CellPress

Review

Global Patterns of Zoonotic Disease in Mammals

Barbara A. Han,[1,*] Andrew M. Kramer,[2] and John M. Drake[2,3]

As the frequency and prevalence of zoonotic diseases increase worldwide, investigating how mammal host distributions determine patterns of human disease and predicting which regions are at greatest risk for future zoonotic disease emergence are two goals which both require better understanding of the current distributions of zoonotic hosts and pathogens. We review here the existing data about mammalian host species, comparing and contrasting these patterns against global maps of zoonotic hosts from all 27 orders of terrestrial mammals. We discuss the zoonotic potential of host species from the top six most species-rich mammal groups, and review the literature to identify analytical and conceptual gaps that must be addressed to improve our ability to generate testable predictions about zoonotic diseases originating from wild mammals.

Where Will Future Zoonoses Come From?

Current understanding about the global distribution of most infectious diseases is surprisingly limited. Even for human infectious diseases, the spatial distributions of the vast majority remain little known [1]. However, the frequency with which new infectious diseases are emerging (**emerging infectious diseases**, IEDs; see Glossary) [2], especially **zoonoses**, underscores the necessity of shifting from a reactionary to a pre-emptive approach to mitigating infectious disease.

Assessing future disease risk requires baseline data – information about where infectious diseases are distributed geographically, taxonomically (with respect to animal reservoirs), and in relation to human populations. Such information is most abundant for records of human infectious disease. Whether looking across multiple diseases to glean generalizable epidemiological insight, or at specific diseases to identify important covariates predicting particular human **outbreaks**, previous studies have combined detailed data on human infectious **disease events** and environmental factors to quantify current and to predict future **disease hotspots** (e.g., [2–6]). Such baseline data provide important starting points for making projections of human disease risk, and can be effectively applied to predict the spread of particular infectious diseases to new areas that are in close proximity, or are located in environments similar to historical outbreak locations (e.g., [6,7]). As one example, data describing the ecology of bat reservoirs of Nipah virus can help to make projections about the types of environments expected to support cases of human disease [5]. Such baseline data can then be applied to identify and manage similar locations where future Nipah outbreaks might be predicted to occur. However, data from past outbreaks may offer little towards efforts to predict outbreaks of completely novel diseases that punctuate the status quo – for example, the emergence of new zoonotic pathogens, such as the Middle East respiratory syndrome coronavirus (MERS-CoV) [8], or outbreaks of known zoonoses in unexpected areas, such as Ebola virus disease in West Africa [9]. Because of their often surprising departures from previous outbreak patterns, some argue that disease events may be inherently unpredictable (e.g., [10]). Predicting outbreaks, caused

Trends

Predicting zoonotic disease events remains a prominent scientific challenge.

In response to increasing frequency of emerging infectious disease events caused by animal-borne (zoonotic) pathogens, recent advances assess the biogeographic patterns of human infectious diseases.

A disproportionate representation of mammal-borne zoonoses among emerging human disease has sparked research emphasis on mammal reservoirs because improved understanding of mammal host distributions may lead to improved predictions of future hotspots for zoonotic disease emergence.

In addition to spatial distributions of animal hosts and human disease, the concept of 'disease risk' is a topic of intense analysis, and has been quantified on the basis of hindsight where regions undergoing frequent or intense human disease events are categorized as possessing numerous factors that interact to increase disease risk.

[1]Cary Institute of Ecosystem Studies, Box AB Millbrook, NY 12545, USA
[2]Odum School of Ecology, University of Georgia, 140 East Green Street, Athens, GA 30602, USA
[3]Center for the Ecology of Infectious Diseases, University of Georgia, Athens, GA 30602, USA

*Correspondence: hanb@caryinstitute.org (B.A. Han).

either by novel pathogens or known pathogens in novel places, remains one of the biggest scientific challenges of our time. We agree that this is a difficult problem, but disagree that it is impossible. This causes us to ask, what types of data are available that may facilitate more effective prediction?

Because most human infectious diseases have animal origins [2,3,11,12], and the majority of emerging human diseases originate from mammals [13,14], better understanding the global distributions of mammal **zoonotic hosts** could provide a first-order prediction of future hotspots for zoonotic disease emergence. Recognizing that a parasite or pathogen is unlikely to persist in all populations of its definitive host(s), we think of the collective geographic ranges of known host species as the maximum potential current geographic range of a zoonosis. Visualizing this potential range offers a baseline from which we can ask basic comparative questions about realized and unrealized risk of zoonotic diseases, and offers a launch point for building predictive models of future zoonotic disease events.

We review here what is known about the geographical distribution of zoonoses carried by wild mammals [15]. We describe global biogeographic patterns of zoonotic hosts across all 27 orders of terrestrial mammals (as confirmed at the species level by the Global Infectious Disease and Epidemiology Network, GIDEON, database [16]), which provides real-time updates of infectious diseases of zoonotic relevance to humans and reports animal hosts to the species level. For zoonotic hosts in each of the six most speciose mammal groups, we review the geographic ranges recorded by the International Union for the Conservation of Nature (www.iucnredlist.org/technical-documents/spatial-data), and address five outstanding research questions about mammal-borne zoonoses.

What Causes High Zoonotic Disease Risk?

Human zoonotic disease risk can be defined as a function of several factors, including the probability of successful transmission of a zoonotic pathogen from an animal host into human hosts (transmission of infection) and the probability of an infection transitioning to a state of disease in human hosts (transition to disease) [17,18]. These components of disease risk rely on several factors that are external to the host–pathogen system. Extrinsic factors, such as urbanization, agriculture, and socioeconomic standing, control host and human population dynamics underlying the frequency of transmissible contacts at the human–wildlife and the wildlife–livestock interfaces [5,17,19–21]. Intrinsic factors (of hosts, pathogens, and vectors) combine with extrinsic factors to contribute to disease risk in humans. Intrinsic factors include life history [22–24], behavior [25,26], **competence** [27–29], and rapid evolutionary changes in animal hosts and pathogens [30–32]; transmission modes and **host breadth** in pathogens [13,33,34]; and differences in host susceptibility, often conferred by prosperity or poverty in human populations [35], and by pristine or degraded communities in wildlife hosts [36]. Thus, regions can have high zoonotic risk for multiple reasons – people living in regions with inherently high **zoonotic potential** may be considered at high risk, but so too can those living in regions with low host and pathogen diversity but increasing external pressures (such as warming or urbanization) that may facilitate the transmission of some zoonoses through a cascade of environmental changes [20,37–39].

Notwithstanding these complexities, areas that are currently experiencing zoonotic outbreaks are places where a high zoonotic risk has been realized as observable disease events. Investigating the features shared in common among regions with high **realized disease risk** (in the form of recurring or new observed outbreaks) is a first step to understanding what triggers these events (e.g., [2,4,5,40]). However, comparing regions with high realized disease risk offers limited utility for forecasting unexpected disease events, which requires quantifying **unrealized disease risk**. Disruptive extrinsic pressures in regions of high zoonotic potential where host or

Glossary

Competence: the degree to which a host can successfully transmit a pathogen to its vector.
Disease event: a general term referring to a collection of human disease cases, including the emergence of novel zoonoses or resurgence of known zoonoses over any temporal or spatial extent.
Disease hotspots: regions where infectious diseases should increase in incidence or geographic range, or regions most likely to generate novel disease events.
Emerging infectious disease (EID): any infectious disease that is increasing in incidence or geographic range.
Host breadth: the range of host species that a given pathogen is able to successfully infect, also commonly referred to as the host range of a pathogen or parasite.
Outbreak: defined by a group of epidemiologically connected disease cases that exceed historical incidence; generally used in this article to refer to the emergence of a zoonotic disease over a relatively short period of time.
Realized disease risk: the component of the overall risk of zoonotic disease in humans that is apparent from current and ongoing disease in human populations.
Reporting bias: bias that arises from infection or disease cases being reported more frequently due to greater resource allocation; thus reporting bias can be high in rich countries.
Richness: the number of unique species within a particular geographic area; richness is a count-based metric for quantifying diversity, which contrasts with other metrics, such as functional trait diversity (the different types of traits represented within a geographic area) or genetic diversity.
Spillover: occurs when a pathogen or parasite successfully infects a human host.
Study bias: bias that can arise when particular organisms (e.g., hosts and pathogens) or geographic areas are better studied than others.
Unrealized disease risk: the component of overall zoonotic disease risk in humans that is not yet apparent, and comprises underlying zoonotic potential (see below); intrinsic features of the host,