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The Science of the Total Environment 274 (2001) 197–207

the Science of the Total Environment
An International Journal for Scientific Research into the Environment and its Relationship with Man

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Infection transmission system models for microbial risk assessment

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Received 17 June 2000; accepted 6 October 2000

Abstract

Chemical risk assessments often focus on measuring exposure as if individuals were subject only to exogenous environmental sources of risk. For infectious diseases, exposure might not only depend on exogenous sources of microbes, but also on the infection status of other individuals in the population. For example, waterborne infections from agents such as *Cryptosporidium parvum* and *Escherichia coli*: O157:H7 might be transmitted from contaminated water to humans through drinking water; from interpersonal contact; or from infected individuals to the environment, and back to other susceptible individuals. These multiple pathways and the dependency of exposure on the prevalence of infection in a population suggest that epidemiological models are required to complement standard risk assessments in order to quantify the risk of infection. This paper presents new models of infection transmission systems that are being developed for the US Environmental Protection Agency as part of a project to quantify the risk of microbial infection. The models are designed to help inform water treatment system design decisions.

Keywords: Microbial risk; Infection transmission system; Epidemic model; Population risk

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0048-9697/01/$ - see front matter
PII: S0048-9697(01)00749-5

1. Introduction

Microbial risk assessments are required for a number of policy decisions to control the spread of infectious diseases. Such risk assessments can inform municipal water treatment decisions designed to control microbial infections in drinking water. An example that underscores the importance of water treatment to control microbial infection is the 1993 outbreak of *Cryptosporidiosis* in Milwaukee. *Cryptosporidium parvum* caused watery diarrhea in a projected estimate of over 400 000 people, the hospitalization of approximately 1000, and played a role in the death in over 50 individuals, most with HIV infection (Hoxie et al., 1997). Microbial risk assessments are also used to assess exposure to pathogens in food. McNab (1998) has indicated that food poisoning may result in 6.5–33 million cases in the US alone, and may be responsible for as many as 9000 deaths per year. Microbial risk assessment is also important in other applications, such as agricultural infection control, and germ warfare preparedness.

A standard methodology for chemical risk assessment is to identify hazards, evaluate exposure, assess the dose–response relationship, and characterize risk. This methodology is also often applied to microbial risk assessment. Microbial hazards, however, may present exposures that typically do not occur for chemical hazards. For example, in addition to the standard exposure assessment to account for exposure to microbes in the environment, microbial infection can also be spread from direct human-to-human contact. Furthermore, the degree of exposure to microbes in the environment may depend on the degree to which infected individuals become a secondary source by further contaminating that environment.

This paper presents a general model for microbial risk assessment based on an infection transmission system model. A simple case study for waterborne *Cryptosporidium parvum* indicates that the effectiveness of plans to control exposure by reducing environmental exposure may depend strongly on infection dynamics. A risk assessment using infection transmission system models may, therefore, play an important role in hazard control programs for microbial agents.

The general idea is to model risk from microbial agents using a dynamic system model to describe infection transmission dynamics. Jacquez (1996) provides an excellent overview of this widely-used technique for modeling infection dynamics, as well as numerous references, but does not focus on risk. Nonetheless, dynamic system models have been used in risk analysis. Haimes (1998) describes how the risk for an individual can vary through time according to some well-defined dynamics. The food industry is concerned with dynamic models of microbial growth in food products (farm-to-fork models) that may affect the health risk of individuals that are susceptible to foodborne infection (McNab 1998). Those dynamic system models quantify a time-dependent change in risk to individuals, but do not capture the phenomena that one person's exposure to microbial hazards may depend strongly on the infection state of other individuals in a population. Some initial work, however, has been done to capture such infection transmission system dynamics. Eisenberg et al. (1996) considered exposure to *Giardia lamblia* from both background environmental sources as well as contamination of reclaimed water in a recreational swimming impoundment with water reclaimed from community sewage. Haas et al. (1999) presented a detailed assessment of microbial risk assessment that built on features of the chemical risk paradigm. They further described an infection model that comprehends human-to-human contact, but did not study structural properties or apply the model to specific microbial agents. Teunis and Havelaar (1999) accounted for secondary infections from human to human, but assumed that endemic levels of infection are not sustainable in populations if all environmental exposure is eliminated.

The framework presented in Section 2 extends the previous work by providing a unified approach for accounting for infection transmission dynamics that models exogenous sources of infection, human-to-human transmission, as well as 'feedback loops' that change exposure because infected individuals raise the risk of susceptible

individuals by recontaminating the environment. The model is less restrictive than Teunis and Havelaar (1999) in that no assumptions are made about the potential for endemic circulation of infection. This is important, for instance, when modeling waterborne agents on the Contaminant Candidate List (CCL) of the US Environmental Protection Agency (US EPA). The CCL is used to focus research efforts for controlling infectious agents in the drinking water system. Viruses on the CCL that can sustain transmission in human populations through either direct or indirect human-to-human transmission include Adenoviruses, Coxsackieviruses, Echoviruses, and Norwalk virus and other Caliciviruses (LeBaron et al., 1990; O'Ryan et al., 1998; Gaulin et al., 1999). In addition the CCL contains a bacterial agent, *Helicobacter pylori*, that is also transmitted directly or indirectly from human to human (Owen, 1998; Di Leo et al., 1999).

This article uses the example of *Cryptosporidium* transmission from both drinking water and secondary transmission to illustrate the infection transmission system ideas. However, other potential environmental repositories for microbial infection, such as food, public swimming facilities, and contamination in day care environments can be similarly modeled with the same conceptual framework. The conclusion is that a standard exposure assessment using the chemical risk paradigm for microbial risks may give misleading conclusions about the effects of hazard reduction interventions, and that an integrated infection transmission system approach can address a number of special concerns for modeling microbial risk.

2. Methods and techniques

First, we present a general infection transmission system model for microbial risk. The model is then used to explain different roles that water might play in an infection transmission system.

2.1. General infection transmission system risk model

A standard chemical risk assessment can be used to account for some microbial hazards. For example, we supposed that the dose–response function for a microbial agent is the well-known exponential model:

$$\text{Probability of infection during elapsed time } t = 1 - e^{-rdt}, \tag{1}$$

where d is the dose of the microbial agent per unit time, r is the probability that an individual microbe survives to initiate infection, and t is the duration of the exposure. Furthermore, we supposed that there is a relatively homogeneous population of S individuals that are susceptible to infection, I individuals that are infected with the microbial agent, and R individuals that are recovered from the infection and are temporarily immune to further infection. If φ is the rate of recovery from infection (so the probability of recovery during a short time Δt is approximately $\rho_1 \Delta t$, and the mean duration of infection is $1/\varphi$), and ρ_2 is the rate of loss of resistance before the individual becomes susceptible again, then the following dynamic system model is appropriate for representing the risk of infection:

$$\frac{dS}{dt} = \text{rate of change of number of susceptible individuals in a population} = -rdS + \rho_2 R \tag{2a}$$

$$\frac{dI}{dt} = \text{rate of change of number of infected individuals in a population} = +rdS - \rho_1 I \tag{2b}$$

$$\frac{dR}{dt} = \text{rate of change of number of recovered individuals in a population} = +\rho_1 I - \rho_2 R \tag{2c}$$

This model ignores birth and death, since they are presumed to occur on a different time scale than the natural course of infection, so the total population size $n = S + I + R$ for this model is

constant. Eisenberg et al. (1998) used a similar model to study the 1993 Milwaukee outbreak of *Cryptosporidiosis*. They simulate outbreaks essentially by changing the dose d to a high level during a specified duration of time to simulate water treatment failure.

The above dynamic system accounts for environmental exposure to a microbial agent, but does not account for secondary infections from human-to-human contact or from recontamination of the environment from infected individuals. The following mathematical infection transmission system model incorporates both of those modes of secondary infection, as well as a time-dependent variable W that represents the concentration of microorganisms in the environment. Table 1 summarizes the notation.

$$\frac{dS}{dt} = -r\varphi WS - c\beta\frac{I}{n}S + \rho_2 R$$

$$\frac{dI}{dt} = +r\varphi WS + c\beta\frac{I}{n}S - \rho_1 I$$

$$\frac{dR}{dt} = +\rho_1 I - \rho_2 R$$

$$\frac{dW}{dt} = -\alpha W + \theta I + \gamma \quad (3)$$

The rate dW/dt of change in environmental contamination W depends on the rate γ of exogeneous introduction of the microbial agent (say, from agricultural reservoirs of infection), the rate θI of contamination of the environment that is proportional to the number of infected individuals, and the rate α that microbes may become non-infectious (e.g. by inactivation or by leaving the environment). In Eq. (2a) above, environmental sources of infection are modeled by a dose–response parameter and a dose, leading to the term rdS. In the system in Eq. (3), the dose $d = \varphi W$ is proportional to the environmental contamination, attenuated by some factor φ that accounts for water treatment and an individual's exposure to drinking water. A similar analysis can be performed for recreational exposure.

A schematic of this infection transmission system is presented in Fig. 1. Individuals flow from susceptible to infected/infectious to recovered states. The flow rates depend on the number of individuals in each state of infection and on water

Table 1
Notation for describing the infection transmission system risk

Notation	Meaning
d	Dose of a microbial agent
r	Parameter of dose–response function
S	The number of susceptible individuals in the population (as a function of time, t)
I	The number of infected individuals in the population (as a function of time, t)
R	The number of recovered individuals in the population (as a function of time, t)
n	The total number of individuals in the population ($n = S + I + R$)
W	The concentration of microbial organisms in the environment (as a function of time, t)
φ	Probability that a microbial organism in the environment actually exposes an individual
c	to a potential infection
β	Probability of infection per contact between infected and uninfected individuals
ρ_1	Rate of recovery (mean duration of infection is $1/\rho_1$)
ρ_2	Rate of loss of resistance to new infection (mean duration of resistance is $1/\rho_2$)
α	Rate for loss of viability of a microbial organism in the environment
θ	Rate of recontamination of the environment per infected individuals
γ	Rate of contamination of the environment from other (e.g. agricultural) sources
R_0	The average number of secondary infections from a single infected individual due to human to human contact in a population of susceptible individuals
R_{0w}	The average number of secondary infections from a single infected individual due to exposure of susceptible individual because of contamination of the environment

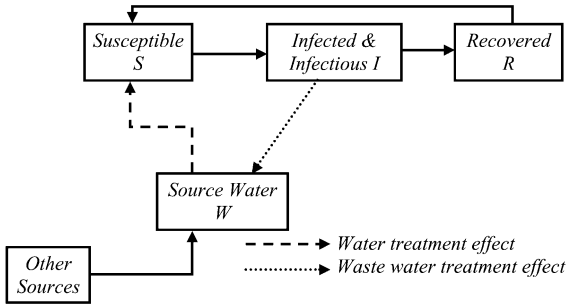

Fig. 1. A generic infection transmission system model that illustrates the flow of infected individuals through a cycle of susceptibility, infectivity, and recovery, as well as the flow of infectious agents into the water system from infected humans and exogenous sources.

contamination levels, as described by Eq. (3). The figure represents waterborne infections, but other sources of infection can be similarly modeled by replacing the source water reservoir for infection with other environmental sources of infection.

For *Cryptosporidium*, values of 0.001 to 0.01 have been used for the dose response parameter r (Eisenberg et al., 1998). For water treatment with a 3-log removal of *Cryptosporidium* oocysts (so that the fraction of remaining oocysts after water treatment is 0.001), and a population that drinks 2 l of water per day, the parameter $\varphi = 0.001 \times 2 = 0.002$. A background rate of 0.24 oocysts/l corresponds to an equilibrium level $W^* = 0.24$ (the * signifies an equilibrium level, when $dW/dt = 0$). If there is no recontamination of the water from infected individuals in the population, that equilibrium level would require $\gamma/\alpha = 0.24$). LeChevallier and Norton (1995) further discuss background rates. The duration of infection may be of the order of 1 week (Osewe et al., 1996), so that $\rho_1 = 1/7$.

A more realistic model for the natural history of infection might be required to accurately model *Cryptosporidiosis* (Osewe et al., 1996). The course of infection may differ in different subpopulations. For instance, small children or individuals with HIV infection may be more susceptible to infection, may have more severe consequences for infection, or may shed different numbers of oocysts. Extra state variables may be required to model the infection. This can be done by modeling each subpopulation explicitly, such as:

$$\frac{dS_1}{dt} = \text{rate of change of number of susceptible individuals in subpopulation 1} = -r\varphi W S_1 - c\beta_1\left(\frac{I_1 + I_2}{n}\right)S_1 + \rho_2 R_1 \quad (4)$$

The inclusion of the potential for asymptomatic and symptomatic infection, partial resistance, and multiple subpopulations can be modeled by modifying Fig. 1 and Eqs. (2a), (2b) and (2c) to reflect the more realistic scenario depicted in Fig. 2.

Similar refinements can be made for the contact process, the environmental contamination and exposure process, the agent survival process, agent enhanced resistance, pathogenicity with animal passage, and population variability.

2.2. Potential roles of water contamination in the infection transmission system

Water may play a variety of roles in the transmission of infection. Some of these roles are categorized here, and their relation to the general model in Eq. (3) is discussed. For a further discussion and analysis of these models, see Chick et al. (2000).

2.2.1. Exogenous exposure with no secondary transmission

A standard risk model presumes that the pri-

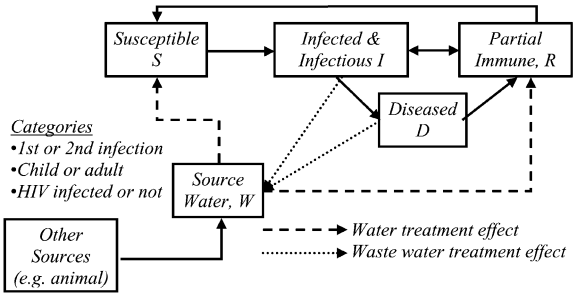

Fig. 2. An infection transmission system model that may be more appropriate for the natural history of infection of the waterborne agent *Cryptosporidium parvum*.

mary and sole source of exposure to a microbial risk is the presence of an exogenous source of pathogens. The standard risk model would assume that secondary transmission is not applicable. This leads to an endemic level of infection circulating in a population. As noted before, the dose–response function in Eq. (1) can be used to develop the infection transmission system risk model in Eqs. (2a), (2b) and (2c). This model can be derived from the general model of infection transmission system risk in Eq. (3) by assuming that there is no recontamination of the environment by humans ($\theta = 0$) and that the water contamination level is at an equilibrium level ($W^* = \gamma/\alpha$), so that the dose per unit of consumed water is $d = \varphi\gamma/\alpha$. The assumption of no secondary human to human transmission is modeled by setting the probability of secondary transmission per contact to $\beta = 0$. Under this model, the endemic prevalence of infected individuals in the population is:

$$I^* = n\frac{r\varphi\gamma/\rho_1\alpha}{1 + r\varphi\gamma/\rho_1\alpha + r\varphi\gamma/\rho_2\alpha} \quad (5)$$

Endemic levels are obtained by setting $dS/dt = dI/dt = dR/dt = dW/dt = 0$.

2.2.2. Exogenous exposure with unsustainable secondary transmission

Haas et al. (1999) and Teunis and Havelaar (1999) considered unsustainable secondary transmission in a population. This approach can be represented by assuming that each infected individual in a population might cause an average of $R_0 < 1$ additional infections through human-to-human contact (assuming all contacts are susceptible), but that there is no recontamination of the environment. This can be modeled in terms of Eq. (3) by setting $R_0 = c\beta/\rho_1$, and constraining $R_0 < 1$, and by setting $\theta = 0$. When $R_0 < 1$, infection will eventually be eliminated from a population through time if the exogenous source of infection is completely removed by some intervention (if γ becomes 0).

With unsustainable secondary transmission, each person infected from water consumption infects an average of R_0 individuals. Each of those individuals infects an average of R_0 individuals, and so on, so that the extended chain of infection infects a total of $1 + R_0 + R_0^2 + ... = 1/(1 - R_0)$, including the initial individual. In a homogenous population with unsustainable transmission, then, a multiplier of $1/(1 - R_0)$ to the risk of infection directly from waterborne infection can be used to approximate the overall risk of infection in a population. If the population is not homogenous (e.g. HIV infected individuals have a different susceptibility to infection) or if $R_0 > 1$, then this multiplier is not a good approximation, as argued in Sections 2.2.3 and 3.

2.2.3. Secondary transmission sustains endemic levels

Human-to-human contact may be sufficient to insure the endemic circulation of an infectious agent, once it is introduced into a population, even if there is not recontamination of the environment ($\theta = 0$). This occurs when an initially infected individual causes $R_0 = c\beta/\rho_1 > 1$ secondary infections, on average, assuming that all contacts are susceptible to infection. Even when there is no exogenous introduction of infection ($\gamma = 0$) and no recontamination of the water ($\theta = 0$), the endemic prevalence of infection will tend towards:

$$I^* = n\left(1 - \frac{1}{R_0}\right)\frac{1/\rho_1}{1/\rho_1 + 1/\rho_2} \quad (6)$$

once infection is introduced, assuming human-to-human transmission is sustainable ($R_0 < 1$).

The potential for sustainable secondary transmission is highly important for evaluating water treatment control decisions. Complete elimination of microbes from drinking water by using extreme water treatment measures (to make $\varphi = 0$ or $\gamma = 0$) will stop the circulation of infection when the chemical risk model (Section 2.2.1) or unsustainable infection model (Section 2.2.2) is presumed, but may have very little effect on the circulation of infection if secondary transmission is sustainable.

2.2.4. Dominant role: water contamination sustains endemic levels

The water system may play a dominant role in

the circulation of infection when infected individuals further contaminate the waterborne environment in sufficient quantities to insure that an endemic level of infection can be sustained. This phenomenon might arise in the context of recreational use of water, as indicated by Eisenberg et al. (1996) or when wastewater is treated near a drinking water intake (Teunis and Havelaar, 1999). This human to environment to human loop of secondary infection may be sufficient to sustain endemic levels of infection. More formally, even without human-to-human transmission ($\beta = 0$) and no continual exogenous source of infection ($\gamma = 0$), non-zero endemic infection levels will continue if $R_{0W} = nr\varphi\theta/\alpha\rho_1 > 1$, once infection is introduced. The term R_{0W} represents the average number of secondary transmissions caused by one individual contaminating the water of an otherwise susceptible population.

Unlike direct human-to-human transmission, water treatment interventions can be used to significantly reduce endemic infection levels when water plays a dominant role in the infection transmission system. This can be achieved by either improving wastewater treatment (to reduce θ) or by improving drinking water treatment (to reduce φ).

2.2.5. Water contamination and secondary transmission jointly sustain endemic levels

It may be possible that endemic levels cannot be sustained directly by human-to-human transmission of waterborne agents ($R_0 < 1$), nor indirectly by water contamination ($R_{0W} < 1$) alone, but that the combination is sufficient to insure the endemic circulation of infection ($R_0 + R_{0W} > 1$), even with 100% efficacy for water treatment. In this case, the role of water in transmitting infection is jointly key with the direct human-to-human mode of infection transmission. In this case, improved water treatment can have a significant effect on the circulation if R_{0W} is changed so that $R_0 + R_{0W} < 1$, but will have a much less significant effect if $R_0 + R_{0W}$ remains above 1. More generally, there may be multiple secondary transmission loops, such as recreational water usage, each of which should be considered when considering the total number of secondary transmissions per index case of infection.

2.2.6. Other potential roles of water in the transmission system

The above five potential roles of water in an infection transmission system lead to rather distinct microbial risk characterizations. The relative impact of infection control programs on curtailing the spread of microbial infection depends strongly on the specific role that water plays in the transmission system. The cost–benefit analysis for water treatment decisions that are intended to control waterborne infections is, therefore, dependent on those potential roles.

There are a number of other roles, however, that may also affect infection transmission dynamics. These arise when considering more realistic aspects of human population dynamics and microbial exposure and transmission. Several complicating factors include:

- Multiple strains (e.g. bovine strains of *Cryptosporidium* that exogenously contaminate the water supply, and human strains that might account for the bulk of secondary transmission).
- Multiple subpopulations within a given community might be more or less susceptible to infection (children or HIV infected adults may have different susceptibility and outcomes resulting from exposure to *Cryptosporidium*).
- Multiple communities might share a common water system, or there may be variation from well to well.
- Multiple environmental reservoirs of infection might be applicable (e.g. public pools, drinking water, food products, toys in a day care setting) to specific subgroups only.
- A more complicated natural history of infection might be more appropriate to account for both the mean and variance of the duration of various stages of infection, and the disease process may vary from strain to strain.
- Other dose–response models (e.g. the beta-Poisson) might be more appropriate.

These and other realistic details regarding

Cryptosporidium transmission should be explored for their possible effects on decisions made on the basis of a microbial risk assessment.

An additional element of model realism that might need exploration involves the role of chance. Crucial decisions on the basis of a model analysis should not be undertaken without considering how the decision might be different if stochastic models were used to account for random effects associated with transmission. For instance, even though secondary infections might theoretically lead to endemic circulation in a population (say, if $R_0 = 1.1$), the probabilistic nature of infection outcomes as a function of exposure might allow for the possibility that infection dies out in a subpopulation. Given this scenario, infections might be amplified when introduced into a specific subpopulation, water might then disseminate infection to another subpopulation, and the initially infected subpopulation might not circulate infection for some extended period of time before infection is reintroduced. For a discussion of similarities and differences between stochastic and deterministic infection transmission system models, see Chick et al. (2001).

3. Results: water treatment control decisions for *Cryptosporidium* risk

Two water treatment options for controlling *Cryptosporidium* include the addition of ozone pretreatment to existing municipal level water treatment, or the localized use of special water filters in the homes of individuals with HIV infection, a subpopulation with particularly severe health consequences associated with cryptosporidiosis. Centralized ozone pretreatment reduces, but does not eliminate, *Cryptosporidium* oocysts from tap water for all individuals in a population. As an extreme case, we supposed that specialized filters on the taps of HIV infected individuals essentially eliminated the risk of infection from drinking water.

We simulated those same two microbial hazard control options using the infection transmission system models for microbial risk in Eq. (3) together with modifications like Eq. (4) to account for distinct HIV infected and immunocompetent subpopulations. We focus on the number of cryptosporidiosis cases in the HIV infected subpopulation, assuming that either ozone pretreatment or filters are used as a control strategy. The control that reduces endemic levels of cryptosporidiosis the most is considered 'better' here. More complicated and appropriate criterion can also be used, but we focus on the simple model to highlight the importance of infection transmissions systems for assessing microbial risk. We indicate that water treatment decisions may also depend on the specific parameter values for the infection transmission system, even for a given role of water in the infection transmission system.

Background levels of oocysts in tap water assuming conventional treatment (tested over the range 0.0001–0.01 oocysts/l), drinking consumption (2 l/day, so that $\varphi\gamma/\alpha$ ranges from 0.0002 to 0.02), the dose–response parameter ($r = 0.005$), the duration of infection (7–20 days $= 1/\rho_1$), and the effectiveness of ozone pretreatment (eliminates another 40% of oocysts remaining after conventional treatment) and filters (complete elimination of oocysts in tap water for HIV subpopulation) were chosen to be compatible with reasonable ranges for *Cryptosporidium* published elsewhere (Eisenberg et al., 1998; Hoxie et al., 1997). The duration of resistance was tested at multiple levels, including $1/\rho_2 = 90$ days, and almost no duration (extremely large ρ_2). We presumed background levels of infection and tested a range of prevalence (0.05–5%) for HIV infection to cover a large number of situations.

Because secondary transmission is not completely understood, and to simplify exposition, we have explored a range of parameters for human-to-human transmission and presumed that secondary infection from recontamination of the environment is negligible ($\theta = 0$). A similar analysis can be performed for the case $\theta > 0$. For immunocompetent individuals (subpopulation 1), the probability β_1 of cryptosporidiosis infection per exposure from contact with an infected individual was presumed to be the no larger than the analogous probability β_2 for HIV infected individuals (subpopulation 2). We distinguish the expected number R_{0i} of secondary infections to subpopula-

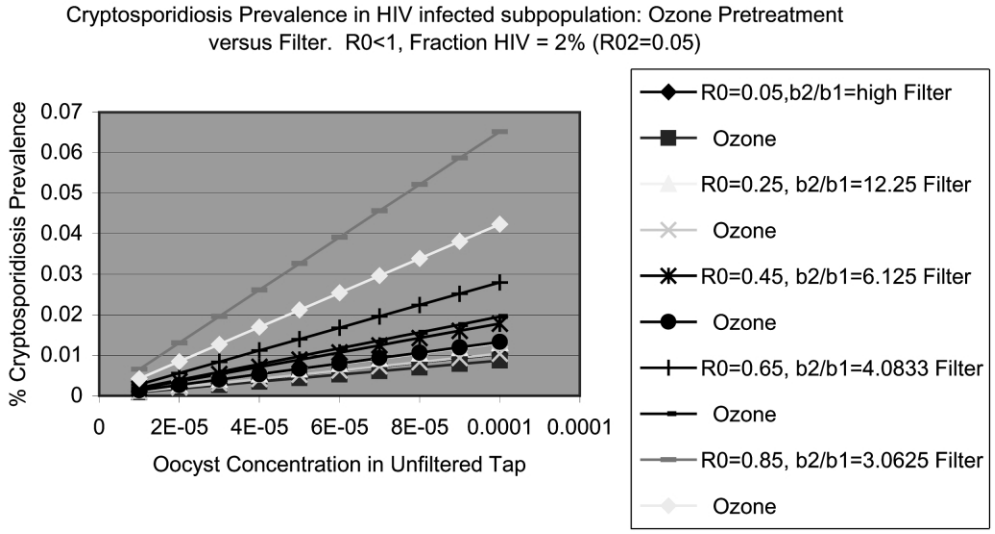

Fig. 3. Endemic cryptosporidiosis prevalence in the HIV subpopulation as a function of the level of secondary transmission and the microbial hazard control for *Cryptosporidium* oocysts and the amount of oocysts in unfiltered tap water.

tion I with an extra subscript, so that $R_0 = R_{01} + R_{02}$.

If secondary transmission plays no role whatsoever (the chemical model of Section 2.2.1 that assumes $R_0 = 0$), our analysis indicates that a specialized filter on the taps of all individuals with HIV infection would essentially eliminate the risk of cryptosporidiosis for that subpopulation. Specialized filters would, therefore, be the preferred microbial hazard control if the chemical risk paradigm were adopted, given our assumptions.

If unsustainable secondary transmission plays a

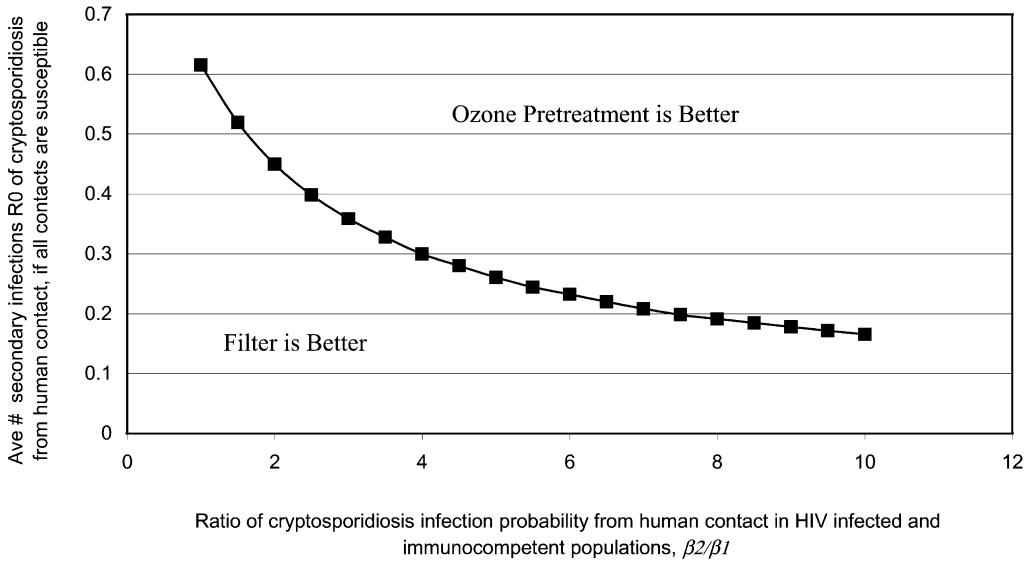

Fig. 4. Policy regions that indicate whether centralized ozone pretreatment or specialized filters in the homes of HIV infected individuals is more successful for reducing the endemic prevalence of cryptosporidiosis in the HIV subpopulation.

role (the model of Section 2.2.2), then HIV infected individuals are still susceptible to cryptosporidiosis through secondary transmission from others that are infected with *Cryptosporidium*. Fig. 3 summarizes simulations that indicate that *Cryptosporidium* transmission can be controlled better by providing a partially effective centralized ozone pretreatment, rather than highly effective filters for HIV infected individuals, when there is unsustainable secondary transmission.

Additional simulations that more thoroughly explore the parameter space indicate that filters are better when the expected number R_0 of secondary transmissions from human-to-human contact (assuming all contacts are susceptible) or the ratio of transmission probabilities β_1/β_2 from human contact are sufficiently small. Otherwise, ozone pretreatment does a better job at reducing *Cryptosporidium* prevalence in the HIV infected subpopulation, as shown in Fig. 4. This graph is specific to a particular set of parameter values input to the simulation, but is representative of a wide range of parameter values. The line that demarcates whether filter or ozone pretreatment is better depends very little on the specific background level of oocysts (over the range 0.0001–0.01 oocysts/l in tap water after conventional treatment, prior to ozone or filters), but that the line is somewhat sensitive to the prevalence of HIV infection in the population (the line is higher for a higher prevalence of HIV, and the line varies up or down by approximately 10% for 10 values of HIV prevalence sampled randomly in the range 0.001–0.05).

4. Conclusion

Microbial risk assessments often proceed in a fashion similar to chemical risk assessments. This approach is appropriate when exposure occurs primarily from an exogenous source of infection, such as when there is essentially no secondary transmission from human to human, and when the magnitude of the exposure does not depend on the number of individuals infected in the population. When human-to-human infection is possible, or when infected individuals can change the exposure of susceptible individuals to microbial agents by contaminating the environment, then the quantification of exposure becomes more complicated. We propose the use of epidemic models of infection transmission to quantify the dynamics of exposure. Not only can exposure and risk change through time, which many other risk assessments comprehend, but they can also depend on the state of infection of the rest of the population, which is not comprehended by most risk assessments.

The importance of an appropriate microbial risk assessment for infection control decisions was illustrated explicitly with a simplified example for a water treatment decision. The best treatment mechanism (centralized at the municipal level vs. local for a particularly sensitive subpopulation) to control *Cryptosporidium* infection was shown to depend upon the level of secondary transmission in the general population.

The use of infection transmission system models to quantify risk is, therefore, an important tool for assisting control decisions for microbial risk. The decisions seem to be sensitive to the values of specific parameters. When the parameters are not known with great certainty, we envision that sensitivity analysis can be used to help decision-makers identify parameters whose values are most important to know in order to make a successful control decision.

Acknowledgements

This work was supported by the US Environmental Protection Agency, National Center for Environmental Assessment in Cincinnati (Reference Number CR-827427-01-0). Discussions with Drs Brenda Boutin, Glenn Suter, Glenn Rice and others at the US EPA NCEA, and Dr Joseph Eisenberg of UC Berkeley during the preparation of this manuscript are greatly appreciated.

References

Chick SE, Adams A, Koopman JS. Analysis and simulation of a stochastic, discrete-individual model of STD transmission with partnership concurrency. Math Biosci, 2000;166(1): 45–68.

Chick SE, Soorapanth S, Koopman JS. Infection transmission systems models to quantify microbial risk for intervention decisions. Working paper. University of Michigan, Department of Industrial and Operations Engineering, 2001.

Di Leo A, Messa C, Russo F, Linsalata M, Amati L, Caradonna L, Pece S, Pellegrino NM, Caccavo D, Antonaci S, Jirillo E. *Helicobacter pylori* infection and host cell. Immunopharmacol Immunotoxicol 1999;21(4):803–846.

Eisenberg JN, Seto EYW, Olivieri AW, Spear RC. Quantifying water pathogen risk in an epidemiological framework. Risk Anal 1996;16:549–563.

Eisenberg JN, Seto EYW, Colford JM, Olivieri AW, Spear RC. An analysis of the Milwaukee *Cryptosporidiosis* outbreak based on a dynamic model of the infection process. Epidemiology May 1998;9(3):255–263.

Gaulin C, Frigon M, Poirier D, Fournier C. Transmission of calicivirus by a foodhandler in the pre-symptomatic phase of illness. Epidemiol Infect 1999;123(3):475–478.

Haas CN, Rose JB, Gerba CP. Quantitative microbial risk assessment. New York: John Wiley & Sons, 1999:449.

Haimes YY. Risk modeling, assessment, and management. New York: John Wiley & Sons, 1998:726.

Hoxie NJ, Davis JP, Vergeront JM, Nashold RD, Blair KA. *Cryptosporidiosis*-associated mortality following a massive waterborne outbreak in Milwaukee, Wisconsin. Am J Public Health Dec 1997;87(12):2032–2035.

Jacquez JA. Compartmental analysis in biology and medicine. 3rd ed.. Ann Arbor, Michigan: BioMedware, 1996.

LeBaron CW, Furutan NP, Lew JF, Allen JR, Gouvea V, Moe C, Monroe SS. Viral agents of gastroenteritis. Public health importance and outbreak management. MMWR — Morbidity & Mortality Weekly Report Apr 27 1990;39(RR-5):1–24.

LeChevallier MW, Norton WD. Occurrence of *Giardia* and *Cryptosporidium* in raw and finished drinking water. J Am Water Works Assoc 1995;87(9):54–68.

McNab WB. A general framework illustrating an approach to quantitative microbial food safety risk assessment. J Food Protect 1998;61(9):1216–1228.

O'Ryan ML, Vial PA, Mamani N, Jiang X, Estes MK, Ferrecio C, Lakkis H, Matson DO. Seroprevalence of Norwalk virus and Mexico virus in Chilean individuals: assessment of independent risk factors for antibody acquisition. Clin Infect Dis 1998;27(4):789–795.

Osewe P, Addiss DG, Blair KA, Hightower A, Kamb ML, Davis JP. *Cryptosporidiosis* in Wisconsin: a case–control study of post-outbreak transmission. Epidemiol Infect 1996;117:297–304.

Owen RJ. *Helicobacter*-species classification and identification. Br Med Bull 1998;54(1):17–30.

Teunis PFM, Havelaar AH. *Cryptosporidium* in drinking water: evaluation of the ILSI/RSI quantitative risk assessment framework. Report no. 284 550 006. The Netherlands: National Institute of Public Health and the Environment, Bilthoven, 1999.