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Human ecology in pathogenic landscapes: two hypotheses on how land use change drives viral emergence

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Abstract

The emergence of novel viral diseases is driven by socioeconomic, demographic and environmental changes. These include land use changes such as deforestation, agricultural expansion and habitat degradation. However, the links between land use change and disease emergence are poorly understood and likely complex. In this review, we propose two hypotheses for the mechanisms by which land use change can lead to viral emergence: 1) by perturbing disease dynamics in multi-host disease systems via impacts on cross-species transmission rates (the 'perturbation' hypothesis); and 2) by allowing exposure of novel hosts to a rich pool of pathogen diversity (the 'pathogen pool' hypothesis). We discuss ways that these two hypotheses might be tested using a combination of ecological and virological approaches, and how this may provide novel control and prevention strategies.

Introduction

Emerging infectious diseases (EIDs), and in particular emerging viruses, are a key threat to global public health, to livestock, wildlife and to ecosystem functioning [1,2]. Some EIDs threaten public health through pandemics with large-scale mortality (e.g., HIV/AIDS). Others cause smaller outbreaks with high fatality rates or lack effective therapies and vaccines (e.g., Ebola virus, rabies, multi-drug resistant TB) [3,4]. As a group, EIDs and re-emerging diseases cause millions of deaths each year, and some single outbreak events (e.g., SARS) have cost the global economy tens of billions of dollars [5]. The World Economic Forum considers EIDs as "major" risks, comprising significant likelihood of occurrence and significant economic threat over the next 10 years, comparable in scale to unsustainable population growth [6,7]. Predicting and preventing the emergence of novel diseases with pandemic potential is therefore a global public health priority [8].

Yet, despite these impacts and perceived importance, our understanding of what causes diseases to emerge is rudimentary. The underlying causes tend to be changes in socioeconomic factors (e.g., increased travel and trade), demography (e.g., population expansion), agriculture (e.g., intensification of livestock production), medical science (e.g., increased antibiotic use) and to the environment (e.g. land use change, deforestation) [2,9,10]. It is thought that these 'drivers' of emergence foster conditions for pathogens to expand host range, and adapt to new niches, and that understanding how they affect the

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process of disease emergence could have use in predicting and combating EID threats [8,11].

The ecology of disease emergence

Human cases of new diseases stimulate intense research. Once reservoir-to-human transmission has occurred for a new EID, and led to human illness or mortality, significant efforts are often made to identify the reservoirs of the causative agent, or its capacity to spread once in the human population. These may have significant broad value for preventing future outbreaks or reducing pandemic threats. Studies that analyze how networks of contact, travel and trade, for example, have been used to predict pandemic spread of new EIDs, and to propose quarantine measures or therapeutic stockpiles to interrupt it [12-14]. These studies, however, are all focused on the later stages of the disease emergence process. There has been much less attention given to the preconditions requisite for epidemics to commence [15].

One key limitation to a fundamental understanding of the process of disease emergence is that new EIDs are caused by previously unknown pathogens, of unknown ecology, in unknown hosts. Another barrier to progress is that this is a fundamentally ecological problem that requires large-scale field studies and interdisciplinary collaboration among the ecological and medical sciences. The process of emergence also likely involves complexity that is often not brought into epidemiological analyses (e.g. the dynamics of seasonally fluctuating wildlife reservoir populations), and they require long-term field and lab commitment [16]. For example, long term studies of Lyme disease ecology have revealed the importance of synchronous tree masting [17], reservoir population changes with habitat fragmentation [18], and loss of predators [19] in the emergence and impact of that disease. Similarly, understanding the relative role of fruit bat population biology and livestock intensification in the emergence of Nipah virus required multi-year collaboration among ecologists, mathematical modelers, virologists, wildlife biologists and veterinary pathologists [16,20]. That said, there are some broad patterns that suggest fruitful avenues of research.

Disease emergence and land use change

Human activity has altered ecosystems on a global scale [21,22]. Changes include deforestation, expansion of agriculture, pollution, eutrophication, depletion of marine fisheries and increased nitrogen fixation [21,22]. Anthropogenic influence on landscapes has increased most rapidly in the last century with global population growth [23]. These changes have led to perturbation of biotic systems (e.g., biodiversity loss and biological invasions) the environment (e.g., water supply, climate), with subsequent direct and indirect impacts on human and wildlife populations [22]. Some impacts are positive (e.g. increased wealth in many regions), but many are negative (e.g. increased risk of drought, famine, emerging diseases).

These changes seem to be particularly important for zoonotic diseases, which account for ~60% of all EIDs [24,25]. Around 1/5 of EID events since 1940 [unpubl. data, updated from 11] and an even higher proportion of zoonotic diseases, have been associated with land use changes, such as agricultural conversion, deforestation and activities associated with the extractive industries (e.g., mining, logging). These statistics support suggestions that increasing interaction among humans, domestic animals and wildlife following land use change is a significant contributor to disease emergence [26,27].

However, despite the relative frequency with which land use change has been associated with disease emergence events [11,18,26,28], land use change/disease emergence

hypotheses tend to be vague or case-specific and currently lack a general theoretical foundation. This limits our ability to derive testable hypotheses and implement tailored management strategies to reduce the risks.

Two hypotheses for disease emergence due to land use change

Current conceptual models tend to focus on two main mechanisms for disease emergence under land use change (Figure 1): **1)** Land use change perturbs disease dynamics in multi-host disease systems by disrupting the cross-species transmission rate (hereafter the 'perturbation' hypothesis); and **2)** Land use change allows exposure of novel hosts to a rich pool of pathogen diversity, influencing the cross-species transmission rate (hereafter the 'pathogen pool' hypothesis). These are not exclusive processes, and may be confounded when considering the mechanisms of disease emergence in dynamic landscapes. This is because human ecology – the presence, distribution and behavior of people - is the common denominator for both. Untangling the two hypotheses to better understand disease emergence and develop control and prevention strategies requires careful consideration of this dynamic coupled natural-human system.

Analyzing land use change and disease emergence

A key limitation to studies of how disease emergence is driven by land use change is, of course, our significant lack of knowledge of the diversity of pathogens present in wildlife in a region, of the ecology of these pathogens, and their impact on different hosts (including should they emerge into people) [8,29]. Unusual or infrequent pathogen transmission between species ("spillover") is the defining characteristic of a zoonosis. Conceptual models place the factors influencing the force of infection from animals to humans into three categories: 1) the prevalence of infection in the animal reservoir, 2) the rate at which humans come into contact with these animals, and 3) the probability that humans become infected when contact occurs [15]. These components interact and are each influenced by diverse properties of natural and human systems, with additional factors associated with pathogen modes of transmission and evolutionary constraints (e.g., phylogeny) [15,30,31].

Under land use change, human ecology directly drives the contact rate among humans and reservoir hosts (e.g., how and when contact with wildlife occurs) and can influence the likelihood of infection given contact (e.g., the type of contact, such as butchering vs cohabitation). Additionally, the human impact on the landscape may simultaneously influence the prevalence of infection in animal reservoirs by perturbing the abundance and distribution of different animal reservoirs [32]. Thus, the interaction of human ecology with biodiversity is fundamentally important to zoonotic disease emergence due to land use change.

Links between biodiversity, disease risk and land use change

Most of the early theoretical models of disease dynamics have concerned single-host single-pathogen systems [33,34]. More recent studies have begun to use a community ecology perspective to understand multi-host disease systems [15,35-40]. Some of these have demonstrated correlations between host diversity and disease risk, both positive and negative [18]. But what are the mechanisms?

Under the 'perturbation' hypothesis, biodiversity has been related to both an increase (via the "amplification effect") and a decrease (via the "dilution effect" or other functionally similar means [35]) of the intrinsic risk of cross-species transmission. There is currently mixed support for which of these outcomes is generally more common or likely from ecosystem perturbation [32,39,41-43]. The underlying mechanisms involve the change in

host species richness, abundance, quality or contact rate, which governs cross-species transmission rates via their effects on pathogen prevalence and the number of infectious individuals [35,39,42]. In order to better understand the way land use change affects risk of disease emergence, understanding the relationships between multiple hosts and multiple pathogens is critical.

Under the ‘pathogen pool’ hypothesis, land use change may foster exposure of hosts (humans and associated species, e.g. livestock, pests) to a pool of microbes harbored by wildlife for which they have no prior exposure. This increases the risk of novel cross-species transmission events. This can be distinguished from the ‘perturbation’ hypothesis because the mechanism focuses on novel contact between novel host-pathogen groups, and not necessarily on perturbing the community ecology of pathogens in reservoirs. Under the ‘pathogen pool’ hypothesis, risk of disease emergence should correlate with the factors that drive contact between novel host-pathogen pairs. This should include aspects of human ecology (our abundance, distribution, behavior) that dictate contact with reservoirs in landscape [44,45], as well as the baseline microbial diversity in reservoirs, referred to in earlier studies as the ‘zoonotic pool’ [46].

Several studies have thus proposed that areas of higher biodiversity (e.g., the tropics) should confer greater risk of zoonotic disease emergence under land use change [11,47]. The assumption is that pathogen diversity is a function of host diversity, such that human activities in highly biodiverse regions result in novel exposure to a more diverse pool of pathogens and an elevated risk of ‘spillover’. However, relationships between host and pathogen biodiversity are often unclear or lack consistent empirical support across taxa [42,48-54]. Thus, testing this hypothesis requires better characterization of viral diversity in wildlife to determine predictable relationships between host and pathogen biodiversity, should they exist. It also requires a better understanding of the factors that drive the microbial diversity within landscapes.

Future perspectives – human ecology and pathogenic landscape?

Despite significant global resources spent on pandemic prevention, new zoonoses, and in particular viral zoonoses, continue to emerge in the human population [55]. Their impact is high, even in the absence of significant mortality (e.g. SARS) and analyses of global and historical trends suggest their emergence is accelerating, even after accounting for reporting bias [11]. The increasing number of zoonotic diseases spilling over from a range of wild animal species is of particular concern. Clearly the global changes promoting novel disease emergence are currently outstripping our potential to leverage fundamental knowledge to predict and prevent pandemics. At the same time, the underlying environmental and socioeconomic drivers continue to accelerate in impact, compounding this problem.

On average, studies suggest that protecting biodiversity or limiting human influence in landscapes should reduce the risk of zoonotic disease emergence [18]. Yet, given our poor understanding of the specific mechanisms involved, there is currently little uptake of this as a disease management option. Elucidating the dominant mechanisms of disease emergence in dynamic landscapes thus remains a critical priority in infectious disease research, and ultimately pandemic prevention.

In this review, we have identified two key hypotheses that could be a priority for future research and that will begin to integrate an understanding of human ecology with host-pathogen community ecology. The long-term result may be a strategy to identify high-risk regions, populations and perhaps even occupations that play the largest role in disease emergence due to land use change. Designing ways to alter land management plans in these regions, or limit exposure for populations at risk may limit exposure to and/or minimize the

consequences of EIDs. Given the high economic and health costs of EIDs, even small gains in risk reduction via novel, tailored strategies could be a highly cost effective way to manage EID risk [56].

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- Emerging viral zoonoses are a critical threat to public health and are driven by socioeconomic and environmental changes
- Our understanding of how environmental changes, in particular land use change causes viruses to emerge is rudimentary
- We propose two hypotheses on how land use change causes disease emergence
- These are: the ‘perturbation’ hypothesis, and the ‘pathogen pool’ hypothesis
- We discuss how these could be tested, using a combination of virological and community ecology studies

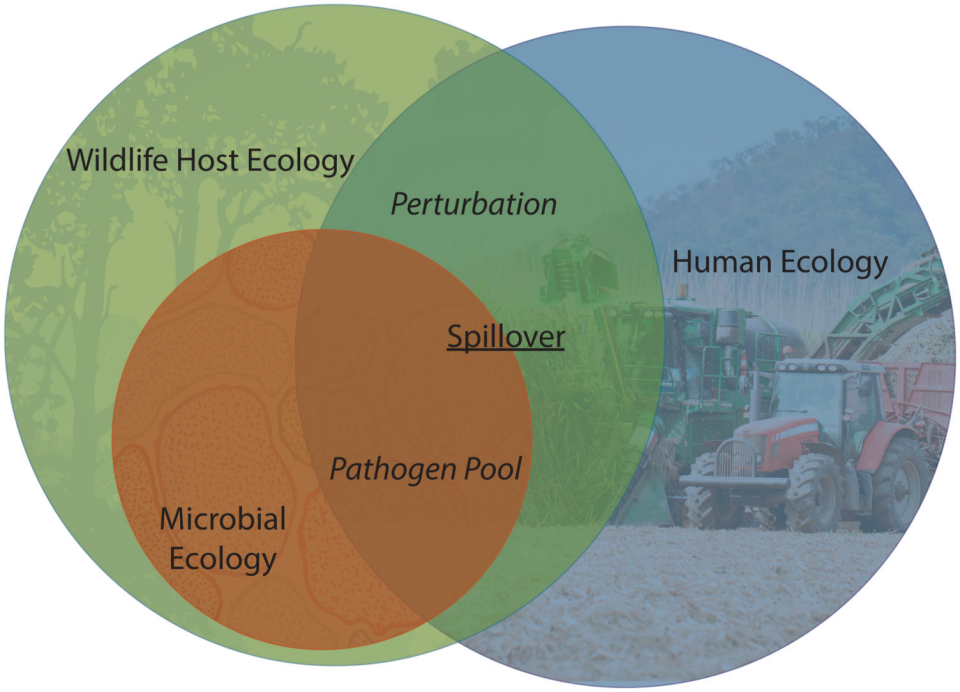

Figure 1.

Conceptual model of how land use change drives the emergence of infectious diseases in people. Land use change is a complex, dynamic process that underpins many of the novel zoonoses identified in humans during the last few decades. While the ultimate goal of public health is to identify and prevent transmission of these pathogens to people (‘spillover’), our mechanistic understanding of what drives them to emerge is poor. We propose two hypotheses which are probably not mutually exclusive. In the ‘pathogen pool’ hypothesis, anthropogenic activities in previously pristine environments bring people into contact with a large reservoir of microbial diversity in wildlife for which humans are naïve. In the ‘perturbation’ hypothesis, land use changes alter the dynamics of pathogen transmission among wildlife, and promote cross-species transmission.