COMMENTARY

Patients as Patches: Ecology and Epidemiology in Healthcare Environments

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The modern healthcare system involves complex interactions among microbes, patients, providers, and the built environment. It represents a unique and challenging setting for control of the emergence and spread of infectious diseases. We examine an extension of the perspectives and methods from ecology (and especially urban ecology) to address these unique issues, and we outline 3 examples: (1) viewing patients as individual microbial ecosystems; (2) the altered ecology of infectious diseases specifically within hospitals; and (3) ecosystem management perspectives for infection surveillance and control. In each of these cases, we explore the accuracy and relevance of analogies to existing urban ecological perspectives, and we demonstrate a few of the potential direct uses of this perspective for altering research into the control of healthcare-associated infections.

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BACKGROUND

Systematic investigation into the effects of urbanization on ecological processes began in earnest after World War II.[1] In the past few decades, the study of how urban environments yield different types of ecosystems from those favored by undisturbed or rural environments has blossomed into its own field: urban ecology. By framing research questions using urbanization, this field has been able to provide insights that might otherwise have remained case-by-case results within ecological research.

Thus far, the field has focused on 3 areas of urban impact: the built environment; the byproducts and processes of human urban life as they affect resources and/or habitats for animals and plants; and the resulting biodiversity of the urban ecosystem.[2] These foci have identified knowledge and data gaps in the understanding of urban ecological processes, have suggested novel hypotheses for scientific investigation, and have enabled concrete and empirically informed planning for more sustainable urban development.

While the complexity of urban ecosystems differs from natural environments,[3] and this difference can largely be attributed to human-related factors, the main populations and communities studied in cities have been plants and animals (eg, McKinney[4]). However, there remains a gigantic yet vastly under-studied realm of the ecology of human urban environments: the urban microbiome.[5]

Here, we consider the healthcare environment as one in which an ecological perspective may be beneficial in improving clinical care and in which the focuses of urban ecology in particular lend themselves to new methods of addressing healthcare-associated infections. While not all healthcare settings are located in what might be considered urban areas, even rural hospitals often feature relatively intense development, a high density of human beings in the same place, and a structurally modified environment. All of these factors are commonly associated with the perspectives and tools of urban ecology.

Applying Urban Microbiome Ecology to Hospital Epidemiology

The healthcare environment represents a complex and medically and economically important environment for pathogens and other human-dependent microbes. Healthcare-associated infections are among the leading causes of death in the United States and have a substantial economic cost.[6] The built environment within the hospital is awash with (1) microbes only infrequently encountered outside the healthcare environment, (2) disinfectants, and (3) an array of antimicrobial agents ranging from drugs used in patient treatment to surfaces designed to be resistant to bacterial colonization. Urban settings in particular, because of their size

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and population density, have greater numbers of emergency care facilities, and academic medical centers, and they offer more specialized resources for treating complicated conditions.[7] Thus, patients may go to several providers simultaneously or in sequence. This diffuses accountability for infections so there is no single obvious "point of failure," but rather a network of institutions struggling to address their infection control problems.[8] Conversely, denser urban settings also support larger institutions with increasing numbers of patients under care, meaning that facilities failing to control hospital-acquired infections may affect a larger number of people.

Viewing hospital settings in an ecological context (Table 1) can yield insights into pathogen dynamics, transmission, and control. An approachable analogy to other ecological disciplines is to view not only the hospital environment as an ecosystem but also each patient as a free-standing ecosystem. This type of thinking is implicit in many current areas of hospital epidemiology research, from the decolonization of patients with chlorhexidine gluconate to manipulating their intestinal microflora to prevent *C. difficile* recurrence. Each patient can be thought of as a "patch," a term denoting a small, self-contained ecosystem that is functionally remote from other habitats, such as an island or an isolated area of green space.[9] The routes of transmission between patients, whether direct contact through the contaminated hands of healthcare workers or contact with a contaminated environment, then become the ecological corridors[10] along which pathogens move from one patch to another. This group of habitat patches is analogous to a metapopulation, where migration between patches and asynchrony in patch dynamics (ie, not all people become infected or recover, at the same time) allow the population to persist over time.[11] Urban ecologists are often interested in whether building dispersal corridors will counteract the effects of habitat fragmentation.[12] By contrast, infection preventionists attempt to intentionally fragment pathogen habitats and disrupt migration between patients, preventing pathogens from persisting over time. Unique to hospital epidemiology is the fact that some of these corridors, such as the hands of healthcare workers, are themselves also microbial habitats and thus could be patches as well. The level of abstraction for using ecological reasoning will depend on the problem in question. For example, while a patient-centric intervention may regard healthcare workers purely as the means by which patients are exposed, a new hand sanitization protocol might focus on the microbial environment of a worker's hands.

Each of these patient environments, by the very fact that they are in a hospital, also undergo significant environmental alterations. These include the direct targeting of a particular pathogen with a pharmaceutical intervention (most commonly an antibiotic or antiviral) as well as the unintended effect of these therapies on other microbes in the patient environment (eg, the impact of broad-spectrum antibiotics on the majority of normal intestinal flora, or a drastic reduction of particular non-target microbial species[13,14]). Such shifts in the patient environment can, in turn, alter immune function[15] and open niches for colonization by microbes acquired post-hospitalization, leading to further changes in community composition.[16] These interactions may yield novel patterns in interpathogen competition and/or commensalism due to the numerous unusual and overlapping selective pressures that exist not only at the level of the patient but among patients as well. For example, the use of proton pump inhibitors may alter a patient's intestinal flora, leaving them susceptible to *C. difficile* infection. In turn, the treatment of this infection with vancomycin may promote the proliferation of vancomycin-resistant *Enterococci*.[17] This complex network of infection risks is borne out of the patient's own microbiome, the hospital's microbial environment, and the interactions between them through treatment.

Above the level of an individual patient, the temporal dynamics of urban life in humans can also impact the ecology of pathogens on the level of both host and hospital. For

TABLE 1. Outline of a Framework for Interpreting Ecological Dynamics in an Urban Hospital Environment

	Ecology Term	Hospital Analog
Landscape	Habitat patch	Patient environment (in this analogy hospital staff are viewed as corridors rather than patches)
	Corridor	Suitable habitat that pathogens can use to migrate between patches
	Heterogeneity	Changes in key parameters that define pathogen habitat suitability across space or time
	Fragmentation	Disrupting connectivity between patches, with the goal of preventing pathogen transmission
Population	Metapopulation	Group of interconnected habitat patches (ie, the hospital environment as a whole)
	Immigration/emigration	Movement of microbes via habitat corridors between patients
	Colonization vs extinction	Infection vs eradication of pathogen from patient
	r/K selection	Different pathogen life history strategies (eg, high/low transmission rate and long-/short-term survival in host)
Community	Richness vs evenness	The absolute number vs relative abundance of microbial species in a community
	Disturbance	Event that alters the patient environment (eg, treatment with antibiotics, cleaning of hospital surfaces)
	Resistance	The extent to which microbial community composition and/or function remains stable in the face of disturbance
	Invasibility	Susceptibility of the patient environment to pathogen establishment

example, many diseases exhibit inherent pathogen-specific seasonality,[18–20] thereby periodically (re)introducing novel microbial competitors into the healthcare environment. Similarly, periodic influxes of cohorts of newly trained doctors, nurses, and other healthcare personnel may lead to a short-term increase in medical errors,[21,22] compromising the deliberate habitat fragmentation caused by infection control policies and allowing ecological corridors between patients to form. This is, in essence, a fluctuating level of habitat heterogeneity, involving anything from relatively mundane daily oscillations in hospital occupancy and the resulting effect on patient care,[23] all the way up to social or political events, such as emergencies, natural disasters, or labor disputes.[24,25] These events can then cascade, altering the microbial environment and competitive landscape in unplanned ways. For example, the use of nurses from different departments to alleviate a temporary staffing shortage may result in combining several infection control cultures and compromising existing protocols.

The dynamics of disease transmission are also different between the healthcare environment and other urban environments, even those entirely created by humans. The near destruction of one's intestinal flora due to antibiotics is a relatively frequent event within hospitals,[26] and while surface-mediated transmission (ie, one individual infects another by way of their shared physical environment) undoubtedly exists in the normal course of urban life, it both occurs at a higher frequency and takes on greater seriousness within the context of the healthcare environment.[27,28]

Ecological Implications of the Patient Environment

As in wildlife ecology, urban patterns of hosts-as-habitats can have considerable impact. Potentially different social conventions regarding intimate contact and sexual partnership in urban settings might alter the success of K-selected pathogens (ie, those that are transmitted rarely or require repeated exposure for successful transmission and therefore must survive within a single host for long periods of time, as is the case with many sexually transmitted infections[29]). The dense patterns of contact among larger numbers of incidentally collocated people might easily be described as favoring *r*-selected pathogens (ie, ones that transmit quickly to new hosts, investing few resources in surviving within any single host for very long) up to a point, but past that point would be expected to shift into boom–bust dynamics wherein periodic large-scale outbreaks sweep through a majority of the population but then die out.[30] Furthermore, as is known from population genetics and metapopulation ecology, increased numbers of potential hosts in regions that can, but do not frequently, interact allow rare neutral mutations to become established more frequently than in fully panmictic populations.

These perspectives are also directly relevant within a healthcare environment, with the associated array of intensive selective pressures. The prevalence of pharmaceutical interventions, disinfection and sterilization products, as well as their varied mechanisms of action and an ever-shifting microbial community, can alter the relative fitness of *r*- versus K-selected species as competitors. This perspective is of immediate practical use, relying on the very well-developed literature about which conditions favor *r*- versus K-selected species (eg, Resnick et al[31] and Phillips et al[32]) and thereby generating practical and testable hypotheses about which pathogens are likeliest to become established as HAIs due to their relative evolutionary fitness among ambient pathogens. For example, *r*-selected species that are characterized by very high rates of reproduction and rapid, explosive growth (eg, norovirus) may be favored in many hospital environments, which, from a microbial perspective, are relatively unstable due to high amounts of environmental disinfection. In contrast, environments with more stable environments and populations, such as long-term care facilities, may favor, or at least be conducive to, the transmission of more K-selected pathogens, such as fungal infections or tuberculosis.

An Ecological Perspective on Infection Surveillance and Control

Understanding the principles of urban ecology that apply to healthcare environments has the potential to inform infection control policy and to improve existing infection surveillance and control programs. Advances in sequencing technology have made the study of infection control problems from a community ecology perspective a technical reality,[33] but this potential has not yet been fully realized. Methodological difficulties arise given the levels of asymptomatic carriage[34] commonly seen in many pathogens important to hospital epidemiology, such as *S. aureus* or *C. difficile.* Despite these hurdles, these technologies are invaluable for quantifying what pathogens exist within a healthcare environment—the first step toward understanding its ecology.

An ecological perspective can help evaluate the relative impacts and unforeseen consequences of vertical infection control programs that combat a single pathogen (eg, targeted screening for CRE colonization when a patient is admitted) versus horizontal infection control programs that target a wide swath of pathogens through a single mechanism (eg, improved hand hygiene compliance).[35–37] Each of these types of programs, or several programs of each type within a hospital, impacts the community dynamics of the pathogens within the hospital and, by extension, within the patient-level environment as well. Understanding these dynamics, such as the potential of one infection control program to increase the prevalence of another type of microbe (ie, through competitive release)[16] allows for more well-controlled programs and may provide explanations for otherwise unanticipated or inexplicable changes in infection rates. The most common example confronting healthcare settings is the epidemiology of *C. difficile*. Treatment protocols that suggest the use of broad-spectrum antibiotics disrupt the normal ecology of the gut, opening up a large niche into which *C. difficile* may then proliferate and cause disease.

Similarly, infection risk analysis and mitigation may also be improved by incorporating urban ecological understanding about how to use observed biodiversity as an indicator of disturbance. Most current patient screening techniques, diagnostic tests, environmental contamination surveys, etc, operate based on the determination of presence/absence, ignoring other community properties, such as relative abundance. However, in ecology, species richness alone is typically an insufficient indicator of ecosystem processes, and the relative abundance of species, or evenness, is also extremely important.[38] For example, urban environments tend to display less evenness as a result of overrepresentation by invasive species and human commensals.[39] These findings align perfectly with *Clostridium difficile* infection, which is driven not necessarily by the presence of the pathogen but rather by the pathogen's relative abundance compared to other organisms within the patient's microbiome.[40,41] Interventions meant to alter microbial abundance, such as the use of fecal microbiota transplantation, are therefore direct means of altering the community ecology of the patient environment.[42] There is no reason that *C. difficile* should be unique in this respect, and save for infections stemming from the introduction of pathogens into an environment where they should not be (eg, central-line–associated bloodstream infections), the ecologically informed inclusion of abundance as part of biodiversity in surveillance and risk analysis may provide better understanding and improved potential for control.

Another aspect of biodiversity, functional diversity, may also be incredibly important from the standpoint of diagnosing and controlling diseases. In urban ecology, function refers to the processes and services performed by ecosystems (eg, nutrient cycling, primary productivity) and is sometimes, but not always, related to the presence or abundance of certain species.[3,43] However, groups of species performing similar functions can lead to functional redundancy, whereby species composition can change without compromising ecosystem processes.[44] Increasing evidence of functional redundancy in the human microbiome[45,46] calls for a broadening of epidemiological focus from the presence or abundance of a particular microbe toward consideration of functionally similar microbes or even specific microbial transcripts (eg, resistance genes).[47] This concept is already being explored through the use of bacterial interference as either a direct treatment[48,49] or as a potential source for new therapeutic agents.[50]

In addition to impacts on ecosystem function, the various components of biodiversity discussed above can influence a community's response to disturbance and invasion. While several authors have considered the implications of ecological resistance and resilience for human-associated microbial communities,[51–53] further insights are uniquely applicable to the healthcare environment. Studies like the Hospital Microbiome Project[54] may ultimately inspire efforts to cultivate surface-associated communities within hospitals that are resistant to pathogen establishment. For example, a recent study found that more diverse microbial communities occur in hospital rooms with windows that open, suggesting the potential for building features to affect microbial community composition, and perhaps indirectly, the movement of pathogens.[55]

Using Urban Ecology to Predict Hospital Epidemiology

With the examples outlined above, we can begin to see how concepts from urban ecology can inform research questions and recommendations in medical ecosystems. Urban ecology has a deep literature base regarding on the impact of urban settings on biodiversity. In general, these studies predict (in temperate regions) that species commonly transported into the urban center by humans (eg, invasives with high propagule pressure) will increase while native species richness declines, although some native species that can adapt to the changes associated with urbanization may increase.[4,39,56] This framework can be applied in medical settings to consider epidemiological outcomes observed already, but with a unifying and explanatory theory by which to predict and describe pathogen dynamics. For example, there should be increasing numbers of outbreaks of rare but often introduced pathogens, such as MRSA when it is endemic in the community, even if it is controlled within a hospital. The incidence of infections that can be easily and effectively treated should decrease (as with the general decline in many infectious diseases in the twentieth century), and correspondingly there should be an increase in diseases that are becoming more difficult to treat, such as antimicrobial-resistant infections. The incidence of infections for which medical treatment increases the host's ability to circulate among the rest of the population while still infectious should increase. Here, this can be the result of treatment suppressing symptoms but not shedding, or as the result of frequent patient transfers within or between hospitals.[8] Likewise, each of the analogies mentioned throughout this review can lead to specific predictions about disease dynamics in healthcare settings.

CONCLUSIONS

Although we have conducted only a surface-level overview of the potential application of ecological perspectives on hospital epidemiology, we believe an increased use of this type of analysis and thinking has immediate potential in helping combat healthcare-associated infections. These infections are directly analogous examples for many of the concepts developed within and between traditional and urban ecological research efforts (eg, invasive species). This perspective on hospital epidemiology puts forth clear and important questions for which existing theory in these disciplines can offer more general solutions, rather than the current case-by-case basis used for disease-specific epidemiological research.

We can already see how to apply this perspective to an astounding diversity of issues confronting infection preventionists: (1) understanding/predicting the likely relative frequencies for different types of pathogens; (2) suggesting critical "corridors" for transmission of pathogens such that surveillance efforts in these locations or populations would be most effective in early detection of outbreaks; (3) informing public health interventions to trade off short-term against long-term outbreak management goals (ie, hospitalizing patients when staffing and resources are already strained during a public health emergency, prioritizing patient treatment and survival at the cost of increased risk for secondary infections, analogous to control strategies studied in population viability analysis); and (4) altering microbial management in healthcare facilities based on understandings of microbial community competition and commensalism dynamics, among others.

Over the past decade, the understanding that the ecology of infectious diseases can help to inform epidemiological research has led to some deep and beautiful insights.[57,58] By taking this understanding a step further, borrowing also from research into the distinct ecological processes that occur in urban settings and how they differ from other environments, we believe we can leverage a greater depth of insight into urban microbial dynamics in direct application to everything from basic epidemiological science to clinical practice. This insight then has the potential to lead to better interventions and improved patient outcomes. Interested researchers may find surprisingly relevant concepts in foundational textbooks in urban ecology[59,60] or through discussions with colleagues in the ecological sciences.

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