Analyzing Pathogen Transmission in the Dialysis Unit: Time for a (Schedule) Change?

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Background and objectives: Infectious diseases and antimicrobial-resistant microorganisms are a growing problem for the dialysis population. The frequency of patient visits and intimate, prolonged physical contact with the inanimate environment during dialysis treatments make these facilities potentially efficient venues for nosocomial pathogen transmission. Isolation measures and infection control practices can be inconvenient and consume limited resources. Quantitative tools for analyzing the effects of different containment strategies can help to identify optimal strategies for further study. However, spatial and temporal considerations germane to the dialysis unit greatly complicate analyses relying on conventional mathematical approaches.

Design, setting, participants, & measurements: A stochastic, individual-based, Monte Carlo simulation tool that predicts the effects of various infection control strategies on pathogen dissemination through the dialysis unit in the face of diagnostic uncertainty was developed. The model was configured to emulate a medium-sized dialysis unit. The predicted consequences of various policies for scheduling patients who were suspected of being infectious were then explored, using literature-based estimates of pathogen transmissibility, prevalence, and diagnostic uncertainty.

Results: Environmental decontamination was predicted to be of paramount importance in limiting pathogen dissemination. Temporal segregation (scheduling patients who were suspected of being infectious to dialysis shifts that are later in the day) was predicted to have the greatest effectiveness in reducing transmission, given adequate environmental decontamination between successive days.

Conclusions: Decontamination of the patient’s environment (chair) can markedly attenuate pathogen dissemination. Temporal segregation could be a simple, low-cost, system-level intervention with significant potential to reduce nosocomial transmission in the dialysis unit.


Infection as a result of transmissible agents is a serious threat to the welfare of individuals who undergo long-term dialysis. Pathogens of particular concern include antimicrobial-resistant bacteria, which are increasingly common, as well as endemic and seasonal viral illnesses, such as influenza and hepatitis C (1–5). In the case of antimicrobial-resistant organisms, management can be more expensive, morbidity higher, and death more likely (6–8). Attempts to change antimicrobial prescribing practices in hopes of limiting the induction or spread of resistance have not proved as effective as hoped, and such interventions do not address horizontal transmission of existing resistant organisms. Similarly, antiviral agents may be of limited efficacy, effective vaccines are not always available, compliance with vaccination programs can be limited, and the quality of the immunologic response to vaccination in patients with ESRD can be poor (9,10).

Unavoidable conditions render the hemodialysis population particularly vulnerable to nosocomial transmission of pathogens. Patients are limited in their ability to forgo dialysis sessions during seasonal outbreaks. The patients have prolonged and intimate contact with environmental surfaces (e.g., the chair) during their treatments. The frequency with which dialysis patients are exposed to the threat of nosocomial transmission is much higher than that in most outpatient populations as a result of the frequency of their visits to the unit. There are repeated contacts between the patient and a health care provider during the dialysis treatment. Finally, the infectious “status” of a patient is not always known with certainty. This could be of particular concern during seasonal outbreaks (e.g., influenza) or when a patient returns after hospitalization, where he or she might have acquired an antimicrobial-resistant organism.

Mathematical techniques have long been applied to problems in infectious disease (11–13); however, there has been growing awareness of the limitations of traditional differential equation–based approaches to pathogen dissemination, limitations that arise from the important effects of contact networks and process stochasticity on pathogen transmission (14–17). Accordingly, newer work in this area has applied individual- or agent-
based modeling approaches, most recently to address the spread of influenza or other agents at the national or metropolitan level (18–25). In such models, each individual in the population is treated as an agent who may or may not be contagious and is explicitly tracked as he or she proceeds through their network of social contacts. Despite the fact that limitations of traditional techniques become more significant as the size of the population examined shrinks, very little work has applied contemporary individual-or agent-based modeling techniques to pathogen dissemination at the level of individual facilities (26,27).

The dialysis unit is characterized by spatial heterogeneity (not every caregiver has contact with every patient), small populations (which exacerbate the influence of stochastic chance events), and diagnostic uncertainty (who is and is not colonized or infected is not always known with certainty). These issues greatly complicate the application of traditional differential equation–based models to explore approaches to limiting pathogen dissemination. We developed an analytic model that addresses spatial heterogeneity, process stochasticity, and diagnostic uncertainty as they apply to pathogen transmission in the dialysis unit. We used this tool to explore the anticipated consequences of three different facility-level infection control strategies. A user-configurable version of the model that is implemented in Microsoft Excel (Microsoft, Redmond, WA) can be downloaded from PandemicDecisions.net.

**Concise methods**

We used an individual-based, Monte Carlo simulation model to predict the effects of various infection control strategies on pathogen dissemination in the dialysis unit. Each individual (patient or caregiver) is considered to be either “infectious” (capable of transmitting the pathogen) or “noninfectious.” The subset of patients who were assigned to each caregiver was explicitly specified, and pathogen acquisition was treated as a stochastic process. We analyzed predicted interactions between pathogen transmissibility, patient assignment policy, population prevalence of the pathogen, and the performance characteristics of a diagnostic screening test.

The model configuration that was used in these analyses is based on clinical practices in an existing medium-sized dialysis unit in a major metropolitan area and incorporates four pods of four dialysis stations, or chairs. Each pod is staffed by one caregiver, who has contact with each patient in that pod at specified intervals, twice per hour in the results presented (Figure 1). All treatments last 4 h. Patients see only one caregiver per treatment. There are 16 patients per shift and three shifts per day (48 total patients).

In the model, a patient can be either infectious or noninfectious. An infectious patient can contaminate the chair, the caregiver, or both with distinct probabilities. An uncontaminated, noninfectious patient can acquire the pathogen from the chair, the caregiver, or both, each with an associated probability. There is a finite probability that a contaminated caregiver will resolve his or her carriage of the pathogen between patient encounters and a (separately specified) probability that the caregiver will resolve his or her contamination between shifts of patients. Each of these probabilities is user-defined in the analytic software.

Similarly, three distinct probabilities govern the decontamination of a dialysis chair. One specifies the probability that a contaminated chair will become decontaminated between caregiver visits. The second specifies the probability that a contaminated chair will be decontaminated between shifts of patients. The third specifies the probability that a chair will be cleared of its contamination, either by pathogen attrition or active decontamination, between successive days.

For each encounter between a contaminated or infectious participant and an uncontaminated participant, a random number between 0 and 1 is drawn. If this number is less than the contamination probability for the class of encounter, then the uncontaminated participant is deemed to become contaminated. A similar approach is applied to model decontamination of chairs and providers.

Contaminated caregivers can immediately transmit the pathogen to other patients (“touch contamination”), have a specified probability of clearing their state of contamination after each encounter (decontami-
nation), and may remain contaminated for the entire day (three shifts). The probability of caregiver decontamination can reflect measures that range from effective hand and fomite cleansing to full barrier precautions.

A screening instrument is used to classify incident patients as high or low risk for being infectious. Patients are assigned to a shift and pod on the basis of their risk status and the containment policy under examination. We assume that the screening instrument can be applied before the patient’s unit visit. The screening instrument could comprise a symptom inventory, knowledge of recent travel, household exposure, membership in a known high-risk group, or a combination of these or other elements. Such screening instruments exist for influenza, severe acute respiratory syndrome, methicillin-resistant Staphylococcus aureus, and vancomycin-resistant Enterococcus (28–32). The number of high-risk incident patients for each day is determined by the user-specified population prevalence of the pathogen and the performance characteristics (sensitivity and specificity) of the screening test (Appendix 1).

Three mitigation strategies are compared with a baseline (high-risk patients are distributed uniformly among the shifts and pods) strategy:

1. Spatial segregation: Patients who are suspected of being infectious are preferentially assigned to four-chair pods that are served by one patient care technician.
2. Temporal segregation: Patients who are suspected of being infectious are assigned appointments later in the day.
3. Spatial + temporal: Patients who are suspected of being infectious are assigned to appointments later in the day and efforts are made to confine them all within four-chair pods that are served by one technician (Figure 2).

The likelihood that a given patient is infectious is calculated on the basis of the risk class of that patient, the performance characteristics of the screening test, and the population prevalence of the pathogen. A random number is generated, and if that number is less than the risk that the patient is infectious, then the patient is deemed infectious.

For each strategy, the model simulates 1 wk (6 d) in the dialysis unit, explicitly tracking each patient, caregiver, and chair as well as their infectious or contamination state through each day. High-risk and infectious patients are distributed identically between sequential days, and the infection control strategies implemented are uniform between days. Caregivers are assumed to be noncontaminated at the beginning of the day and can experience repeated cycles of contamination and decontamination during the day. In contrast, once contaminated, a chair can remain contaminated between successive days; the probability of this occurring is defined as outlined previously. Chairs are assumed to start the week uncontaminated. Once a patient has become contaminated, he or she is considered contaminated for the remainder of that shift. The number of patient contamination events is counted, the system is reseeded with an appropriately randomly generated distribution of high-risk patients, and the simulation is repeated. After 100 cycles, the total number of contamination events is used to calculate the contamination rate per 1000 patient-days for the class of patient under consideration.

Results

Predictions are presented as the anticipated number of contamination events (a noninfectious patient acquires the pathogen) per 1000 patient-days. Results from analyses are presented for a pathogen prevalence of 20% in incident patients (20% of incident patients are infectious) and three broad ranges of screening test characteristics: 95% sensitive/95% specific, 40% sensitive/92% specific, and 96% sensitive/54% specific. These performance characteristics correspond roughly to the case in which the patient’s infectious status is relatively well known, as with testing for methicillin-resistant Staphylococcus aureus or hepatitis C; the ability to ascertain influenza cases from verbal historical information alone; and the ability to ascertain severe acute respiratory syndrome from historical information alone (28,29). This spectrum was chosen to illustrate the effects of various strategies under various levels of uncertainty.

In Figures 3 through 5, the probability of an infectious patient’s contaminating his or her chair during the course of a 4-h treatment was varied from 18 to 87% (midrange 58%), and the corresponding likelihood of the patient’s caregiver’s acquiring the pathogen on his or her hands was varied from 2 to 17% (midrange 8%). These midrange values are consistent with the contamination rates measured by Grabsch et al. (33) and Smith et al. (34) for vancomycin-resistant Enterococcus. The probability of between-shift decontamination of contaminated chairs was
systematically varied from 0% (no decontamination) to 50%, and the probability of between-day decontamination of contaminated chairs was varied from 0% (no decontamination) to 100%. Results are grouped by the performance characteristics of the screening test.

Figure 6 depicts the anticipated effects of increasing the likelihood of caregiver contamination from approximately 2.5% per encounter to approximately 22.5% per encounter at each level of screening test performance and chair contamination probability. The between-shift and between-day chair decontamination probabilities were set at 0 and 100%, respectively. This reflects the consequences of an increase in the relative importance of caregiver cross-transmission in the setting of suboptimal between-shift but optimal between-day decontamination.

Increasing the between-encounter chair decontamination probability or the between-day probability of chair decontamination reduces the rate of patient contamination events for all containment strategies (Figures 3 through 5). This effect is most marked for temporal segregation and temporal + spatial segregation. Absent a high level of between-day environmental decontamination, temporal segregation has little effect and could potentially increase dissemination (Figures 3 and 5). In the presence of a sensitive and specific screening instrument, spatial segregation is less subject to this limitation.
The effects of both temporal and spatial segregation depend strongly on the performance characteristics of the screening instrument. Moreover, the effects of these "social distancing" interventions are generally smaller than those of environmental decontamination. These findings persist at higher levels of environmental decontamination (data not shown).

In the setting of complete end-of-day decontamination, temporal segregation uniformly reduced the predicted rate of transmission. Spatial segregation was less effective than temporal segregation in reducing the generation rate in this context (Figure 6). Combining spatial and temporal segregation added little to temporal segregation alone. Increasing caregiver-mediated transmission attenuated the differences among containment strategies. The effectiveness of spatial segregation was more dependent on the performance characteristics of the screening instrument than was the effectiveness of temporal segregation. These findings were robust over a wide range of transmissibilities and at prevalence levels both higher and lower than those presented (data not shown).

**Discussion**

Traditional mathematical analyses of pathogen dissemination are predicated on large, well-mixed populations that comprise susceptible, infected, and resistant individuals (SIRS models [35]). These models best predict disease transmission under conditions of homogeneous mixing and large populations. The characteristic
spatial intricacy and small populations of the dialysis unit violate both of these conditions. In contrast, individual-based models are spatially and temporally explicit and are appropriate to the heterogeneous and ordered contact networks of the dialysis unit. A Monte Carlo simulation approach is well suited to the probabilistic nature of the transmission process, variability in colonization pressure, and diagnostic uncertainty. Most model inputs reflect macroscopic system characteristics that are largely determined by unit policy; we based our system parameters on the clinical practices in a medium-sized dialysis unit in a major metropolitan area. System characteristics that are not determined solely by policy can be measured. For example, the decontamination probability may reflect a system characteristic as simple as the likelihood of effective postencounter hand washing; the range that we chose for this parameter (which is at least partially determined by unit policy) is in reasonable accordance with literature reports (36,37). Because “transmissibility” is more difficult to ascertain, we generated predictions for scenarios in which the likelihood of the patient’s contaminating his or her chair during a 4-h treatment ranged from 18 to 87% and the likelihood of the patient’s contaminating the hands of his or her provider ranged from 2 to 17%. Although data are sparse, these values are commensurate with the likelihood of environmental and caregiver contamination with vancomycin-resistant *Enterococcus* measured during dialysis procedures as measured by Grabsch et al. (33) and in the outpatient setting as measured by

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**Figure 5.** Predictions for baseline and interventions at population prevalence of 20%, screening test sensitivity of 96%, and screening test specificity of 54%. Probability of chair decontamination between shifts rises from 0 (left column) to 50% (right column); probability of chair decontamination between successive days rises from 0 (top row) to 100% (bottom row). Solid line, baseline; ○, spatial segregation; △, temporal segregation; □, temporal + spatial segregation.
Smith et al. (34). Moreover, the ordering of the strategies remains the same at all levels of transmissibility.

A number of simplifying assumptions were made in developing the model, none of which is crucial to this approach and all of which were used solely to simplify the presentation. Incorporation of direct patient-to-patient, caregiver-to-caregiver, and caregiver-to-environment transmission would be relatively straightforward but would not contribute substantively to the message of this communication. Interventions targeted specifically to high-risk patients (e.g., barrier precautions, focused decontamination procedures) are readily incorporated. However, such interventions are equally applicable to spatial and temporal segregation. We chose instead to focus on one unique set of resource-sparing strategies, approaches that could add a system-based additional layer of “protection” from pathogen transmission.

Similarly, the results presented do not incorporate variability in individual “contagiousness.” Although clinically relevant, such modifications do not qualitatively change our results (38,39). The results presented do not address time-dependent changes in the likelihood of transmission from a previously contaminated surface (as a result of “spontaneous” pathogen attrition). Experimental data suggest that relevant pathogens, particularly bacterial pathogens, can survive on surfaces for durations that are longer than the time scale of our analyses (40–45). Such relatively prolonged pathogen survival consid-
erably reduces the anticipated effect of pathogen attrition on system dynamics at this time scale.

Finally, we do not address the effects of repeated contamination of the same patient as regards an increase in pathogen burden for that patient or allow patients to transition from “contaminated” to “infectious” over sequential dialysis days. Both of these considerations are patient specific and require additional assumptions regarding pathogen survival, patient clearance, and the degree to which a patient “spreads” a pathogen from one site (e.g., his or her hands) to another (e.g., his or her chest). These important biologic questions merit further evaluation but are beyond the scope of this analysis.

Conclusions

Our results highlight the importance of environmental decontamination in attenuating pathogen transmission in the dialysis unit. Moreover, they suggest that temporal segregation might be an effective, low-cost approach to reducing pathogen dissemination in the hemodialysis unit if a high level of environmental decontamination between days can be ensured and infectious patients can be expeditiously identified.

Health care institution-level epidemiologic models could be applied to either endemic, nonseasonal pathogens of considerable importance or highly contagious agents that are seasonal or episodic in nature (e.g., the influenza virus). Moreover, similar quantitative tools could be used to weigh the overall costs of a particular strategy against the savings resulting from the attenuation of pathogen transmission, thereby facilitating the optimal deployment of increasingly scarce resources while improving patient safety.

Appendix

Patient Risk Class and Infectious Status

The probability that a high-risk or low-risk patient is infectious is calculated from the population prevalence and the sensitivity and specificity of the test:

1. Probability of true positive = sensitivity * prevalence
2. Probability of false positive = (1 − specificity)(1 − prevalence)
3. Probability of true negative = (specificity) * (1 − prevalence)
4. Probability of false negative = (1 − sensitivity) * prevalence
5. Probability of being assigned high-risk status = Prob(true positive) + Prob(false positive)

Probability that a patient categorized as high risk is infectious is as follows:

6. Prob(high risk and infectious) =

\[
\frac{\text{Prob(true positive)}}{\text{Prob(true positive)} + \text{Prob(false positive)}}
\]

Probability that a patient categorized as low risk is infectious is as follows:

7. Prob(low risk and infectious) =

\[
1 - \frac{\text{Prob(true negative)}}{\text{Prob(true negative)} + \text{Prob(false negative)}}
\]

A random number is generated for each patient and is compared with the relevant probability (equation 6 or 7). If the random number is less than the calculated probability, then the patient is designated as infectious.

Transmission Probabilities for Different Classes of Encounter

The dialysis treatment is broken into eight 30-min periods. The overall transmissibility is the likelihood that an infectious patient will contaminate his or her chair during a 30-min portion of his or her treatment; a 20% overall transmissibility indicates a 20% chance of contamination during a 30-min interval.

The transmission probabilities for all other types of encounter (e.g., infectious patient → caregiver) are expressed as a fraction of the probability of chair contamination in a 30-min period:

Transmission probability encounter type X = (overall transmissibility) * (multiplier for encounter type X).

The probabilities that a caregiver or chair will be decontaminated between patient visits or between shifts are specified directly.

Table 1. Transmission multipliers and decontamination probabilities

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contamination probabilities</td>
<td>Varies</td>
</tr>
<tr>
<td>patient to caregiver multiplier</td>
<td>Varies</td>
</tr>
<tr>
<td>environment to caregiver multiplier</td>
<td>0</td>
</tr>
<tr>
<td>caregiver to patient multiplier</td>
<td>Varies</td>
</tr>
<tr>
<td>caregiver to environment multiplier</td>
<td>0</td>
</tr>
<tr>
<td>Sanitization probabilities</td>
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<td>probability of hand hygiene, caregiver during shift</td>
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</tr>
<tr>
<td>probability of hand hygiene, caregiver between shifts</td>
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</tr>
<tr>
<td>probability of environmental decontamination during shifts</td>
<td>0</td>
</tr>
<tr>
<td>probability of environmental decontamination between shifts</td>
<td>Varies</td>
</tr>
<tr>
<td>probability of environmental decontamination between days</td>
<td>Varies</td>
</tr>
</tbody>
</table>
For the simulations presented, the transmission multipliers and decontamination probabilities are shown in Table 1.

The probability that a patient will contaminate his or her chair during a 4-h treatment is then given by the following:

\[
\text{Probability of chair contamination at 4 hours} = 100 \cdot (1 - (1 - \text{probability of overall transmissibility}))^6
\]

The probability that a patient will contaminate his or her caregiver’s hands during a 4-h treatment is given by the following:

\[
\text{Probability of caregiver contamination at 4 hours} = 100 \cdot (1 - (1 - \text{transmission multiplier} \cdot \text{probability of overall transmissibility}))^6
\]

The values used for overall transmissibility ranged from a 2.5% probability of chair contamination per 30 min to a 22.5% chance of caregiver hand contamination during a 4-hour treatment. The values used for overall transmissibility ranged from a 2.5% probability of chair contamination per 30 min to a 22.5% chance of caregiver hand contamination during a 4-hour treatment. The values used for overall transmissibility ranged from a 2.5% probability of chair contamination per 30 min to a 22.5% chance of caregiver hand contamination during a 4-hour treatment.

Acknowledgments

This work was supported by National Institute of Allergy and Infectious Diseases grant 1R21AI55818 (J.R.H.).

We express our gratitude to the anonymous reviewers for insightful suggestions.

Disclosures

None.

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