American Journal of Epidemiology
Vol. 170, No. 2
DOI: 10.1093/aje/kwp116
Advance Access publication May 27, 2009
© The Author 2009. Published by the Johns Hopkins Bloomberg School of Public Health.
All rights reserved. For permissions, please e-mail: journals.permissions@oxfordjournals.org.

## Practice of Epidemiology

# Dynamics and Control of Infections Transmitted From Person to Person Through the Environment

**Sheng Li, Joseph N. S. Eisenberg, Ian H. Spicknall, and James S. Koopman**

*Initially submitted November 17, 2008; accepted for publication April 13, 2009.*

The environment provides points for control of pathogens spread by food, water, hands, air, or fomites. These environmental transmission pathways require contact network formulations more realistically detailed than those based on social encounters or physical proximity. As a step toward improved assessment of environmental interventions, description of contact networks, and better use of environmental specimens to analyze transmission, an environmental infection transmission system model that describes the dynamics of human interaction with pathogens in the environment is presented. Its environmental parameters include the pathogen elimination rate, $\mu$, and the rate humans pick up pathogens, $\rho$, and deposit them, $\alpha$. The ratio, $\rho N/\mu$ ($N$ equals population size), indicates whether transmission is density dependent (low ratio), frequency dependent (high ratio), or in between. Transmission through frequently touched fomites, such as doorknobs, generates frequency-dependent patterns, while transmission through thoroughly mixed air or infrequently touched fomites generates density-dependent patterns. The environmental contamination ratio, $\alpha/\gamma$, reflects total agent deposition per infection and outbreak probability, where $\gamma$ is defined as the recovery rate. These insights provide theoretical contexts to examine the role of the environment in pathogen transmission and a framework to interpret environmental data to inform environmental interventions.

communicable diseases; disease transmission, infectious; environmental medicine; environment and public health; epidemiologic methods; fomites; influenza, human; intervention studies

Abbreviations: EITS, environmental infection transmission system; SIR, susceptible-infectious-recovered.

Human infections that pass from one person to another commonly do so through environmental media, such as air, fomites, food, hands, and water. Infection transmission models for non-vector-borne infections, however, rarely specify the mode of transmission or the vehicle that carries infection from one person to another. Instead, most models assume that the dynamic details of environmental transmission can be approximated by a point contact process (1–5). With the exception of sexually transmitted diseases, however, the environment often plays a major role in transmission, especially for enteric and respiratory diseases. Moreover, these environmental processes provide important points of intervention. To promote a transmission system framework that explicitly accounts for environmental process dynamics, we present a transmission model with environmental components that mediate transmission. We call this an *environmental infection transmission system* (EITS) model.

A number of approaches have been presented for incorporating environmental processes of non-vector-borne infections in transmission models. One approach is to collapse across environmental dynamics, resulting in a static description of the environment (6). Another approach is to explicitly formulate environmental pathogen dynamics. This has been done for water-mediated transmission in deterministic (7–11) and stochastic (12) formulations, as well as for air- and fomite-mediated transmission of influenza (13). We both generalize and abstract these approaches in our EITS framework.

Much of the previous work on defining transmission rates in this area has focused on the household to define contact and to estimate transmission probabilities (14–17). Other

Correspondence to Dr. Joseph N. S. Eisenberg, Department of Epidemiology, University of Michigan, 109 South Observatory Street, Ann Arbor, MI 48109 (e-mail: jnse@umich.edu).



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

attempts to define contact have relied on conversational encounters (3, 18, 19), direct touching (3), or simultaneous presence in a room (4, 5). Conversational contact is likely relevant to airborne transmission. Direct touching could transmit environmentally acquired pathogens. The simultaneous presence of both transmission modes could generate vastly different transmission probabilities in different venues depending upon environmental conditions, human behaviors in those venues, the survival characteristics of the agent as it transits in air or on fomites, and the dose required to initiate infection.

By explicitly modeling environmental processes that mediate transmission, our EITS models differentiate air, water, and fomite pathways of transmission (and even different classes of fomite transmission). We will demonstrate how this framework provides paths to the following: 1) developing transmission parameters that can be independently measured in environmental field studies, including survival rates of pathogens in the environment, the transfer coefficient from fomites to hands, and many more; 2) formulating transmission processes specific for air, water, food, and fomites in a manner that facilitates assessment of potential environmental control effects and the interpretation of environmental pathogen measurements; and 3) developing mechanistic theory on environmentally based transmission rates, analogous to how vector-borne transmission rates are largely defined by entomologic factors that are easily measured in the field.

## MATERIALS AND METHODS

### Model assumptions

We present a basic EITS model with the following assumptions:

1. All individuals are identical except that one is either $S$ (completely susceptible), $I$ (infected and infectious), or $R$ (completely immune).
2. The total population size is constant.
3. The environment is a single, fixed-size, homogeneous compartment.
4. Humans are the only source of pathogens, and individuals are uniformly exposed to pathogens in the environment.
5. In the environment, pathogens instantaneously and thoroughly mix, and they do not replicate.
6. Once picked up from the environment, pathogens can instantaneously infect $S$ at a rate that is independent of prior pathogen pick up.
7. Pathogen levels in the environment diminish via first-order dynamics through pick up of pathogens by humans, die off, and environmental decontamination.

### EITS deterministic compartmental model

As shown in Figure 1, our EITS deterministic compartmental model includes 2 types of state entities: 1) humans, which are divided into $S$, $I$, and $R$ states, and 2) live pathogens in the environment, $E$. The model is based on the following ordinary differential equations:

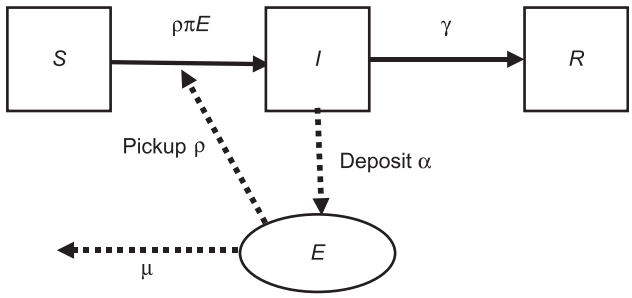


**Figure 1.** A schematic representation of flow of individual (solid lines) among states and flow of pathogens in the environment (dotted lines) for the environmental infection transmission system (EITS) model.

$$\begin{aligned}
\tfrac{dS}{dt} &= -S\rho\pi E \\
\tfrac{dI}{dt} &= S\rho\pi E - \gamma I \\
\tfrac{dR}{dt} &= \gamma I \\
\tfrac{dE}{dt} &= \alpha I - E\big(\big(S + I + R\big)\rho + u\big).
\end{aligned} \tag{1}$$

$\rho$ is the fraction of $E$ picked up by each person per unit of time; $\pi$ is the probability that a susceptible individual becomes infectious per pathogen $E$ picked up; $\gamma$ is the rate per individual and per unit of time of recovery from and acquisition of immunity to infection; $\alpha$ is the number of pathogens per unit of time deposited into the environment by an infectious individual; and $\mu$ is the rate at which pathogens are eliminated from the environment by any means (naturally dying, being killed by decontamination processes, or being cleaned or otherwise removed from the environment).

We used Berkeley Madonna software (20) to numerically solve the ordinary differential equations in equation 1.

### Stochastic compartmental model

Our EITS stochastic model is Markovian. All state entities and transmission rates are defined similarly to those in the EITS deterministic compartmental model. One difference is that the state variables ($S$, $I$, $R$, $E$) are discrete integers in the stochastic model rather than continuous as in the deterministic compartmental model. Our stochastic models allow for only a single event to occur at any given time; the specific event is randomly determined by the transition rates (Table 1). In deterministic compartmental models, on the other hand, events happen continuously and simultaneously. The outputs of these 2 model structures converge as the initial numbers of infected individuals and environmental pathogens are large. As these initial values decrease, the chance of stochastic die out increases. This phenomenon does not occur in a deterministic model.

The Gillespie algorithm (21) is applied to simulate the stochastic transmission process and to randomly execute a single event at various time steps on a continuous time scale. This model was coded and run in JAVA software (Sun Microsystems, Inc., Santa Clara, California).

Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

**Table 1.** Event and Transition Rates for the EITS Stochastic Model

| Event | Result | Transition Rate |
|---|---|---|
| Infection | $(S, I, R, E) \rightarrow (S-1, I+1, R, E)$ | $S \times \rho \times E \times \pi$ |
| Removal | $(S, I, R, E) \rightarrow (S, I-1, R+1, E)$ | $I \times \gamma$ |
| Depositing | $(S, I, R, E) \rightarrow (S, I, R, E+1)$ | $I \times \alpha$ |
| Pathogen decrease | $(S, I, R, E) \rightarrow (S, I, R, E-1)$ | $E \times (\rho \times (S+I+R) + \mu)$ |

Abbreviation: EITS, environmental infection transmission system.

### Choice of parameter values

To illustrate the behavior of the EITS, we chose to parameterize our model for influenza (Table 2) such that the environment corresponds to 1) frequently touched fomites, such as a door handle, that are touched by many different individuals; 2) infrequently touched fomites, such as floors or ledges; or 3) air inside a building. Any real situation might incorporate all 3 of these pathways simultaneously. We isolated these 3 conditions for the sake of clarifying the dynamics related to each condition separately. The population size, $N$ ($N = S + I + R$), represents the number of people in a public indoor venue. We used a point estimate for the recovery rate derived from previous influenza models (22, 23). Except for the recovery rate, $\gamma$, all parameters vary by route of transmission. Infectivity, $\pi$, differs between air and fomite because the different routes of infection, inhalation for air and touched membrane for fomites, have different dose-response characteristics as illustrated from empirical studies (24–26). Estimates on environmental elimination rates, $\mu$, are based on experimental studies in air (27) and on nonporous surfaces (28). Considering the particle size distribution of excretions, only the smaller particles stay suspended in air and are respirable, whereas larger particles rapidly settle onto surfaces where they may be picked up; thus, there is a route-specific deposit rate, $\alpha$, for each pathway. We assume that frequently touched fomites have smaller surface areas than infrequently touched fomites and, therefore, receive proportionally less contamination. The deposit rate is governed by physical and behavioral factors, such as sneezing or cough rates and deposition and aerosolization fractions, among others that are derived from a variety of empirical studies (29–35). Analogously, the pick-up rate, $\rho$, is governed by physical and behavioral factors, such as breathing, touching rates, and transfer efficiencies among surfaces, hands, and membranes (36–41). In order to compare across the 3 scenarios, we parameterized the scenarios to have the same $R_0$. For more parameterization details, refer to the Web-only supplement accompanying this paper. (This information is posted on the *Journal*'s website (http://aje.oxfordjournals.org/).)

## RESULTS

### Mathematical analysis of EITS model structure and behavior

In the EITS model, pathogens are picked up by humans at a rate, $\rho N$, and eliminated from the environment at a rate, $\mu$. The fraction of live environmental pathogens picked up by humans, therefore, is

$$f_E = \frac{\rho N}{\rho N + \mu}. \tag{2}$$

This fraction ranges from near zero when elimination is much larger than the pick up to near 1 if the pick up is much larger than elimination. Another important metric is the average time pathogens persist in the environment, $t_E$:

**Table 2.** Parameter Values for an Influenza EITS Model Based on Data From the Literature

| Parameter | Parameter Estimates | | | Notes[a] |
|---|---|---|---|---|
| | Air | Frequently Touched Fomite | Infrequently Touched Fomite | |
| Recovery rate, 1/day ($\gamma$) | 0.2 | 0.2 | 0.2 | Based on empirical probability distribution. |
| Infectivity ($\pi$) | 0.0517 | 0.0000693 | 0.0000693 | Based on exponential dose-response model. Route of transmission: air = inhalation; fomite = membrane. |
| Elimination rate, 1/day ($\mu$) | 8.64 | 2.88 | 2.88 | Loss in air comes from deaths, and loss on fomites reflects loss on nonporous surfaces. |
| Deposit rate, pathogens/infected/day ($\alpha$) | 693 | 5,244 | 1,040,177 | Contamination based on cough and sneezing rates. Deposition is based on size distribution from sneezing, where preevaporative particles with a diameter of <20 μm are assumed to remain in air. |
| Pick up, 1/person/day ($\rho$) | 0.0000877 | 0.297 | 0.0000145 | Based on breathing rates and touching rates. Exposure duration is assumed to be 8 hours/day. |

Abbreviation: EITS, environmental infection transmission system.

[a] References for model parameterization are in the Web-only supplement (http://aje.oxfordjournals.org/).



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

**Table 3.** Initial Conditions and Basic Statistics for the EITS Models

| Parameter | Airborne | Frequently Touched Fomite | Infrequently Touched Fomite |
|---|---|---|---|
| Total population ($N$) | 1,000 | 1,000 | 1,000 |
| Initial $S$ ($S_0$) | 999 | 999 | 999 |
| Initial $I$ ($I_0$) | 1 | 1 | 1 |
| Initial $R$ ($R_0$) | 0 | 0 | 0 |
| Initial $E$ ($E_0$) | 0 | 0 | 0 |
| Basic reproductive number ($R_0$) | 1.80 | 1.80 | 1.80 |
| Environmental persistence time ($t_E$) | 0.115 | 0.003 | 0.345 |
| Fraction of pick up from the environment ($f_E$) | 0.010 | 0.990 | 0.005 |

Abbreviation: EITS, environmental infection transmission system.

$$t_E = \frac{1}{\rho N + \mu}. \tag{3}$$

For our 3 environmental transmission pathways (air, frequently touched fomites, infrequently touched fomites), the parameter values defined in Table 2 generate fractions of live environmental pathogens picked up by humans of 0.01%, 99.04%, and 0.50%, respectively. They generate average persistence times of 0.115, 0.003, and 0.345 days (Table 3). These values reflect the fact that frequently touched fomites are picked up at a high rate and, therefore, have a low environmental persistence time compared with infrequently touched fomites. Air is more similar to infrequently touched fomites with respect to persistence and fractional pick up. The specific relation between these 2 transmission routes depends on pathogen- and environment-specific factors.

The basic reproductive number, $R_0$, represents the expected number of secondary cases caused by introducing a single primary case into a totally susceptible population. As shown in the Web supplement, $R_0$ can be written as follows:

$$\frac{\alpha}{\gamma} \times \frac{\rho N}{\rho N + \mu} \times \pi. \tag{4}$$

$R_0$ can be considered as the product of 1) total pathogens deposited by an infectious individual during his/her contagious period, $\frac{\alpha}{\gamma}$; 2) the proportion of pathogens picked up while still alive, $\frac{\rho N}{\rho N+\mu}$; and 3) the infectivity of pathogens, $\pi$. Based on the parameter values presented in Table 2, $R_0 = 1.8$ for the 3 model scenarios.

When the total pickup rate is much larger than the elimination rate ($\rho N >> \mu$), $R_0$ approaches $\alpha \times \frac{\pi}{\gamma}$ and is independent of population size, $N$. This results in a frequency-dependent mass action formulation and corresponds to a frequently touched fomite, such as a door handle or a frequently used workspace. When the total pick-up rate is much smaller than the elimination rate ($\rho N << \mu$), $R_0$ approaches $\alpha \times \frac{\rho N}{\mu} \times \frac{\pi}{\gamma}$ and is proportional to the population size, $N$. This corresponds to a density-dependent mass action formulation, such as either 1) airborne transmission with rapid, thorough mixing of air or 2) surface contamination where individuals infrequently touch the surface and the majority of agents die or are disinfected before the next person touches it. This density-dependent formulation is similar to the case addressed by Noakes et al. (6) in an airborne transmission model. Therefore, according to the ratio, $\rho N/\mu$, the EITS model can characterize airborne- or fomite-mediated transmission and, within fomite-mediated transmission, either frequently or nonfrequently touched surfaces. Multiple pathways can also be modeled, each with unique parameterizations.

By rearranging equation 4, we get

$$R_0 = \pi \times \left(\frac{\alpha}{\gamma}\right) \times \left(\frac{\frac{\rho N}{\mu}}{\frac{\rho N}{\mu} + 1}\right). \tag{5}$$

This reformulation of $R_0$ brings out 2 important ratios: $(\rho N)/\mu$, the environmental persistence ratio, an indicator of the importance of pick up compared with environmental elimination pathogens from the environment; and $\alpha/\gamma$, the contamination ratio, a measure of the pathogen deposition magnitude from an infectious individual. The condition, $\rho N/\mu >> 1$, corresponds to frequently touched fomites. Under this condition, environmental contamination, $\alpha/\gamma$, is more likely to be picked up than to die off. The condition, $\rho N/\mu << 1$, corresponds to infrequently touched fomites. Under this condition, environmental processes attenuate pathogen levels before humans are exposed.

These frequency- and density-dependent relations can also be appreciated by transforming our EITS model into an instantaneous contact model corresponding to the classic Kermack-McKendrick susceptible-infectious-recovered (SIR) model (42). To this end, we assume that the dynamics of $E$ can be ignored, such that $dE/dt = 0$. Under these conditions:

$$E = \frac{\alpha I}{(S + I + R)\rho + \mu}.$$

Substituting $E$ into equation 1, we have

$$\begin{aligned} \frac{dS}{dt} &= -\frac{\alpha\pi\rho}{\rho N+\mu} SI \\ \frac{dI}{dt} &= \frac{\alpha\pi\rho}{\rho N+\mu} SI - \gamma I, \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{6}$$

where the term $\frac{\alpha\pi\rho}{\rho N+\mu}$ is equivalent to the single transmission rate parameter in the classic SIR model. The $R_0$ of this instantaneous contact SIR model is

$$R_0 = N\left(\frac{\alpha\pi\rho}{\rho N + \mu}\right)\left(\frac{1}{\gamma}\right). \tag{7}$$

This is the same as that derived previously from our EITS model with environmental dynamics. The Kermack-McKendrick SIR model is formulated as density-dependent contact, and its $R_0$ is proportional to the population size. As in the EITS model, the formulation of this instantaneous contact SIR model can be considered as either density- or



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

frequency-dependent contact on the basis of the environmental persistence ratio, $\rho N/\mu$.

### Analyses of dynamics of the EITS model

Figure 2 compares the influenza dynamics for the 3 EITS model scenarios (air, frequently touched fomites, and infrequently touched fomites) with the SIR model configuration shown in equation 6. The final cumulative incidence is similar for all 3 EITS transmission pathways and the SIR configuration, reflecting that they were all parameterized to have the same $R_0$ (Figure 2A). The SIR configuration dynamics are the fastest, although frequently touched fomite transmission exhibits similar dynamics. Air transmission dynamics are slower, and the infrequently touched fomite transmission is even slower.

These dynamic differences are reflected in the different environmental persistence times, $\frac{1}{\rho N+\mu}$, for the 3 EITS model scenarios. Environmental persistence time is greatest for the infrequently touched fomites and, therefore, their time to peak infection prevalence is longer than for the other scenarios (Figure 2B). On the other hand, the pathogen environmental persistence time is short in the case of the frequently touched fomites, so their time to peak infection prevalence is the shortest.

The specific timing and dynamics will vary by the specific parameterization. For example, decreasing the pick-up rate and the elimination rate by the same fraction ($\rho N/\mu$ remains constant) results in slower dynamics, lower peak prevalence, and unchanged final cumulative incidence. However, the general features of the EITS model are that 1) environmental pathogen dynamics will slow the epidemic curve, 2) environmental transmission will attenuate peak incidence and prevalence, and 3) different routes of environmental transmission will exhibit different dynamics.

### Intervention effects in the EITS deterministic compartment model

To gain insights into environmental infection control dynamics, we assess 2 types of interventions. The first affects the elimination rate parameter, $\mu$, which corresponds to environmental decontamination. The second affects the pathogen pick-up rate parameter, $\rho$. The pick-up rate, $\rho$, has no simple intervention analog but could be thought of as a behavioral change that decreases environmental contact, an altered transfer efficiency, or a dilution of the environmental surface area to be touched. To illustrate intervention effectiveness in different scenarios and how interventions impact dynamics and risk, we examine 2 simple scenarios: 1) increasing the elimination rate, $\mu$, by 25%; and 2) reducing the pathogen pick-up rate, $\rho$, by 25%. As shown in Figure 3, both interventions have little effect on the dynamics of epidemics for the frequently touched fomite scenario. Frequently touched objects, such as doorknob handles, have a high pick-up rate, so that a small increase in the elimination rate or a decrease in the pick-up rate will have very little impact on transmission. This can also be explained by noting that $R_0$ for frequently touched fomites is approximately independent of both the elimination and pick-up rates. For the air and the infrequently touched fomite scenarios, however, these 2 interventions can lead to lower cumulative incidence, slower dynamics, and a smaller peak of live pathogens in the environment. Although reducing pathogen pick up is more effective than environmental decontamination, the efforts required by these 2 interventions will affect the choice of intervention. The reason why these 2 interventions are effective for air and infrequently touched fomites is that the elimination rate and pick-up rate are approximately proportional to $R_0$ in these 2 scenarios.

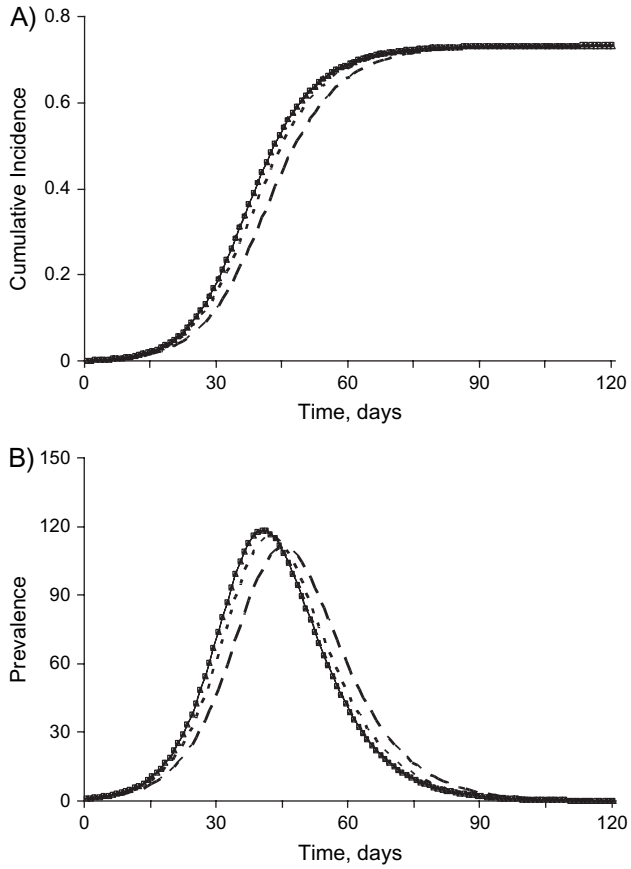


**Figure 2.** Cumulative incidence (A) and prevalence (B) using the environmental infection transmission system (EITS) deterministic compartmental model. EITS model scenarios include transmission through infrequently touched fomite (dashed line), air (dotted line), and frequently touched fomite (solid line with square). Corresponding instantaneous contact susceptible-infectious-recovered (SIR) model (solid line with triangle) is shown for comparison, which has similar dynamics to the EITS frequently touched fomite scenario. $R_0 = 1.8$, and simulations are seeded with 1 infectious individual. Parameter values are shown in Table 2.

### Stochastic model analyses

The EITS stochastic model was first analyzed to explore how an environmental contamination event affects the probability of an outbreak. To this end, we varied the initial level of environmental contamination to assess its impact on the probability of an outbreak's occurring, defined as the proportion of simulations that resulted in attack rates of >0.05



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

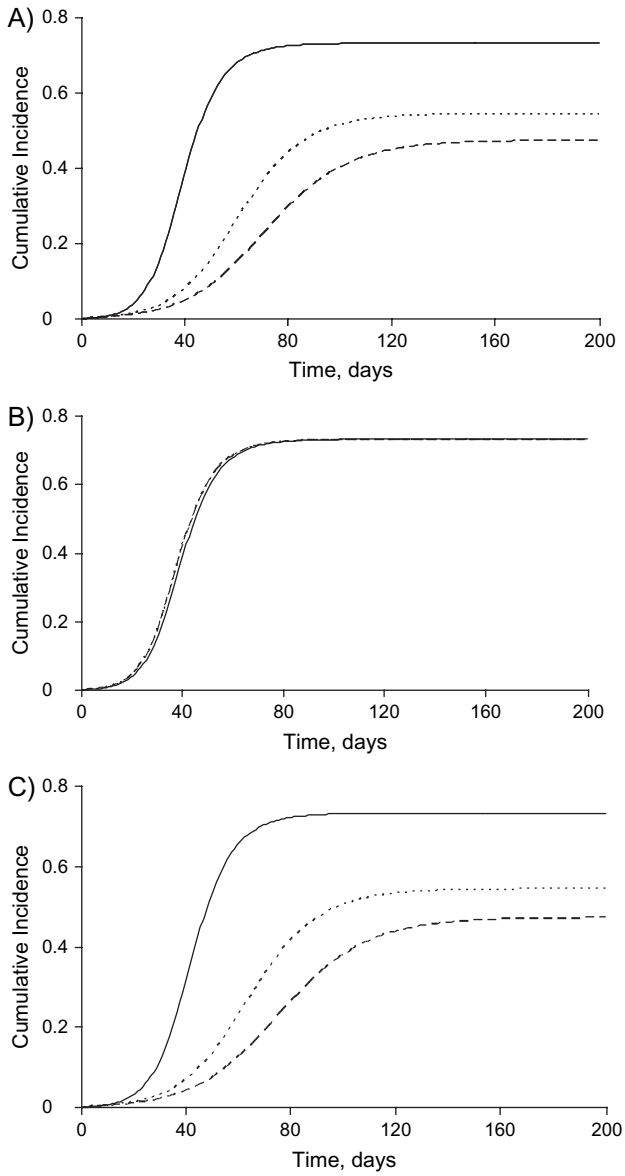


**Figure 3.** Comparing the effectiveness of environmental decontamination (dotted line), decreasing environment contact (dashed line), and no intervention (solid line) by using the environmental infection transmission system (EITS) deterministic compartmental model for air (A), frequently touched fomite (B), and infrequently touched fomite (C) scenarios. Parameter values for the "no intervention" scenario are shown in Table 2. Environmental decontamination corresponds to increasing the elimination rate by 25%. Decreasing environmental contact corresponds to decreasing the pick-up rate by 25%.

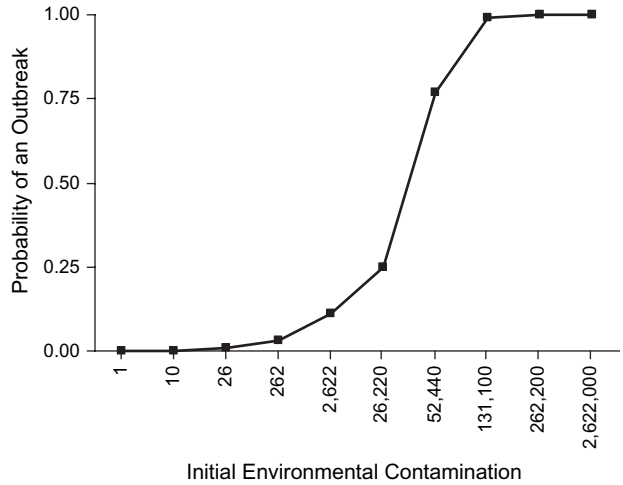


**Figure 4.** Probability of an outbreak for different initial environmental contamination levels by using the environmental infection transmission system (EITS) stochastic model and the frequently touched fomite scenario. Simulations use the parameter sets for the frequently touched fomite scenario shown in Table 2. Initial conditions are $I_0 = 0$, $E_0 = (1, 10, 26, 262, 2{,}622, 26{,}220, 52{,}440, 131{,}100, 262{,}200, 2{,}622{,}000)$.

(simulation details are defined in Figure 4). The relation between the outbreak probability and $E_{(t=0)}$ is sigmoidal; that is, above a threshold contamination level, there is a region in which the probability of an epidemic increases exponentially with $E_{(t=0)}$. At higher initial contamination levels, the probability of an outbreak levels off. Using the probability of outbreak as an additional risk measure in microbial risk assessments may be an important complement to the currently used measures that generally rely on mean values.

We also explored the influences of human contamination, through shedding from infectious individuals, on the dynamics of epidemics (simulation details defined in Figure 5). An infectious individual sheds, on average, $\frac{\alpha}{\gamma}$ pathogens into the environment during his/her contagious period. As shown in Figure 5, when fixing $R_0$ and the initial conditions, increasing the contamination ratio, $\frac{\alpha}{\gamma}$, results in an increase in the probability of an outbreak. The relation in Figure 5 holds for any proportional change in the elimination rate, pick-up rate, and infectivity parameter values where $R_0$ remains constant, suggesting that, as long as $R_0$ is constant, these 3 parameters do not have significant influence on the probability of an outbreak. The reason that the contamination ratio can affect the probability of an outbreak, even when $R_0$ is constant, is that, when infectious individuals excrete fewer pathogens into the environment, reflected by a small contamination ratio, $\frac{\alpha}{\gamma}$, this smaller number of environmental pathogens has a higher chance of extinction, preventing the initiation of an outbreak.

The results shown in Figures 4 and 5 also hold for both the infrequently touched fomite and air scenarios (data not shown).

## DISCUSSION

Commonly, the mechanisms of transmission through the environment are not explicitly formulated in non-vector-borne infectious disease population dynamic models, except for some models that focus on enclosed hospital settings (31) or water-borne outbreaks (7–12). In this paper, we



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

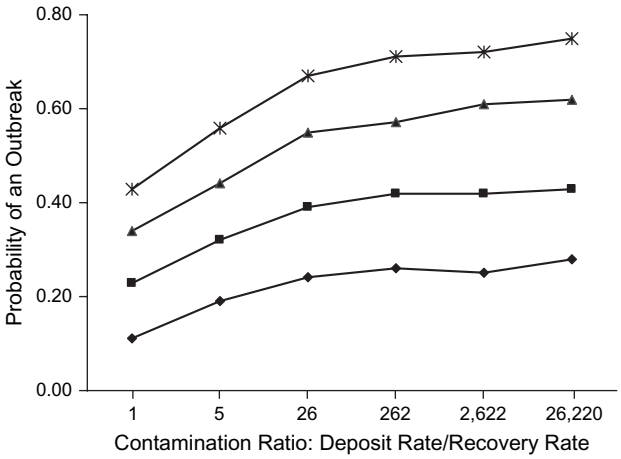


**Figure 5.** Probability of an outbreak for different levels of contamination excreted per person. $R_0$ equals 4.0, 2.5, 1.8, and 1.3 for these 4 curves from top to bottom. For each curve, the infectivity is decreased proportionally with the contamination ratio so that $R_0$ remains constant. Simulations use the parameter sets for the frequently touched fomite scenario shown in Table 2 ($\gamma = 0.2$, $\mu = 2.88$, $\rho = 0.2972$ for all simulations). For $R_0 = 1.8$, $[\pi, \alpha] = [1.810, 0.2]$, [0.362, 1], [0.072, 5.2], [6.9e-3, 52.4], [6.9e-4, 524.4], [6.9e-5, 5,244]; for other $R_0$ curves, infectivity is increased or decreased proportionally, and $[\pi, \alpha]$ is varied analogously. The initial condition is $I_0 = 1$, $E_0 = 0$.

present a basic conceptual framework of environmentally mediated population infection transmission for non-vector-borne infectious diseases by incorporating environmental mechanisms into epidemic models.

By use of the EITS framework presented here, the transmission rate and $R_0$ are formulated by well-defined and measurable environmental factors, similar to how vector-borne transmission is formulated by using entomologic factors. Although we focus on air and fomite transmission, a potential generalization of this framework would be incorporating pathogen dynamics within different environmental settings, such as other vectors, food, and water.

The adoption of an EITS framework provides a theoretical basis for understanding and modeling intervention efficacy in realistically detailed situations involving diverse venues where transmission takes place. The parameters of the EITS model reflect physical events on which data can be readily gathered by using newly developed methodologies and for which a considerable body of data and theory already exists. In contrast, contact rates and transmission probabilities in specific venues are abstract and not feasibly measurable in most situations, except in uniform places with repeated and prolonged contact, such as households.

The EITS framework also helps to identify and relax unrealistic mass action assumptions, such as no time passing between pathogens leaving one person and reaching another. It also provides a way to conceptualize the extent to which transmission is a density- or frequency-dependent contact process (1, 2). In reality, most transmissions occur between these 2 extremes, and the EITS formulation reflects this. As the environmental persistence ratio, $\rho N/\mu$, increases, transmission becomes more density dependent and, as this ratio decreases, it becomes more frequency dependent.

Another theoretically valuable focus is found in the contamination ratio, $\alpha/\gamma$, a measure of the total amount of pathogens shed by infectious individuals. This ratio and the magnitude of a contamination event are both indicators of the probability that an outbreak will occur, suggesting that stochastic "die out" is more likely when environmental contamination is low.

EITS models will eventually help us to define the role of different transmission modes in sustaining or amplifying transmission. Multiple transmission modes have been recognized for many other infections than those in our example, such as cholera, hepatitis A, and cryptosporidiosis (43–45). The EITS model framework provides leverage for using detailed environmental data and well-established parameters reflecting pathogen characteristics to analyze different transmission modes and the role they play in endemic and epidemic situations.

Although including more realistic details than classic SIR models, the EITS models presented here are abstract in order to serve heuristic purposes. Future EITS models will relax current model assumptions. The specific choices of which assumptions to relax will depend on the research question. For example, with only a single environmental compartment, our models may not accurately capture contact patterns or pathogen dynamics in the environment. In fact, our preliminary analysis pointed out that a key way to relax the homogeneous environment assumption is to distinguish frequently touched fomites from infrequently touched fomites. Additionally, a more refined understanding of transmission patterns might require model structure that accounts for detailed contact patterns between people and the environment.

Our simple EITS models identify key elements and important data gaps of the environmental infection transmission system. They provide an initial step in motivating improved environmental measurements that would complement human case data and might be more informative and more cost-effective to gather than such data. EITS models incorporating more realistic details than those presented here can be used to help design future environmental data collection efforts. They also can provide a basis for analyzing focused environmentally based interventions, such as decontamination of specific surfaces, water, or air, as well as hygiene and sanitation efforts.

## ACKNOWLEDGMENTS

Author affiliations: Department of Epidemiology, University of Michigan, Ann Arbor, Michigan (Sheng Li, Joseph N. S. Eisenberg, Ian H. Spicknall, James S. Koopman); and Center for the Study of Complex Systems, University of Michigan, Ann Arbor, Michigan (Sheng Li, Joseph N. S. Eisenberg, James S. Koopman).

This research was supported by the US Environmental Protection Agency Science to Achieve Results (STAR) Program and by US Department of Homeland Security



Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

University Programs grant R83236201 to Dr. Jim Koopman and Dr. Joseph N. S. Eisenberg.

The authors thank Dr. Rick L. Riolo and Josep M. Serra for their contributions to this study.

Conflict of interest: none declared.

## REFERENCES

1. Anderson RM, May RM. *Infectious Diseases of Humans: Dynamics and Control*. New York, NY: Oxford University Press; 1992.
2. Diekmann O, Heesterbeek JAP. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*. New York, NY: John Wiley & Sons, Inc; 2000.
3. Mossong J, Hens N, Jit M, et al. Social contacts and mixing patterns relevant to the spread of infectious diseases [electronic article]. *Plos Med*. 2008;5(3):e74.
4. Eubank S, Guclu H, Kumar VS, et al. Modelling disease outbreaks in realistic urban social networks. *Nature*. 2004; 429(6988):180–184.
5. Del Valle SY, Hyman JM, Hethcote HW, et al. Mixing patterns between age groups in social networks. *Soc Networks*. 2007; 29(4):539–554.
6. Noakes CJ, Beggs CB, Sleigh PA, et al. Modelling the transmission of airborne infections in enclosed spaces. *Epidemiol Infect*. 2006;134(5):1082–1091.
7. Eisenberg JN, Seto EY, Olivieri AW, et al. Quantifying water pathogen risk in an epidemiological framework. *Risk Anal*. 1996;16(4):549–563.
8. Eisenberg JN, Brookhart MA, Rice G, et al. Disease transmission models for public health decision making: analysis of epidemic and endemic conditions caused by waterborne pathogens. *Environ Health Perspect*. 2002;110(8):783–790.
9. Eisenberg JN, Lei X, Hubbard AH, et al. The role of disease transmission and conferred immunity in outbreaks: analysis of the 1993 cryptosporidium outbreak in Milwaukee, Wisconsin. *Am J Epidemiol*. 2005;161(1):62–72.
10. Soller JA, Olivieri AW, Crook J, et al. Risk-based approach to evaluate the public health benefit of additional wastewater treatment. *Environ Sci Technol*. 2003;37(9):1882–1891.
11. Soller JA. Use of microbial risk assessment to inform the national estimate of acute gastrointestinal illness attributable to microbes in drinking water. *J Water Heath*. 2006;4(suppl 2): 165–186.
12. Eisenberg JN, Scott JC, Porco T. Integrating disease control strategies: balancing water sanitation and hygiene interventions to reduce diarrheal disease burden. *Am J Public Health*. 2007;97(5):846–852.
13. Atkinson MP, Wein LM. Quantifying the routes of transmission for pandemic influenza. *Bull Math Biol.* 2008;70(3): 820–867.
14. Dingle JH, Badger GF, Jordan WS. *Illness in the Home*. Cleveland, OH: The Press of Western Reserve University; 1964.
15. Fox JP, Hall CE. *Viruses in Families*. Littleton, MA: PSG Publishing Company, Inc; 1980.
16. Longini IM Jr, Koopman JS, Monto AS, et al. Estimating household and community transmission parameters for influenza. *Am J Epidemiol*. 1982;115(5):736–757.
17. Becker N. An estimation procedure for household disease data. *Biometrika*. 1979;66(2):271–277.
18. Wallinga J, Edmunds WJ, Kretzschmar M. Perspective: human contact patterns and the spread of airborne infectious diseases. *Trends Microbiol.* 1999;7(9):372–377.
19. Wallinga J, Teunis P, Kretzschmar M. Using data on social contacts to estimate age-specific transmission parameters for respiratory-spread infectious agents. *Am J Epidemiol*. 2006; 164(10):936–944.
20. Macey R, Oster G, Zahnley T. *Berkeley Madonna User's Guide, Version 8.0*. Berkeley, CA: University of California; 1993. (http://www.berkeleymadonna.com). (Accessed January 31, 2009).
21. Gillespie DT. Exact stochastic simulations of coupled chemical reactions. *J Phys Chem.* 1977;81(25):2340–2361.
22. Elveback LR, Fox JP, Ackerman E, et al. An influenza simulation model for immunization studies. *Am J Epidemiol*. 1976; 103(2):152–165.
23. Longini IM Jr, Halloran ME, Nizam A, et al. Containing pandemic influenza with antiviral agents. *Am J Epidemiol*. 2004;159(7):623–633.
24. Alford RH, Kasel JA, Gerone PJ, et al. Human influenza resulting from aerosol inhalation. *Proc Soc Exp Biol Med*. 1966; 122(3):800–804.
25. Couch RB, Douglas RG Jr, Fedson DS, et al. Correlated studies of a recombinant influenza-virus vaccine. 3. Protection against experimental influenza in man. *J Infect Dis*. 1971; 124(5):473–480.
26. Hayden FG, Treanor JJ, Betts RF, et al. Safety and efficacy of the neuraminidase inhibitor GG167 in experimental human influenza. *JAMA*. 1996;275(4):295–299.
27. Hemmes JH, Winkler KC, Kool SM. Virus survival as a seasonal factor in influenza and poliomyelitis [letter]. *Nature*. 1960;188(4748):430–431.
28. Bean B, Moore BM, Sterner B, et al. Survival of influenza viruses on environmental surfaces. *J Infect Dis*. 1982;146(1): 47–51.
29. Loudon RG, Roberts RM. Droplet expulsion from the respiratory tract. *Am Rev Respir Dis*. 1967;95(3):435–442.
30. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogens. *J Occup Environ Hyg*. 2005;2(3):143–154.
31. Nicas M, Sun G. An integrated model of infection risk in a health-care environment. *Risk Anal*. 2006;26(4):1085–1096.
32. Murphy BR, Chalhub EG, Nusinoff SR, et al. Temperature-sensitive mutants of influenza virus. 3. Further characterization of the ts-1(e) influenza A recombinant (H3N2) virus in man. *J Infect Dis*. 1973;128(4):479–487.
33. Duguid JP. The size and duration of air-carriage of respiratory droplets and droplet-nuclei. *J Hyg (Lond)*. 1946;44:471–479.
34. Loudon RG, Brown LC. Cough frequency in patients with respiratory disease. *Am Rev Respir Dis*. 1967;96(6): 1137–1143.
35. Dick EC, Jennings LC, Mink KA, et al. Aerosol transmission of rhinovirus colds. *J Infect Dis*. 1987;156(3):442–448.
36. Guyton AC, Hall JE. *Textbook of Medical Physiology.* 10th ed. Philadelphia, PA: WB Saunders Company; 2000.
37. ICRP publication 66. Human respiratory tract model for radiological protection. International Commission on Radiological Protection. *Ann ICRP.* 1994;24(1–3):36–54, 231–299.
38. Rheinbaben F, Schunemann S, Gross T, et al. Transmission of viruses via contact in a household setting: experiments using bacteriophage straight phiX174 as a model virus. *J Hosp Infect*. 2000;46(1):61–66.
39. Sattar SA, Springthorpe S, Mani S, et al. Transfer of bacteria from fabrics to hands and other fabrics: development and application of a quantitative method using *Staphylococcus aureus* as a model. *J Appl Microbiol.* 2001;90(6):962–970.
40. Nicas M, Best D. A study quantifying the hand-to-face contact rate and its potential application to predicting

Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017

respiratory tract infection. *J Occup Environ Hyg*. 2008;5(6):347–352.
41. Rusin P, Maxwell S, Gerba C. Comparative surface-to-hand and fingertip-to-mouth transfer efficiency of gram-positive bacteria, gram-negative bacteria, and phage. *J Appl Microbiol.* 2002;93(4):585–592.
42. Kermack WO, McKendrick AG. A contribution to the mathematical theory of epidemics. *Proc R Soc Lond A*. 1927;115(772):700–721.
43. Swerdlow DL, Malenga G, Begkoyian G, et al. Epidemic cholera among refugees in Malawi, Africa: treatment and transmission. *Epidemiol Infect*. 1997;118(3):207–214.
44. Hutin YJ, Sabin KM, Hutwagner LC, et al. Multiple modes of hepatitis A virus transmission among methamphetamine users. *Am J Epidemiol*. 2000;152(2):186–192.
45. Yoder JS, Beach MJ; Centers for Disease Control and Prevention (CDC). Cryptosporidiosis surveillance—United States, 2003–2005. *MMWR Surveill Summ*. 2007;56(7):1–10.

Downloaded from http://aje.oxfordjournals.org/ at University of North Texas on January 2, 2017