate of the associated infection risk is made as follows. Given $C_F = 1 \times 10^6$ mL^{-1}, particles with d_{eq} values in the range 10–100 μm are expected to carry a total of 5.2 pathogens. We assume that all particles in this d_{eq} range rapidly become uniformly distributed within the conceptual right circular cone between the HCW and the patient. This cone has volume 0.079 m^3, so the expected airborne pathogen concentration near the HCW is (5.2) $\div$ (0.079 m^3) = 66 m^{-3}. Approximately 50% of the particles in this d_{eq} range in an inspired air volume enter the head airways region and, of those that enter, essentially 100% deposit in the head airways. For a breathing rate of 1.2 m^3 hour^{-1} with 15 breaths minute^{-1}, the inspired volume per breath is 1.3×10^{-3} m^3. Therefore, the HCW's expected deposited dose of inspirable pathogens in the first breath following the cough is (66 m^{-3}) $\times$ (1.3×10^{-3} m^3) $\times$ $0.5 = 4.3 \times 10^{-2}$ pathogens. Given $\alpha = 0.069$, the infection risk per cough due to inspirable pathogens is $1 - \exp(-0.069 \times 4.3 \times 10^{-2}) = 3.0 \times 10^{-3}$.

Again, this risk is conditioned on the HCW being at close range at the moment the patient coughs. If there is 0.05 probability that the HCW is at arm's length during the cough, the unconditional infection risk per cough due to inspirable pathogens is $3.0 \times 10^{-3} \times 0.05 = 1.5 \times 10^{-4}$. If a HCW is present during three coughs, infection risk due to inspirable pathogens is $1 - (1 - 1.5 \times 10^{-4})^3 = 4.5 \times 10^{-4}$. For the specified scenario, infection risk due to droplet spray (0.021) is 50-fold greater than infection risk due to inspirable pathogens (4.5×10^{-4}). However, if both C_F and α were to increase fivefold ($C_F = 5 \times 10^6$ mL^{-1}, $\alpha = 0.35$), infection risk due to droplet spray versus inspirable pathogens would increase to 0.024 versus 0.011, respectively, which is only a two-fold difference.

6. DISCUSSION

6.1. Combining Risks

Let R_A denote infection risk due to hand-to-mucous-membrane contacts, R_B denote infection risk due to droplet spray, R_C denote infection risk due to inspirable pathogens, and R_D denote infection risk due to respirable pathogens. Because infection can occur only once, the overall infection risk is computed by the inclusion-exclusion formula:

$$\begin{aligned} \mathrm{E}[R] = {} & R_A + R_B + R_C + R_D - R_A R_B - R_A R_C \\ & - R_A R_D - R_B R_C - R_B R_D - R_C R_D \\ & + R_A R_B R_C + R_A R_B R_D + R_A R_C R_D \\ & + R_B R_C R_D - R_A R_B R_C R_D. \end{aligned} \tag{7}$$

In the hypothetical example, $R_A = 0.029$, $R_B = 0.021$, $R_C = 4.5 \times 10^{-4}$, and $R_D = 8.3 \times 10^{-6}$. The overall expected infection risk is 0.050 per Equation (7). To be strict, the contributory risks R_A and R_D should account for the increase in pathogen loads N_1, N_2, and N_3 due to each of the three patient coughs while the HCW is the room. If the coughs were evenly spaced at 2.5, 7.5, and 12.5 minutes after room entry, then $R_A = 0.031$ and $R_D = 1.8 \times 10^{-5}$, and the adjusted overall expected infection risk would be 0.052.

In this scenario, infection risk is driven by hand-to-mucous-membrane contact and by exposure to droplet spray. We do not mean to argue, however, that, these two exposure routes are always more important than inhalation. For example, if the HCW knew the patient had a disease transmitted by hand-to-mucous-membrane contact, the HCW would usually wear protective gloves, which, in turn, would make the HCW conscious of avoiding touching her or his face with gloved hands; in effect, the rate parameter λ_{45} would be zero. If the HCW had no cause to be located close to the patient, the potential for droplet spray exposure would be eliminated. If the HCW's activities involved disturbing bed linens such that respirable pathogens were resuspended into air at the rate of, say, 0.1% per hour ($\lambda_{21} = 1.7 \times 10^{-5}$ minute^{-1}), the expected inhaled dose would be $\mathrm{E}[D_6] = 0.17$; given $\alpha = 0.069$, the infection risk due to respirable pathogens would be 0.012.

6.2. Estimating the Efficacy of Biocidal Textile Coatings

The Fig. 1 model permits a first-pass assessment of the efficacy of different controls that might be applied singly or in combination. In this regard, one of us (Dr. Sun) has developed methods to coat textile surfaces with biocidal finishes that rapidly kill both bacteria[22] and viruses[23] via oxidation. When tested against surrogate microbes, survival after two minutes of contact was equal to or less than 1×10^{-6} of the initial load for most organisms. The latter findings indicate that $\lambda_{27} \geq 6.9$ minute^{-1}, which corresponds to a half-time of 0.1 minute or less.

In our hypothetical scenario with $\lambda_{27} = 1.2 \times 10^{-2}$ minute^{-1} (corresponding to a pathogen half-life of one hour), the dose of viable pathogens to the mucous membrane was $E[D_5] = 0.46$. If the bed linens were coated with a biocidal finish such that $\lambda_{27} = 6.9$ minute^{-1}, the new dose would be $E[D_5] = 0.054$, which corresponds to an approximate 90% reduction in dose and infection risk associated with hand-to-mucous-membrane contact, and a 50% reduction in overall infection risk to 0.025. This outcome suggests that a biocidal coating on textiles could significantly reduce the incidence of HCW infections due to hand-to-mucous-membrane contact.

This substantial reduction in overall infection risk predicted by the model happens to be consistent with two intervention studies demonstrating the importance of hand-to-mucous-membrane contact in the transmission of common respiratory tract diseases. In the first study, mothers in a treatment group periodically applied a virucidal iodine solution to their fingers upon the first appearance of common cold symptoms in a sick family member, whereas control mothers applied a nonvirucidal placebo solution. The infection rate among the treatment mothers was decreased by 66% relative to the control group.[2] In the second study, handwashing at least five times daily was actively promoted among groups of U.S. Navy personnel, but was not promoted among control subjects living in different barrack housing on the same base. Subsequent to implementing the handwashing program, the rate of outpatient visits for respiratory illness to the base medical clinic was reduced by 45% among the treatment group, but did not change among the control group.[24] Although neither study identified the specific pathogens involved in subjects who became ill, it is believed that most respiratory tract infections are due to viral pathogens.

Although handwashing with virucidal solutions and the use of protective gloves should completely eliminate the hand-to-mucous-membrane exposure route and, in theory, be superior to a biocidal finish on textiles, handwashing and glove use are less reliable control measures. The reason is that the HCW must strictly adhere to glove use and/or thorough handwashing when attending all patients for whom disease diagnoses are still pending. If the HCW takes time-saving shortcuts during a busy work shift by not always wearing gloves or washing hands, the control measures are compromised. In contrast, the biocidal finish is always in place, and its efficacy does not rely on the behavior of the HCW. The biocidal finish would also reduce potential inhalation exposure to pathogens resuspended into room air from textile surfaces, whereas handwashing and glove use practices would have no effect on this exposure pathway.

7. CONCLUSIONS

We have presented an integrated model of pertinent source-environment-receptor pathways associated with infection risk in a health-care setting. As evident in our hypothetical example, assumptions are required to specify numerous system parameters because relevant published data are not available (for example, the frequency with which a HCW's hands contact surfaces while in a patient room) and because the value of a given parameter is not constant across different scenarios (for example, the rate at which a pathogen loses viability). At the same time, a benefit of the model, and of modeling in general, is that it identifies the key elements of the system under study and the associated information needed to make accurate estimates of system performance. In turn, this information can be collected by reviewing published literature and conducting prospective experimental and/or observational studies.

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APPENDIX: INFECTION RISK DUE TO RESPIRATORY DROPLET SPRAY

For simplicity, we assume that the particles in each diameter range in Table I are uniformly distributed between the range endpoints. The mean initial volume $\overline{v}_0$ of a particle in a given diameter range (Table I, Column 5) is computed as follows:

$$\overline{v}_0 = \frac{\pi\left(d_{0,\max}^4 - d_{0,\min}^4\right)}{24\left(d_{0,\max} - d_{0,\min}\right)}.$$

The expected number of pathogens carried by a particle with mean volume is the product $\overline{v}_0 \times C_F$. Table I, Column 5, lists the expected number of pathogens per particle given $C_F = 1 \times 10^6$ mL^{-1}. The actual number of pathogens in a particle with mean volume in a given diameter range is treated as a Poisson random variable with the corresponding expected value listed in Column 5. Table I, Column 6, lists the expected number of particles per cough in each diameter range; these are average values based on the particle counts in 90 coughs. The actual number of particles in a cough in a given diameter range is treated as a Poisson random variable with the expected value listed in Column 6. The probability that any particle with $d_{eq} > 144$ μm in droplet spray strikes the mucous membranes of a HCW facing a patient at arm's length is estimated to be 3.9×10^{-3}. According to the Poisson thinning principle, the expected number of particles with $d_{eq} > 144$ μm in a given diameter range that strike a mucous membrane is the product of 3.9×10^{-3} and the expected number of particles per cough listed in Column 7.

For particles with $d_{eq} > 144$ μm in a given diameter range, the pathogen dose to the mucous membranes is an integer random sum D described as follows:

$$D = \sum_{i=1}^{N} X_i,$$

where N is the number of particles that strike a mucous membrane, and X_i is the number of viable pathogens in the ith particle. Again, both X and N are treated as Poisson random variables. Given a random dose D, infection risk due to the particles in the given diameter range is computed by $R = 1 - (1 - \alpha)^D$.

The expected random dose is $E[N] \times E[X]$. Although both N and X are Poisson random variables, the random sum D is not a Poisson random variable; thus, Equation (6) of the main text may not be used to compute $E[R]$. Instead, for each diameter range for which $d_{eq} > 144$ μm, we randomly generated 10^5 values of D, computed the associated infection risk, and equated the mean risk with the unconditional risk value $E[R]$. Table I, Column 8, lists the $E[R]$ value due to the particles in each diameter range. Finally, the $E[R]$ values for all the relevant diameter ranges were combined using an inclusion-exclusion formula (analogous to Equation (7) of the main text) to compute the infection risk per cough due to droplet spray exposure.

REFERENCES

1. Buxton Bridges, C., Kuehnert, M. J., & Hall, C. B. (2003). Transmission of influenza: Implications for control in health care settings. *Clinical Infectious Diseases*, *37*, 1094–1101.
2. Hendley, J. O., & Gwaltney, J. M. Jr. (1988). Mechanisms of transmission of rhinovirus infections. *Epidemiologic Reviews*, *10*, 242–258.
3. Institute of Medicine. (2001). In M. J. Field (Ed.), *Tuberculosis in the Workplace* (pp. 25–27). Washington, DC: National Academy Press.
4. Haas, C. N., Rose, J. B., & Gerba, C. P. (1999). *Quantitative Microbial Risk Assessment* (pp. 266–268, 275–277). New York: John Wiley & Sons, Inc.
5. Loudon, R. G., & Roberts, R. M. (1967). Droplet expulsion from the respiratory tract. *American Review of Respiratory Diseases*, *95*, 435–442.
6. Nicas, M., Nazaroff, W., & Hubbard, A. (2005). Toward understanding the risk of secondary airborne infection: Emission of respirable pathogens. *Journal of Occupational Environmental Hygiene*, *2*, 43–51.
7. Loudon, R. G., & Roberts, R. M. (1967). Cough frequency in patients with respiratory disease. *American Review of Respiratory Diseases*, *96*, 1137–1143.
8. Murphy, B. R., Chalhub, E. G., Nusinoff, S. R., Kasel, J., & Chanock, R. M. (1973). Temperature-sensitive mutants of influenza virus. IV. Further characterization of the ts-1 [E] influenza A recombinant (H_3N_2) virus in man. *Journal of Infectious Diseases*, *128*, 479–487.
9. Bean, P., Moore, B. M., Sterner, B., Peterson, L. R., Gerding, D. N., & Balfour, Jr. (1982). Survival of influenza virus on environmental surfaces. *Journal of Infectious Diseases 146*, 47–51.
10. Hinds, W. C. (1999). *Aerosol Technology*, 2nd ed. (pp. 62–64, 235–245). New York: John Wiley & Sons, Inc.
11. Sattar, S. A., S. Springthorpe, H. H., Mani, S., Gallant, M., Nair, R. C., Scott, E., & Kain, J. (2001). Transfer of bacteria from fabrics to hands and other fabrics: Development and application of a quantitative method using *Staphylococcus aureus* as a model. *Journal of Applied Microbiology*, *90*, 962–970.
12. Rheinbaben, F. V., Schunemann, S., Grob, T., & Wolff, M. H. (2000). Transmission of viruses via contact in a household setting: Experiments using bacteriophage ϕX174 as a model virus. *Journal of Hospital Infection*, *46*, 61–66.
13. Sattar, S., Jacobsen, H., Springthorpe, V. S., Cusack, T. M., & Rubino, J. R. (1993). Chemical disinfection to interrupt transfer of rhinovirus type 14 from environmental surfaces to hands. *Applied and Environmental Microbiology*, *59*, 1579–1585.
14. Hendley, J. O., Wenzel, R. P., & Gwaltney, J. M., Jr. (1973). Transmission of rhinovirus by self-inoculation. *New England Journal of Medicine*, *288*, 1361–1364.
15. Rusin, P., Maxwell, S., & Gerba, C. (2002). Comparative surface-to-hand and fingertip-to-mouth transfer efficiency of gram-positive bacteria, gram-negative bacteria, and phage. *Journal of Applied Microbiology*, *93*, 585–592
16. National Institute for Occupational Safety and Health. (1976). *A Guide to Industrial Respiratory Protection* NIOSH Publication No. 76-189. Cincinnati, OH.
17. Nicas, M., Hubbard, A., Jones, R., & Reingold, A. (2004). infectious dose of variola (smallpox) virus. *Applied Biosafety*, *9*, 118–127.
18. Alford, R. H., Kasel, J. A., Gerone, P. J., & Knight, V. (1966). Human influenza resulting from aerosol inhalation.

Proceedings of the Society for Experimental Biology and Medicine, *122*, 800–804.
19. Douglas, R. G., Jr. (1975). Influenza in man. In Kilbourne, E. D. (Ed.), *The Influenza Virsues and Influenza* (pp. 395–447). New York: Academic Press.
20. Centers for Disease Control and Prevention. (1997). *Guideline for Isolation Precautions in Hospitals, Part II. Recommendations for Isolation Precautions in Hospitals*. Garner, J. S., & the Hospital Infection Control Practices Advisory Committee. Available at http://www.cdc.gov/ncidod/hip/ISOLAT/isopart2.htm (accessed November 10, 2005).
21. Khan, T. A., Higuchi, H., Marr, D. R., & Glauser, M. N. (2004). Unsteady flow measurements of human microenvironment using time resolved particle image velocimetry. RoomVent 2004, Coimbra, Portugal, September 5–8, 2004.
22. Sun, G., Xu, X., Bickett, J. R., & Williams, J. F. (2001). Durable and regenerable antibacterial finishing of fabrics with a new hydantoin derivative. *Industrial & Engineering Chemistry Research*, *40*, 1016–1021.
23. Panangala, V. S., Liu, L., Sun, G., Worley, S. D., & Mitra, A. (1997). Inactivation of rotavirus by new and polymeric water disinfectants. *Journal of Virological Methods*, *66*, 263–268.
24. Ryan, M. A. K., Christian, R. S., & Wohlrabe, J. (2001). Handwashing and respiratory illness among young adults in military training. *American Journal of Preventive Medicine*, *21*, 79–83.