Zoonoses 2

Drivers, dynamics, and control of emerging vector-borne zoonotic diseases

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This is the second in a **Series** of three papers about zoonoses

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Emerging vector-borne diseases are an important issue in global health. Many vector-borne pathogens have appeared in new regions in the past two decades, while many endemic diseases have increased in incidence. Although introductions and emergence of endemic pathogens are often considered to be distinct processes, many endemic pathogens are actually spreading at a local scale coincident with habitat change. We draw attention to key differences between dynamics and disease burden that result from increased pathogen transmission after habitat change and after introduction into new regions. Local emergence is commonly driven by changes in human factors as much as by enhanced enzootic cycles, whereas pathogen invasion results from anthropogenic trade and travel where and when conditions (eg, hosts, vectors, and climate) are suitable for a pathogen. Once a pathogen is established, ecological factors related to vector characteristics can shape the evolutionary selective pressure and result in increased use of people as transmission hosts. We describe challenges inherent in the control of vector-borne zoonotic diseases and some emerging non-traditional strategies that could be effective in the long term.

Introduction

In the past three decades, many vector-borne pathogens (VBPs) have emerged, creating new challenges for public health.[1] Some are exotic pathogens that have been introduced into new regions, and others are endemic species that have greatly increased in incidence or have started to infect local human populations for the first time. Here, we review the drivers of these processes. Of particular interest are zoonoses that are maintained by transmission in wildlife but also affect people who have been bitten by infected vectors. Additionally, we draw from lessons learned from diseases that now use only people as transmission hosts, such as malaria and dengue.

Clinicians have an important role alongside disease ecologists and epidemiologists in the study of the causes of an outbreak and minimisation of the burden of disease, because the effectiveness of control is improved by rapid identification.[2,3] In many cases, clinicians are on the first line of detection of these epidemics because clusters of patients present with novel sets of symptoms; evidence of new outbreaks then has to be passed to public health agencies for appropriate management. New high-throughput technologies for detection and identification of novel genetic material in samples taken from patients can greatly aid this process.[4,5] Additionally, data obtained via mobile phones and online social networks checked against expert assessment of plausibility offer the potential to detect changes in spatial and

Key messages

- Many vector-borne zoonotic diseases have emerged in the past three decades
- Emergence in new regions is caused primarily by pathogen movement due to trade and travel, whereas local emergence is driven by a combination of environmental changes that affect vectors and wildlife hosts and social changes (eg, poverty and conflict) that affect human exposure to vectors
- Pathogens introduced into novel regions often cause explosive epidemics followed by declining incidence, whereas pathogens that emerge locally because of land-use or social changes usually show consistent increases
- Vector-borne diseases are highly sensitive to climate, but the past and future effects of climate change on vector-borne disease will probably be less than will those of changes in land use and social factors
- Land use and increasing human populations exert selective pressure on vector-borne pathogens to be able to infect and be transmitted by people and vectors associated with human development
- Control of vector-borne zoonotic diseases needs combined efforts by clinicians and public health officials to treat patients and promote behaviour likely to minimise risk of infection, and by disease ecologists, urban planners, and medical entomologists to advise on development, restoration of ecological communities, and vector control to reverse the ecological drivers of transmission

Search strategy and selection criteria

We searched PubMed and ISI Web of Knowledge with the terms "emerging infectio*", "vector-borne diseas*", "zoonos*" or names of specific vector-borne infections, in combination with "control", "exotic", "climate change", "socio-econom*", "land use", or "evolution" for reports published in any language before July, 2012. Searches were done at all stages, from the initial drafting of the paper to submission of the revised and final version. We also relied on our own familiarity with the scientific literature. We largely selected reports from the past 6 years, but did not exclude older publications that were informative and useful. We also searched the reference lists of reports identified by our searches and selected those that we judged to be relevant. Reviews and book chapters are cited to provide readers with comprehensive sources of references, but primary research is also included where possible within the space allowed. Our reference list was modified on the basis of comments from peer reviewers.

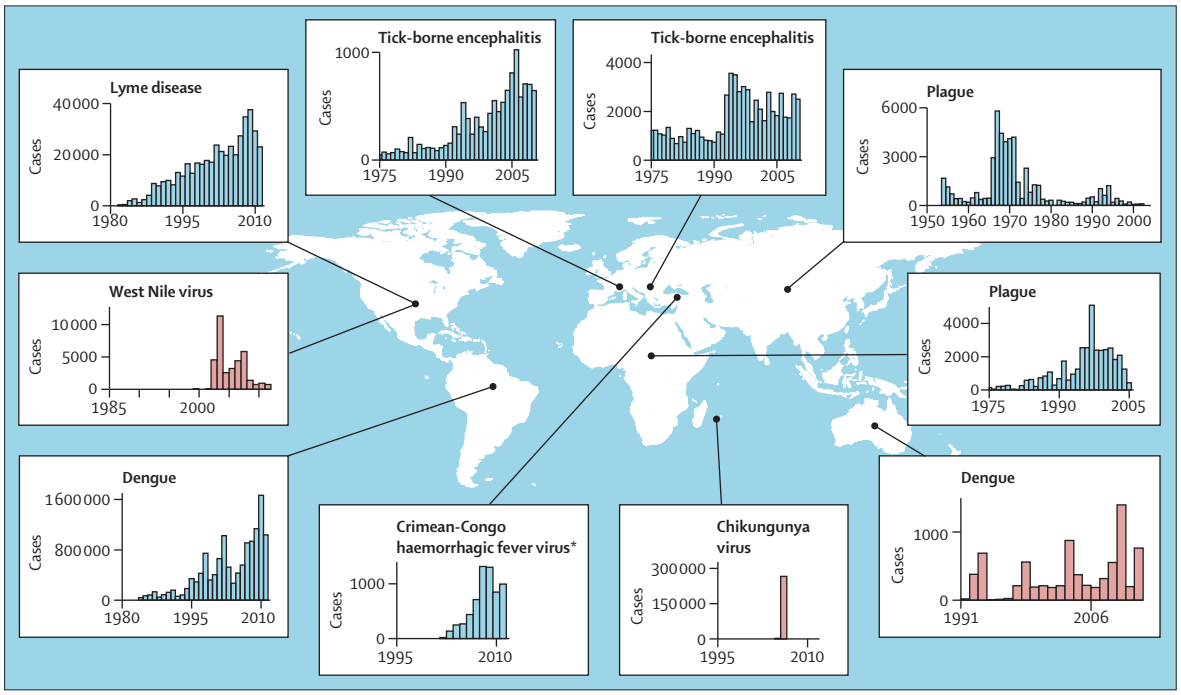

Figure 1: **Temporal patterns of reported cases for selected introduced vector-borne pathogens (red) and endemic or long-established diseases (blue)**
Introduced pathogens can cause notable epidemics followed by a decreased incidence (eg, West Nile virus in the USA[7] and chikungunya virus in Réunion[8]), or sporadic epidemics from repeated introductions and local transmission (dengue in Australia[9]). The incidence of some endemic or long-established zoonotic vector-borne diseases has increased greatly in the past several decades (Lyme disease in North America,[10] plague in Africa,[11] and dengue in South America[12]), but could show different trajectories (plague in Africa *vs* plague in Asia[11]), even in neighbouring regions (tick-borne encephalitis in eastern [ex-communist] and western [historically free market] Europe) because of socioeconomic differences. *Crimean-Congo haemorrhagic fever virus is shown as endemic to Turkey because there is evidence of its presence there many years before its appearance in people.

temporal patterns of illness in real time so that new epidemics can be detected early.[6]

West Nile virus and chikungunya virus are among the best understood zoonotic VBPs to have emerged in the past two decades and show just how explosive epidemics can be in new regions (figure 1). In 1999, the New York City Department of Health (NY, USA) reported a cluster of patients with meningoencephalitis associated with muscle weakness; epidemiological evidence suggested that an arbovirus (ie, a virus transmitted by arthropod vectors) was a probable cause.[13] Clinicians and veterinarians collaborated to identify the aetiological agent as West Nile virus, but unfortunately identification and initial control efforts did not prevent the virus spreading from the east to the west coast of North America within 4 years,[7,14] causing national epidemics in 2002 and 2003.

Similarly, on the Indian Ocean island of Réunion in 2005, hundreds of patients had painful and disabling polyarthralgia, and a subset presented with neurological signs or fulminant hepatitis.[15] A second wave of such symptoms in 2006 exceeded all expectations, eventually affecting more than a third of the entire population of 770 000 people.[15] The causative agent was identified as chikungunya virus, which is also causing continuing epidemics in India, with several million cases so far.[15–17] Other introductions of VBPs have caused smaller outbreaks but have been important in the expansion of the range of human populations at risk. For example, dengue virus has spread to Hawaii,[18] Zika virus to the Micronesian island of Yap,[19] and chikungunya virus to Europe.[20] Whether the outbreak of chikungunya in Europe died out naturally because of the arrival of the temperate autumn or was interrupted by mosquito control efforts is unclear.

These past experiences—together with increases in the known drivers of pathogen introduction—suggest that future introductions are likely (table). A key challenge arises from the non-specificity and similarity of symptoms caused by many of these viruses, especially Zika virus, dengue, and chikungunya virus that all present with acute fever similar to many diseases endemic in the tropics, such as malaria.[12,19] This difficulty makes rapid identification methods[22] and high-quality laboratory-based diagnoses necessary for accurate surveillance and appropriate treatment. Recent advances in identification of unknown pathogens with deep sequencing and microarrays should enable rapid identification of novel or introduced pathogens.[23] A key need is to develop diagnostics for point-of-care use for infection and exposure to allow for proper assessments of case fatality ratios and disease burden.

The emergence of endemic VBPs is usually thought to be a qualitatively different process from the arrival of

	Regions at risk	Endemic region	Pathways for introduction*
Japanese encephalitis virus	Americas	Asia	Infected livestock
Rift Valley fever virus	Americas, southern Europe	Africa, Asia	Infected livestock
Venezuelan equine encephalitis virus	Europe, Asia, Africa	Americas	Infected livestock
Chikungunya virus	Europe, Americas, Australia	Africa, Asia	Infected people
Mayaro virus	Africa, Asia, Europe	South America	Infected people
Zika virus	Europe, Americas	Africa, Asia	Infected people
Crimean-Congo haemorrhagic fever	North Africa, east Asia, central and western Europe	Africa, Asia, Europe	Infected livestock
Dengue virus	Southern Europe	Southern hemisphere	Infected people
West Nile virus	Central Europe, Turkey	Africa, Asia, Europe, Australia	Migratory or dispersing birds
Sindbis virus	Northern Europe	Africa, Asia, Australia	Migratory or dispersing birds

*Infected mosquitoes transported via aeroplanes are a potential pathway for all these pathogens (except Crimean-Congo haemorrhagic fever which is tick borne) in addition to pathways listed.[21]

Table: **Important pathogen threats for introduction into new regions and range extensions within endemic regions, and probable sources and pathways for introduction**

exotic ones, but in some cases increases in incidence of endemic VBPs result more from spread into new areas than increases in local transmission. A combination of local spread and an increase in transmission potential in situ is also possible. Lyme disease is perhaps the best understood example of a mixed emergence. Reported cases (and estimated illnesses) have roughly tripled since 1990 in the USA (figure 1), appeared increasingly in Canada,[24] and apparently increased by between two and ten times in various parts of Europe where diagnosis and reporting are more variable. Evidence for the importance of local invasion in the USA comes from counties in the states of Wisconsin and Virginia, where Lyme cases have only been reported in the past decade and few if any cases occurred previously.[10] By contrast, in the state of Connecticut—where the first cases of Lyme were detected 30 years ago—incidence of the disease has hardly risen in the past decade.[10]

In Europe and Eurasia, the substantial rise in cases of Lyme disease and other tick-borne diseases, including babesiosis, ehrlichiosis, and rickettsiosis, and tick-borne encephalitis, is due as much or more to upsurges within pre-existing ranges of the vector ticks (principally *Ixodes ricinus* and *Ixodes persulcatus*) as to the establishment of enzootic cycles in new places. Zoonotic VBPs with other types of vectors also represent an important and growing threat in some places, such as those that cause Chagas disease, plague, and leishmaniasis.[25] Strong evidence suggests that ecological and human factors have had important roles in establishment of the differential patterns of increased incidence of all these diseases, while increasing awareness and testing by clinicians has contributed to improved reporting of cases.

Differences in the drivers of emergence of exotic and endemic VBPs have important implications for their subsequent dynamics, where they will emerge, and the efforts that can be made to control or eliminate them. We consider each of these aspects in turn, illustrated by some of the more notable examples across the globe. We argue that viewing emerging endemic pathogens as invading at a local scale can be used to take a prospective approach to prevention and control.

Emergence of exotic versus endemic pathogens

Arrival of exotic pathogens

The main driver of pathogen introductions in the past five decades—the accelerating increase in trade and travel—is well known. What is less discussed is that four centuries of trade and travel set the stage for many present pathogen introductions. In the 17th to 19th centuries, shipping traffic resulted in the transport of larvae of several important mosquito species, such as *Aedes aegypti* (a vector of dengue, yellow fever, chikungunya virus, and others), *Culex pipiens* (a vector of West Nile virus) and *Culex quinquefasciatus* (a vector of West Nile virus and filariasis).[26–28]

Some pathogens (eg, *Plasmodium vivax*) were introduced to new continents and became established coincident with or shortly after these early vector introductions because they cause chronic infections in people that are still infectious after weeks or months of travel.[29] Other pathogens that have only short periods of infectiousness in people, including yellow fever virus and dengue virus, could also reach distant regions centuries ago because pathogen transmission cycles could occur aboard ships in which vectors were present and could reproduce.[28]

The growth in air travel enabling global transit in a single day (figure 2) has accelerated introductions because it has allowed many pathogens that cause acute infectiousness (eg, chikungunya and West Nile viruses) to reach other continents within the few days that hosts are infectious, and even during the latent period for some diseases.[21] Several of these pathogens were also aided by the 20th century introductions of another key vector, *Aedes albopictus*.[31,32] Thus, the most recent wave of pathogen introductions, and those likely to occur in the near future, take place against the backdrop of centuries of vector introductions that enable establishment.

A key result of an already well established vector population and a highly suitable environment (including hosts and climate) is that many introduced pathogens cause explosive epidemics in which a large fraction of the population at risk is infected in the first few years after introduction (figure 1). High vector populations (relative to host abundance) result in a high basic reproduction number (R_0) of the pathogen, and if the host population is immunologically naive to the introduced pathogen, as is usually the case, then the effective pathogen reproduction number (R_{eff}) is close to the maximum R_0. This high R_{eff} leads to another common pattern, which is that the intense and rapid initial spread of a novel pathogen is frequently followed by a substantial decrease in case

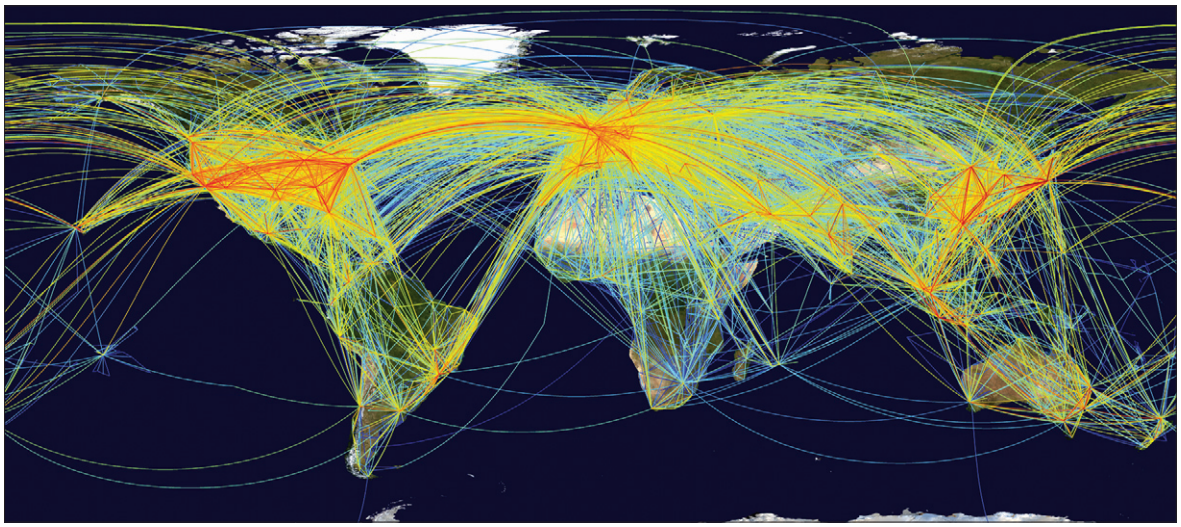

Figure 2: **The global aviation network**
Lines show direct links between airports, and the colour indicates passenger capacity in people per day (thousands [red]; hundreds [yellow]; tens [blue]). Routes linking regions at similar latitudes (in the northern or southern hemisphere) represent pathways that pathogens can move along to reach novel regions. Notably, air traffic to most places in Africa, regions of South America, and parts of central Asia is low. If travel increases in these regions, additional introductions of vector-borne pathogens are probable. Adapted from Hufnagal and colleagues.[30]

burden shortly after introduction, especially on a local scale, as the fraction of the population that is immune to infection rises.[14] This pattern both contrasts with, and has similarities to, the emergence of endemic diseases.

Emergence of endemic pathogens

Emergence of endemic VBPs is frequently associated with changes in land use[33] or socioeconomic conditions,[34] and these transitions control the dynamics of disease emergence. For pathogens affected by land-use change, the rise in case numbers is often gradual (figure 1), paralleling changes in the pathogen's abiotic and biotic environment. By contrast, the increased incidence of endemic disease driven by changes in socioeconomic conditions can be abrupt if the shift is rapid, such as that caused by political upheavals, military conflicts, or natural disasters (figure 1).

Changes in land use affect VBPs by altering the interactions and abundance of wildlife and domestic hosts, vectors, and people, with some diseases better understood than are others.[33] In the Amazon and east Africa, deforestation increases standing water and sunlight and enhances the breeding success of some mosquito species, which can increase risk of malaria. Further increases in urbanisation frequently eliminate anopheline mosquito habitat and have reduced malaria elsewhere.[35] In northeastern North America, reforestation during the 20th century is thought to have allowed recolonisation by deer and the consequent expansion of the range of ticks (*Ixodes scapularis*), underpinning the emergence of Lyme disease in the mid-20th century.[36] Deer (*Odocoileus virginianus* in the USA and *Capreolus capreolus* in Europe) have a key role in feeding adult *Ixodes* ticks, although they are actually incompetent hosts for the Lyme disease bacterial spirochaetes. Additionally, in the past three decades, fragmentation of forests in eastern regions of Canada and the USA and changes in predator communities[37] have altered the host community for ticks and the Lyme bacterium *Borrelia burgdorferi*, and might have increased relative abundance of small mammals (white-footed mice [*Peromyscus leucopus*], eastern chipmunks [*Tamias striatus*], and shrews [*Sorex* spp and *Blarina brevicauda*]) that are the principal transmission hosts for Lyme disease spirochaetes. These changes in the host community can result in increased spirochaete infection prevalence in nymphal ticks.[38] A key remaining question is how fragmentation and hunting-induced changes in the host community affect the abundance of infected nymphal ticks, which is the key metric for disease risk.

Changes in land use might also be responsible for recent emergent foci of Crimean-Congo haemorrhagic fever virus within its large range through parts of Africa, Asia, southeastern Europe, and the Middle East. By contrast with typical sporadic outbreaks of only a few cases, an exceptional epidemic occurred in Turkey, starting with about 20 cases in 2002, and rising to nearly 1400 cases by 2008 (figure 1). Most infections occurred in agricultural and animal husbandry workers via tick bites and direct contamination from infected animals. Changes in land cover associated with political unrest and reduced agricultural activities might have allowed colonisation by wildlife and subsequent tick population growth, as is thought to have precipitated the first recorded epidemic of Crimean-Congo haemorrhagic fever in Crimea in 1944–45.[39] The case fatality rate (5%) in Turkey has been

much lower than is usually observed (20–30%),[39,40] creating some uncertainty about the cause of this epidemic. This uncertainty emphasises the need for accurate and systematic diagnosis through effective point-of-care methods.

Increases in incidence can also result from changes in socioeconomic and human activities, such as expansion into risky new habitats for exploitation or dwelling, or land-cover change, such as reforestation of previously agricultural areas.[36,41–43] Human infection with VBPs increases with the product of entomological risk (the abundance of infected vectors) and exposure of people to vectors, which can change independently and sometimes synergistically. For example, the incidence of dengue is higher on the Mexican side of the Mexico–Texas border than on the other,[44] where open windows compensate for the absence of air-conditioning but expose people to mosquito biting.

Exposure to ticks, paradoxically, might be higher in people of high and low income than in those with intermediate income (figure 3). Incidence of Lyme disease in parts of Europe has been shown to be higher in people with high income living in new homes in broad-leaf woodlands where wildlife co-occur, including rodents and birds that serve as reservoirs for spirochaetes and ticks.[45] Generally, outdoor recreational opportunities associated with wealth can result in increased exposure to vectors. Conversely, hardship precipitated by population displacements due to civil conflict, loss of protective housing through natural disasters, or use of natural environmental resources driven by economic transitions can lead to increased contact between people and vectors.[34,46] A clear example comes from a large upsurge of tick-borne encephalitis in 2009, immediately after the economic downturn in three eastern European countries that already had high background poverty and where foods are harvested from forests for subsistence and commerce.[47] Human activities resulting in exposure to VBPs is sometimes reflected in different seasonal patterns, such as cases of tick-borne encephalitis in different parts of Europe (figure 4). In eastern Europe, the timing of cases matches the season of forest food harvest more closely than the seasonal pattern of tick abundance, while in western Europe the earlier peak of cases coincides with summer recreational activity.

Poverty and wealth, however, probably affect final disease outcomes asymmetrically, because economic duress restricts the potential for ameliorative actions (eg, limiting of outdoor activities, protection from vector bites, or costly vaccination in the case of tick-borne encephalitis). This hypothesis could partly explain the difference between a large upsurge (two to 30 times) in reported tick-borne encephalitis cases in the early 1990s in central and eastern Europe after the fall of Soviet rule and a gradual and steady increase in western Europe (figure 1).[34] Political and civil unrest that commonly occur with armed conflict could also account for the sudden re-emergence of plague in Vietnam in the late 1960s and in Madagascar and Mozambique at the end of the 1980s.[48] Failure of public health services and overcrowded, unsanitary living conditions increased human contact with flea-bearing rodents and decreased routine surveillance, allowing rapid emergence with no warning. These examples of social strife enabling new epidemics of vector-borne diseases will probably recur, and awareness and investment in public health infrastructure can help to reduce their effect.

Understanding of the mechanistic processes linking land use and socioeconomic conditions with disease enables prediction of future trends and control or mitigation. Economic and public health assistance could be targeted towards populations at high disease risk because of social strife caused by conflict or natural disasters, and urban planning could be used to minimise the use of risky habitat by people for living and recreation. Unfortunately, although correlations exist between land use and disease incidence or measures of risk, rigorous and mechanistic analyses that identify causal factors that are needed for intelligent urban planning are absent in most cases. For example, in the USA, specific types of land use (agriculture and urbanisation) are associated with a higher incidence of West Nile virus in people at the county scale, but the mechanism underlying this pattern is unknown.[14,49] This gap in our knowledge makes it difficult to anticipate and avoid future epidemics associated with rapid urbanisation and land-use change.

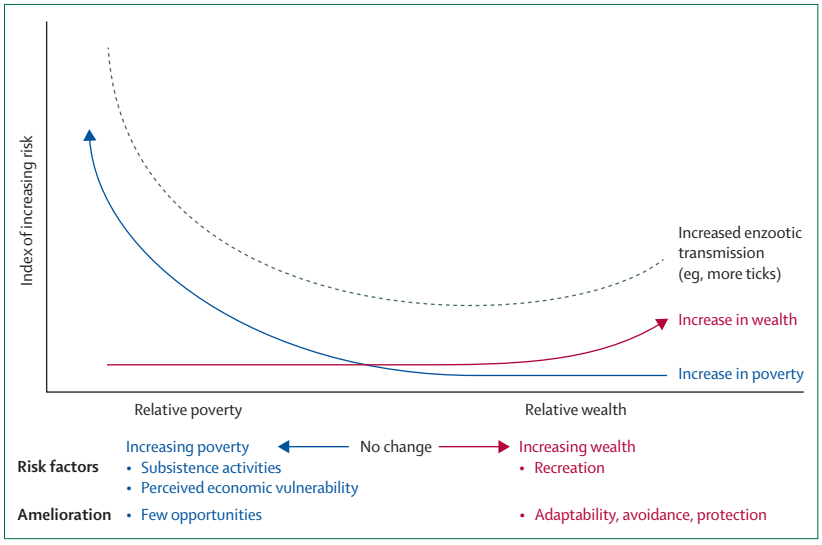

Figure 3: **Interactions between economic status and disease risk**
Interactions are particularly applicable where contact with infectious agents is largely due to human activities outdoors, such as tick-borne diseases. Human activities take place against a backdrop of variable inherent risk from zoonotic vector-borne pathogens, which is measured as the density of host-seeking infected vectors such that the overall risk curve can rise or fall.

Climate change and vector-borne diseases

Although several components of vector-borne disease systems (principally the vector and the pathogen) are highly sensitive to climate, evidence shows that climate change has been less important in the recent emergence of

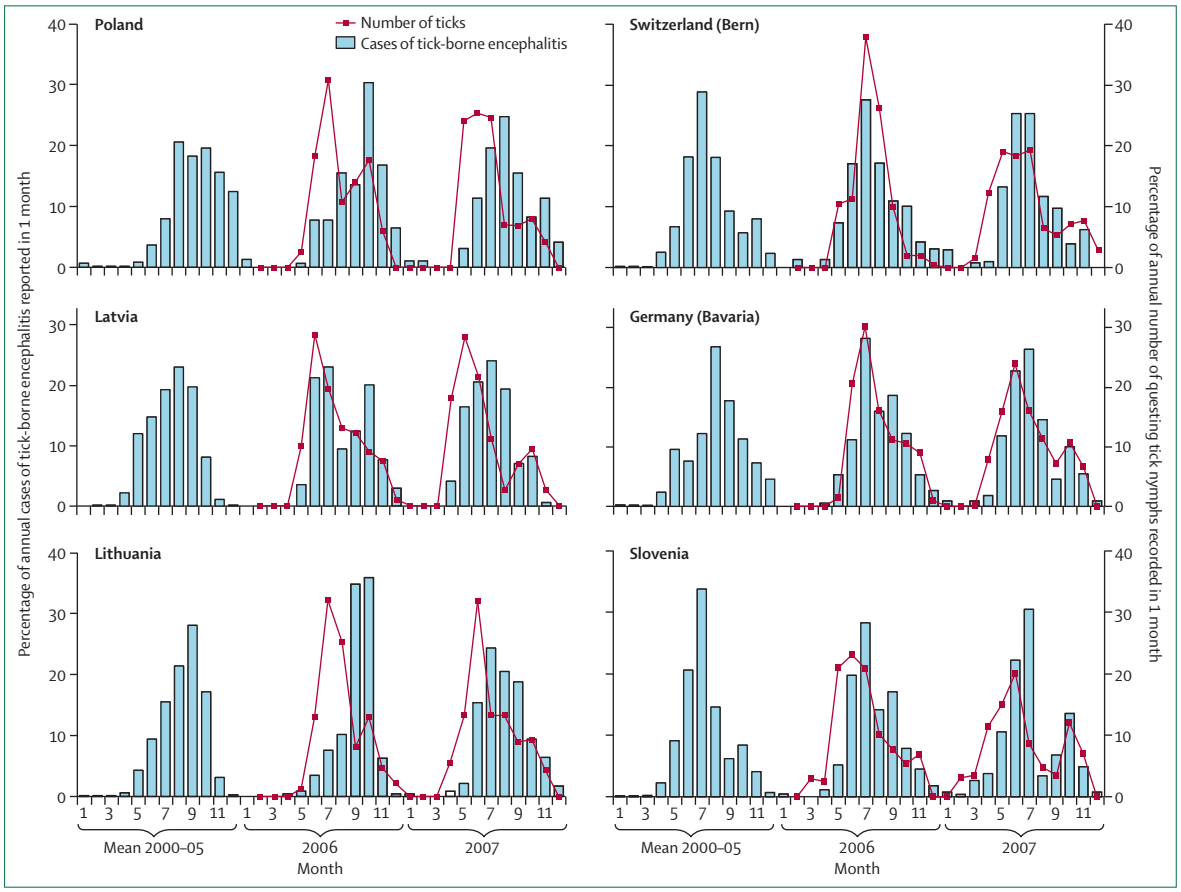

Figure 4: **Seasonal patterns of tick-borne encephalitis cases and abundance of questing nymphal ticks (*Ixodes ricinus*)**
The data for ticks are lagged by 1 month to account for the interval between a tick bite and diagnosis of tick-borne encephalitis.

vector-borne diseases than have changes in land use, animal host communities, human living conditions, and societal factors, probably because of countering influences of climate (panel). An exception seems to be the increased transmission of VBPs with warming along the cold latitudinal and altitudinal edges of their present distribution. The differential effect of climate at the edge and core of a pathogen's distribution stems partly from the non-linear relation between the fraction of the population exposed in an epidemic and transmission potential (which can be quantified as R_0). Specifically, initial increases in R_0 to more than one (ie, allowing pathogen spread to create an epidemic) lead to large rises in case burden, but further increases in R_0 have diminishing effects, especially for pathogens with sterilising immunity. Expansions in the distribution of a disease might have disproportionate effects on public health if the newly exposed populations have little immunity. Examples of VBP range expansions along cold edges are dengue virus in Texas, USA,[59] Lyme disease in Canada,[24] and tick-borne encephalitis at increasing altitude in Slovakia.[60]

In core transmission areas, not only are the effects of climate change less important than other factors, but warming might even decrease transmission if decreases in vector survival overwhelm other factors (panel).[61] An analysis of several decades of severe malaria incidence (the best studied disease with respect to climate change) at five locations spanning a range of elevations in western Kenya identified initial rises in incidence followed by two decades of decreases at two locations and increases with high variability in three others.[62] These mixed patterns challenge expectations that continuing climate change will lead to increased malaria and suggest that changes in transmission potential of malaria and other VBPs are primarily driven instead by a mix of factors such as demographic shifts, land-use change, interventions (eg, bednets), drug resistance, and climate. The relative contributions of each factor can be rigorously assessed only by careful comparisons of the same pathogen over time and with valid accurate baseline data, which were lacking in a previous study.[63]

Evolution of vector-borne pathogens

One underappreciated aspect of growing human populations, global land-use change, and the introduction of human commensal vectors is the selective pressure

exerted on pathogens, causing them to evolve to take advantage of new environments, including hosts and vectors. Both West Nile virus and chikungunya evolved rapidly (a feature typical of viruses and especially RNA viruses[64]) after being introduced to new locations and encountering new anthropophilic vectors. The original genotype of West Nile virus (NY99) was replaced by another (WN02)[65] that differs by three consensus nucleotide changes and exhibits increased transmission efficiency in *C pipiens* and *Culex tarsalis* mosquitoes.[66,67] Similarly, on Réunion between 2005 and 2006, one nucleotide change occurred in chikungunya virus that increased infection in the recently introduced mosquito species *Aedes albopictus*.[68] The same genetic change appeared independently in viruses isolated from Réunion, west Africa, and Italy, but was not identified in mosquitoes from India at the start of the continuing epidemics there in 2006.[69] When *A albopictus* rather than *A aegypti* became the main vector in India from 2007, however, the same genetic substitution spread rapidly and subsequent substitutions seem to be enabling even more efficient virus circulation and persistence, which could presage further expansion of the chikungunya virus.[68]

More generally, the transmission of many VBPs is less efficient when the vector feeds on several hosts, only some of which can be infected by the pathogen.[70] It is no coincidence that the dominant human VBPs malaria and dengue are transmitted most intensely where they are vectored by mosquitoes that feed almost entirely on people. What has been less appreciated is the selective pressure imposed on zoonotic pathogens (especially those for which people are still a dead-end host) to adapt to be efficiently transmitted by human specialist vectors like *Anopheles gambiae, A aegypti*, and, to a slightly lesser extent, *A albopictus* (which sometimes feeds on non-human mammals and birds) where people are highly abundant. As the abundance of human commensal vectors increases with urbanisation and deforestation, so do the opportunities for strictly human transmission of pathogens.

Control of VBPs

Novel introductions and increases in incidence of endemic VBPs draw attention to the need for effective control and treatment of individuals with associated diseases. A key challenge in the attempt to control many VBPs is that they are zoonotic and transmission intensity in vectors is driven primarily by wildlife reservoirs. As a result, the dominant method used to control directly transmitted pathogens—vaccines—protects only individuals with financial and logistical access and has no effect on underlying transmission intensity. Thus, natural or vaccine-acquired herd immunity has no protective effect in people, and exposure is governed primarily by contact with vectors.

Control of zoonoses in wildlife is difficult at best, and eradication is often impossible.[42] Vaccines for wildlife hosts—in development for West Nile virus[71] and field tested at a small scale for Lyme borreliosis[72]—offer some reasons for optimism, but substantial work remains

Panel: Climate change and vector-borne disease

It is now well established in the scientific community that climate change has played and will play a mixed and minor part in the emergence of most vector-borne pathogens (VBPs) and diseases generally.[50,51] Nonetheless, a persistent stream of reviews are published that claim that climate change is a primary driving force. These reviews stem from two semi-independent assumptions that have developed in the past decade: first, that climate change will lead to more widespread and more abundant VBPs as more of the planet starts to closely resemble the tropics where VBPs are presently most abundant; and second, that the arrival of exotic and upsurges of endemic VBPs are due to climate changes. Both these assumptions originate from plausible arguments, because the natural distribution and intensity of VBPs are indeed highly sensitive to climate.[9] They were partly inspired by repeated publications of highly influential and visually arresting maps at the end of the 20th century that presented predictions of expanding malaria derived from mathematical models. Problematically, these models were not parameterised with data for key variables (eg, vector abundance).[52] The belief that warming will intensify VBPs is reinforced by speculative reports that describe the general coincidence of increased disease incidence with warming in recent decades.[53,54] Spatiotemporal analyses of variation in long trends suggest that in many cases climate has not consistently changed in the right way, at the right time, and in the right places to account for the recorded epidemiology of emergent VBPs.[55]

The effects of climate on transmission are several, non-linear, and act in opposing directions. Thus, prediction of the overall effect of climate and climate change on vector-borne disease systems needs a complete understanding and parameterisation of VBP models.[56,57] Specifically, higher temperatures increase three aspects of transmission for vector-borne pathogens: vector biting rate, vector development rate, and pathogen replication (thereby reducing the extrinsic incubation period or the time between a vector feeding on an infected host and being able to transmit the pathogen). However, they frequently decrease a fourth, vector survival, especially when associated with moisture stress. As a result, increased temperatures might lead to increases or decreases in transmission depending on the relative effects of these factors.[57] A key challenge is that biological models frequently have difficulty accurately predicting changes in vector abundance, which is the most variable factor in the transmission potential of VBPs.

The best science clearly suggests that effects of climate change on VBPs will be variable, as would be expected from all such complex systems.[58] Thus, although continuing climate change could increase transmission or distributions of some VBPs in the future, for most diseases other factors will be more important and, crucially, be manageable with public health initiatives (eg, drug treatment, vaccines, and bednets). These factors include changes in the biotic elements of the environment (eg, wildlife hosts), drug resistance, reduced health service provision, and political and socioeconomic factors that change human exposure and susceptibility to infections.

Governments and public health agencies want predictions of the disease burden and risk in the future. To obtain such predictions, a robust understanding of how all aspects of climate affect rates of the processes involved in transmission needs to be developed,[57] and the breadth of analyses should be expanded to include all potential factors affecting incidence of infection and prevalence of disease, both biological and non-biological. Predictions will necessitate truly cross-disciplinary collaborations, marrying biologists' pursuit of improved models of vector abundance, infection prevalence, and pathogen evolution (eg, drug resistance) with understanding from medical and social scientists about developments in treatment and interventions, land-use change, and human societal factors. Such cooperation would further our knowledge, which is presently based on assumptions about what global warming will do, to a more evidence-based set of predictions.

before they can be deployed as effective instruments on a large scale. Additionally, for vector-borne pathogens, transmission is thought to be frequency dependent, such that culling of livestock or wildlife that decreases host abundance (short of eradication) might increase transmission. Vectors are likely to seek out, feed on, and infect the hosts that remain after culling efforts, and the remaining hosts will subsequently be fed on by a greater number of susceptible vectors per host than they were before culling.[73] Control of frequency-dependent pathogens by culling would thus be expected to result in short but intensified epizootics that could lead to additional human infections, with the exact public burden depending in part on patterns of vector feeding on people and other hosts.[70,74]

Another control strategy used for VBPs, active or passive use of animals to divert vector feeding away from people to protect them against infection (so-called zooprophylaxis[75]), has had mixed effects. Feeding on additional alternative hosts sometimes results in increased vector densities, which could result in higher transmission even if a smaller proportion feed on people.[76,77] A more recent incarnation of this basic idea—termed the dilution effect—postulates that naturally occurring biodiversity could, in some instances, also divert vectors from infectious hosts.[78] As with empirical attempts of zooprophylaxis, the effects of biodiversity, or, more accurately, variable host community assemblages, are not uniform with respect to risk of infection, because of the complexity of interactions between hosts, vectors, and pathogens.[79,80] The more direct strategy of vector control targeted at larval mosquitoes (including elimination of larval habitat) has been more effective than has zooprophylaxis and has even resulted in local eradication of a disease.[81] Additionally, new techniques to develop vectors resistant to pathogens by infecting them with naturally occurring intracellular insect parasites (eg, *Wolbachia*) offer some promise.[82]

In many cases, the most effective long-term public health strategies will combine efforts by clinicians and public health officials to treat and alter the behaviour of patients to avoid infection with actions by others to reverse the ecological drivers of transmission. Behavioural change is especially important at the leading edge of invading endemic or exotic pathogens where personal protective behaviours are often absent. Reversal of ecological drivers of disease emergence necessitates identification of the causes of increases in incidence and subsequent targeting with appropriate control measures, which needs integration between researchers, public health agencies, the government, and the public. For example, risk related to specific types of land use could be ameliorated by urban planning and management of host and vector communities through landscaping, hunting, or restoration of ecological communities.

Similarly, increases in incidence related to socioeconomic changes could be reduced with prudent development and assistance after disasters and social upheaval.[83] The vaccination campaign against tick-borne encephalitis, for example, targeted children in Latvia in response to the massive upsurge in incidence in the early 1990s. This campaign, together with a reduction in high-risk activities in tick-infested forests (presumably as a result of enhanced awareness), effectively reduced the mean national incidence by 74% by 1999, with the greatest reductions in counties where incidence was previously highest.[84] Even modest changes in societal structure and socioeconomic development can increase exposure to zoonoses; an awareness of changing risk would allow communication of appropriate warnings to alert unsuspecting members of the public. Prevention of the introduction of foreign pathogens is far more difficult than is control of endemic VBPs because it is an inevitable result of the globalisation of trade and travel. History suggests that successful control needs prompt identification, swift action, and occasionally draconian social measures.

Conclusions

VBPs impose an important global burden on public health, including widespread human diseases that were formerly zoonotic, such as malaria and dengue, as well as zoonotic diseases for which people are dead-end hosts, such as Lyme disease, West Nile virus, and Crimean-Congo haemorrhagic fever. Widespread land-use change, globalisation of trade and travel, and social upheaval are driving the emergence of zoonotic VBPs, including along local invasion fronts. Recognition that a large fraction of the public health burden of both endemic and exotic VBPs comes from infection at the invading front would enable prospective action to address the ecological and sociological drivers of transmission. Financial and technological hurdles persist in developing countries, making diagnosis and control difficult where the diseases are stubbornly most prevalent. Inadequate knowledge prevents populations in developed countries from taking actions that would minimise the diseases' effects. Development projects that address disease can help to overcome these challenges, and clinicians and public health professionals can play important parts in the reduction of the burden of vector-borne disease.

Contributors

AMK and SER conceived the ideas and wrote the report.

Conflicts of interest

We declare that we have no conflicts of interest.

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