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

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Abstract

Emerging vector-borne diseases represent an important issue for global health. Many vector-borne pathogens have appeared in new regions in the past two decades, and many endemic diseases have increased in incidence. Although introductions and local emergence are frequently considered distinct processes, many emerging endemic pathogens are in fact invading at a local scale coincident with habitat change. We highlight key differences in the dynamics and disease burden that result from increased pathogen transmission following habitat change compared with the introduction of pathogens to new regions. Truly *in situ* 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 and suitable conditions for a pathogen, including hosts, vectors, and climate. Once established, ecological factors related to vector characteristics shape the evolutionary selective pressure on pathogens that may result in increased use of humans as transmission hosts. We describe challenges inherent in the control of vector-borne zoonotic diseases and some emerging non-traditional strategies that may be more effective in the long term.

Introduction

Over the past three decades vector-borne pathogens (VBPs) have been on the move, creating new challenges for public health (Fig. 1).¹ Some are exotic pathogens that have been introduced into new regions, and others are endemic species that have shown large increases 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 infect humans bitten by vectors. We also draw from lessons learned from diseases that now use only humans as transmission hosts such as malaria and dengue.

Clinicians have a vital role to play, alongside disease ecologists and epidemiologists, in studying the causes of an outbreak and minimizing the burden of disease because the efficacy of control is improved by rapid identification.^{2, 3} In many cases, clinicians are on the first line of detection of these epidemics as clusters of patients present with novel sets of symptoms and this evidence of new outbreaks must be passed to public health agencies for appropriate management. New high-throughput technologies for detection and identification

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of novel genetic material in samples taken from patients can significantly aid this process.^{4, 5} In addition, data obtained via mobile phones and online social networks, checked against expert assessment of plausibility, offers the potential for detecting changes in spatial and temporal patterns of illness in real time such that new epidemics may be detected early.⁶

West Nile virus (WNV) and Chikungunya virus (CHIKV) are among the best-understood zoonotic VBPs to have emerged in the last two decades and show just how explosive epidemics can be in new regions (Fig. 1). In 1999, the New York City Department of Health reported a cluster of patients with meningoencephalitis associated with muscle weakness and epidemiological evidence suggested that an arbovirus was a likely cause.⁷ Clinicians and veterinarians collaborated to identify the aetiological agent as WNV, but identification and initial control efforts, unfortunately, did not prevent the virus spreading from the east to the west coast of North America within four years, and causing significant national epidemics in 2002 and 2003. Similarly, in 2005 in the Indian Ocean island of La Réunion there was an epidemic of hundreds of patients with a painful and disabling polyarthralgia, and a subset presented with neurological signs or fulminant hepatitis.⁸ The second wave of the epidemic in 2006 exceeded all expectations, eventually infecting over a third of the entire population of 770,000 people. The causative agent was identified as CHIKV, which is also causing on-going epidemics in India with several million cases to date.^{8–10} Other introductions of VBPs have caused smaller outbreaks but have been significant in expanding the range of human populations at risk, including dengue virus to Hawaii,¹¹ Zika virus (ZIKV) to the Micronesian island of Yap,¹² and CHIKV to Europe.¹³ In the case of CHIKV it is not clear whether the outbreak died out naturally due to the arrival of the temperate autumn or was interrupted by mosquito control efforts.

These past experiences, together with increases in the known drivers of pathogen introduction that we describe below, suggest that future introductions are likely. Zoonotic VBPs that are likely to be introduced into new regions include Rift Valley Fever and Japanese Encephalitis viruses (JEV) in the Americas, Venezuelan equine encephalitis virus in Eurasia or Africa, Crimean-Congo Haemorrhagic Fever virus (CCHFV) in new parts of Eurasia, and others (Table 1).¹ A key challenge arises from the non-specificity and similarity of symptoms caused by many of these viruses, especially ZIKV, dengue and CHIKV that all present with acute fever similar to many diseases endemic in the tropics such as malaria.^{12, 14} This makes rapid identification tools¹⁵ and high quality laboratory-based diagnoses necessary for accurate surveillance and appropriate therapy. Recent advances in identifying unknown pathogens using deep sequencing and microarrays should enable more rapid identification of novel or introduced pathogens.¹⁶ A key need is to develop diagnostics for point-of-care use for both 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 exotic VBPs, but in some cases increases in incidence 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, and Lyme disease is perhaps the best understood example of a mixed emergence. Reported cases (and estimated illnesses) have approximately tripled since 1990 in North America (Fig. 1), appeared increasingly in Canada,¹⁷ and apparently increased 2- to 10-fold in various parts of Europe where diagnosis and reporting are less certain. Evidence for the importance of local invasion comes from the states of Wisconsin and Virginia where Lyme cases have appeared recently in counties where few if any cases occurred previously, while in the state of Connecticut, where the first cases of Lyme were detected 3 decades ago, there is little upward trend in incidence in the last decade (<http://www.cdc.gov/lyme/stats/index.html>). In contrast, in Europe and Eurasia, the significant rise in cases of Lyme disease and other tick-borne

diseases, including babesiosis, ehrlichiosis, and rickettsiosis, and tick-borne encephalitis (TBE), is due as much or more to upsurges within pre-existing ranges of the vector ticks, principally *Ixodes ricinus* and *I. persulcatus* as to the establishment of enzootic cycles in new places. Zoonotic VBPs with other types of vectors that also represent an important and growing threat in some places include those that cause Chagas disease, plague, and leishmaniasis.¹⁸ Strong evidence suggests that ecological and human factors have played significant roles in determining the differential patterns of increased incidence of all these diseases, while increasing awareness and testing by clinicians has contributed to better reporting of cases.

Emergence of exotic versus endemic pathogens

Differences in the drivers of emergence of exotic and endemic VBPs have important implications for their subsequent dynamics, where they are likely to 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 (Fig. 1). We argue that viewing emerging endemic pathogens as invading pathogens at a local scale can be used to take a prospective approach to prevention and control.

Arrival of exotic pathogens

The main driver of recent pathogen introductions, the accelerating increase in trade and travel over the past five decades, is well known. What is less discussed is that four centuries of trade and travel set the stage for many current pathogen introductions. In the 17th to 19th centuries shipping traffic resulted in the introduction of several important mosquito species by transporting larvae alongside traded goods, including *Aedes aegypti* (a vector of dengue, yellow fever, CHIKV and others), *Culex pipiens* (a vector of WNV) and *Cx. quinquefasciatus* (a vector of WNV, and filariasis).^{19–21} Some pathogens, such as *Plasmodium vivax* malaria, were introduced to new continents and became established coincident with or shortly after these early vector introductions because they cause chronic infections of humans such that humans were still infectious after weeks or months of travel.²² Other pathogens that have only short periods of infectiousness in humans, including yellow fever virus and some dengue virus strains, were also able to reach distant regions centuries ago because pathogen transmission cycles often occur aboard ships where vectors are present and can reproduce.²¹ The recent growth in air travel enabling global transit in a single day (Fig. 2) has accelerated pathogen introductions because it has allowed many more pathogens that cause acute infectiousness, including many subtypes of dengue virus, CHIKV, and WNV, to reach other continents within the few days that hosts are infectious, and even during the latent period for some diseases.²³ Several of these pathogens were also aided by the 20th century introductions of another key vector, *Ae. albopictus*.^{24, 25} 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 facilitate establishment.

A key consequence of having 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 very large fraction of the population at risk is infected in the first few years after introduction (Fig. 1). High vector populations (relative to host abundance) result in a high basic reproductive ratio or R_0 of the pathogen, and if the population is immunologically naïve to the introduced pathogen, as is usually the case, then the effective pathogen reproductive ratio, R_{eff} , is close to the maximum, R_0 . This 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 burden shortly after introduction, especially on a local scale.²⁶ This both contrasts with, and has similarities to, the emergence of endemic diseases.

Emergence of endemic pathogens

The emergence of endemic VBPs is frequently associated with changes in land use²⁷ or socio-economic conditions, and this determines the dynamics of disease emergence. For endemic pathogens driven by land use change, the rise in case numbers frequently shows a gradual increase (Fig. 1) paralleling changes in the pathogen's abiotic and biotic environment. In contrast, the rate of increase in incidence for endemic disease emergence driven by changes in socio-economic conditions can be much more abrupt if the rate of change in socio-economic conditions is rapid, such as that caused by political upheavals, military conflicts or natural disasters.

Changes in land use influence VBPs by altering the interactions and abundance of wildlife and domestic hosts, vectors, and humans with some overall impacts being clearer than others.²⁷ In the Amazon and East Africa, increased standing water and sunlight as a result of deforestation enhance the breeding success of some mosquito species, which may increase the risk of malaria, whereas further increases in urbanization frequently eliminate Anopheline mosquito habitat and have reduced malaria elsewhere.²⁸ In northeastern North America reforestation during the 20th century is thought to have permitted re-colonization by deer and the consequent expansion of the range of ticks (*Ixodes scapularis*), underpinning the emergence of Lyme disease in the mid-20th century.²⁹ Deer (*Odocoileus virginianus* in the USA, and *Capreolus capreolus* in Europe) serve a key role in feeding adult *Ixodes* ticks, although they are actually incompetent hosts for the Lyme disease bacterial spirochetes. In addition, more recent fragmentation of forests in eastern North America and changes in predator communities³⁰ has altered the host community for ticks and the Lyme bacteria, *Borrelia burgdorferi* and may have resulted in greater 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 spirochetes. These changes in the host community may result in a higher spirochete infection prevalence in nymphal ticks.³¹ A key remaining question is to determine how fragmentation and hunting-induced changes to the host community affect the abundance of infected nymphal ticks, which is the key metric for disease risk.

Changes in land use may also be responsible for recent emergent foci of CCHF within its extensive range through parts of Africa, Asia, southeastern Europe and the Middle East. In contrast to typical sporadic outbreaks consisting 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 (Fig. 1). The majority of infections occurred amongst agricultural and animal husbandry workers via tick bites and direct contamination from infected animals. It has been hypothesized that changes in land cover associated with political unrest and reduced agricultural activities permitted colonization by wildlife with consequent tick population growth, as is thought to have precipitated the first recorded CCHF epidemic in Crimea in 1944–45.³² Interestingly, the case fatality rate (5%) in Turkey has been much lower than is usually observed (30–50%), creating some uncertainty as to the cause of this epidemic. This uncertainty highlights the need for accurate and systematic diagnosis through effective point-of-care diagnostic tools.

Increases in incidence can also result from changes in socio-economic 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.^{29, 33–35} Human infection with VBPs increases with the product of entomological risk (the abundance of infected vectors) and exposure of humans to vectors, which can change independently, and sometimes synergistically. Exposure to ticks, paradoxically, may be higher in wealthy and poor people than those with intermediate financial standing (Fig. 3). Incidence of Lyme disease in parts of Europe has been shown to be higher amongst wealthy people living in new homes within

broad-leaf woodlands where wildlife, including rodents and birds that serve as reservoirs for spirochetes, and ticks co-occur.³⁶ More generally, greater outdoor recreational opportunities associated with increased 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 greater use of the natural environmental resources driven by economic transitions can lead to greater contact between humans and vectors.^{37, 38} A clear example comes from a significant upsurge of TBE in 2009 immediately following the economic downturn in three eastern European countries already suffering high levels of background poverty and where foods are harvested from forests for subsistence and commerce.³⁹

Human activities resulting in exposure to VBPs is sometimes reflected in different seasonal patterns, such as cases of TBE in different parts of Europe (Fig. 4). In eastern Europe, the relatively later 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 the peak in summer recreational activity. More simply, the incidence of dengue, for example, is higher on the poorer Mexican side of the Mexico-Texas border,⁴⁰ where open windows compensate for the absence of air-conditioning but expose people to high mosquito biting.

The effects of poverty and wealth, however, are likely to be asymmetrical in determining final disease outcomes (Fig. 3) because economic duress limits the potential for ameliorative actions (e.g., limiting outdoor activities, protection from vector bites, or costly vaccination in the case of TBE, etc). This hypothesis may partly explain the difference between a marked upsurge (2- to 30-fold) in reported TBE cases in the early 1990s in central and eastern Europe after the fall of Soviet rule and a more gradual and steady increase in western Europe (Fig. 1).³⁸ Political and civil unrest that commonly occur with armed conflict may 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.⁴¹ Failure of public health services and over-crowded 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 facilitating new epidemics of vector-borne diseases are likely to occur again and awareness can help in reducing their impact.

Understanding the mechanistic processes linking land use and socio-economic conditions to disease facilitates prediction of future trends and control or mitigation. Economic aid could be targeted towards populations at high disease risk from recent social strife caused by conflict or natural disasters, and urban planning could be used to minimize the overlap and use of risky habitat by humans. Unfortunately, in many cases, while correlations exist between land use and disease incidence or some measure of risk, rigorous and mechanistic analyses linking increases in incidence to land use needed for intelligent urban planning are lacking. For example, in North America certain types of land use (agriculture and urbanization) are linked with higher WNV incidence in humans at the county scale, but the mechanism underlying this pattern is unknown.^{26, 42} This gap in our knowledge makes it difficult to anticipate and avoid future epidemics associated with rapid urbanization and land use change.

Climate change and vector-borne disease systems

Although several components of vector-borne disease systems (the vector and the pathogen) are highly sensitive to climate, evidence shows that climate change has been less important in the recent emergence of vector-borne diseases than changes in land use, human living conditions, and societal factors, likely to be a result of countering influences (Box 1). An exception to this appears to be the increased transmission of VBPs with warming along the

cold latitudinal and altitudinal edges of their current distribution. The differential influence of climate at the edge and core of a pathogen's distribution stems in part from the nonlinear relationship between the fraction of the human population exposed and transmission intensity; the latter can be quantified as R_0 , the pathogen reproductive ratio. Specifically, initial increases in R_0 above the critical value of 1 for an epidemic (i.e. allowing pathogen spread) lead to large increases in case burden, but beyond that, increases in R_0 have diminishing impacts, especially for pathogens with sterilizing immunity. It should be noted that expansions in the distribution of a disease may have disproportionate impacts on public health if newly exposed populations there have little immunity. Examples of VBP range expansions at cooler edges include dengue virus in Texas,⁴³ Lyme disease in Canada,¹⁷ and TBE at increasing altitude in Slovakia.⁴⁴

Box 1

Climate change and vector-borne disease: the need to resolve the controversy and confusion

Although it is now well established in the scientific community that climate change has played and will play a mixed and relatively minor role in the emergence of most VBPs and diseases in general,^{68, 69} there is nonetheless a persistent stream of review articles that claim that climate change is a significant driving force for the emergence of VBPs. These reviews stem from two semi-independent assumptions that have grown up over the past decade: a) that climate change will lead to more widespread and more abundant VBPs as more of the planet more closely resembles the tropics where VBPs are currently most abundant; b) that the observed recent arrival of exotic, and upsurges of endemic, VBPs are due to climate changes to date. Both of these assumptions originate in plausible general biological arguments, as the natural distribution and intensity of VBPs are indeed highly sensitive to climate.⁷⁷ They were partly inspired by repeated publications of highly influential and visually arresting maps at the end of the 20th century that presented predictions from mathematical models that were not parameterized with data for key variables (e.g. vector abundance).⁷⁰ Belief is bolstered by speculative papers that describe the general coincidence of increased disease incidence with warming over recent decades.^{71, 72} Spatio-temporal analyses of variation around long-trends suggests 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 observed epidemiology of emergent VBPs.⁷³

The effects of climate on transmission are multiple, non-linear, and act in opposing directions. Thus, predicting the overall impact of climate and climate change on vector-borne disease systems requires a complete understanding and parameterization of VBP models.^{74, 75} Specifically, higher temperatures increase three aspects of transmission for vector-borne pathogens, vector biting rate, vector development rate, 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), but frequently decrease a fourth, vector survival, especially when associated with moisture stress. As a result, increased temperatures may lead to increases or decreases in transmission depending on the relative impacts of these factors.⁷⁷ A key challenge is that biological models frequently have difficulty accurately predicting changes in vector abundance, the most variable factor in the transmission potential of VBPs.

The best science clearly indicates that climate change impacts on VBPs will be variable, as one would expect from all such complex systems.⁷⁶ Thus, while continuing climate change may increase transmission or distributions of some VBPs in the future, other factors will frequently play a more significant role and, importantly, be more tractable to public health initiatives. These include changes in the biotic elements of the environment

(e.g. wildlife hosts), drug resistance, reduced health service provision, and political and socio-economic 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 do so, we must develop a more robust understanding of how all aspects of climate influence the rates of the processes involved in transmission,⁷⁴ and also expand the breadth of analyses to include all the potential factors influencing incidence of infection and prevalence of disease, both biological and non-biological. Predictions will require truly cross-disciplinary collaborations, marrying biologists' pursuit of better models of vector abundance, infection prevalence and pathogen evolution (e.g. drug resistance) with understanding from medical and social scientists about developments in treatment and interventions, land use change, and human societal factors. Doing so would move our knowledge from its current state, based on assumptions about what global warming will do, to a more evidence-based set of predictions.

In core transmission areas, not only are the effects of climate change minor compared with other factors, but warming may even decrease transmission if decreases in vector survival through heat and moisture stress overwhelm other influences.⁴⁵ A recent analysis of several decades of severe malaria incidence (the most well studied disease with respect to climate change) at five locations spanning a range of elevations in western Kenya revealed initial increases in incidence followed by two decades of declines at two locations and increases with higher variability in three others.⁴⁶ These mixed patterns challenge simple expectations that ongoing climate change will lead to increased malaria and suggest that changes in malaria and other VBP transmission potential are driven instead by a mix of factors including demographic shifts, land use change, interventions (e.g., bed nets), drug resistance, and climate. The relative contributions of each factor can only be rigorously assessed by careful comparisons of the same pathogen over time and with valid accurate baseline data, in contrast to a recent study.⁴⁷

There are likely to be many more emerging zoonotic VBPs in the near future and it is critical that assessment of the causes of emergence focus more on changing land use and socioeconomic factors and public health measures (e.g. drug treatment, vaccines, bed nets) that determine human exposure than on climate driven changes in enzootic potential.

Evolution of vector-borne pathogens

One under-appreciated aspect of increased 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 the new environments, including hosts and vectors. Both WNV and CHIKV evolved rapidly (a feature typical of viruses and especially of RNA viruses⁴⁸) after being introduced to new locations and encountering new anthropophilic vectors. Specifically, the originally introduced genotype of WNV (NY99) was replaced by another genotype (WN02)⁴⁹ that differs by three consensus nucleotide changes and exhibits increased transmission efficiency in *Culex pipiens* and *Cx. tarsalis* mosquitoes.^{50, 51} Similarly, on La Réunion a single nucleotide change occurred in CHIKV between 2005 and 2006 that increased infection in the recently introduced mosquito species, *Ae. albopictus*.⁵² The same genetic change appeared independently in viruses isolated from La Réunion, West Africa and Italy, but was not identified in mosquitoes from India in 2006 at the start of the ongoing epidemics there.⁵³ When *Ae. albopictus* rather than *Ae. aegypti* became the main vector in India from 2007, however, the same genetic substitution spread rapidly and subsequent substitutions appear to be facilitating even more efficient virus circulation and persistence, which may presage further expansion of CHIKV ranges.⁵²

More generally, the transmission of many VBPs is relatively inefficient when the vector feeds on a range of hosts, only some of which are infectious for the pathogen.⁵⁴ 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 humans. What has been less appreciated is the selective pressure currently imposed on zoonotic pathogens (i.e. those for which humans are still a dead end host) to adapt to being transmitted efficiently amongst abundant humans by human specialist vectors like *Anopheles gambiae*, *Ae. aegypti* and, to slightly lesser extent, *Ae. albopictus*, which sometimes feeds on non-human mammals and birds. As the abundance of human commensal vectors increases with urbanization and deforestation, the opportunities for strictly human transmission of pathogens increase.

Control of vector-borne pathogens

Novel introductions and increases in incidence of endemic VBPs (Fig. 1) highlight the need for effective control and treatment of individuals suffering from associated diseases. A key challenge in attempting to control many VBPs is that they are zoonotic and transmission intensity is driven primarily by wildlife reservoirs. As a result, the dominant tool used against directly transmitted pathogens, vaccines, only protects those with financial and logistical access to the vaccine, and has no impact on underlying transmission intensity. Thus, there is no protective effect of natural or vaccine acquired “herd immunity” in humans, and exposure of people is governed primarily by their contact with vectors.

Managing or treating zoonoses of wildlife is difficult at best, and eradication is nearly impossible.³⁴ Vaccines for wildlife hosts, in development for WNV,⁵⁵ and field tested at a small scale for Lyme borreliosis,⁵⁶ offer some reason for optimism, but substantial work remains before they can be deployed as an effective tool on a large scale. In addition, for insect-borne pathogens, transmission is thought to be frequency-dependent, such that livestock or wildlife culling that decreases host abundance (short of eradication) may actually increase transmission. This is because vectors are likely to seek out, feed on, and infect the hosts that remain following culling efforts, and the remaining hosts will subsequently also be fed on by a greater number of susceptible vectors per host.⁵⁷ Control of frequency-dependent pathogens by culling would thus be expected to result in short but intensified epizootics that may result in additional human infections, with the exact public burden depending in part on patterns of vector feeding on humans and other hosts.^{54, 58}

Active or passive use of animals to divert vector feeding away from humans to protect them against infection, so-called zooprophylaxis,⁵⁹ has met with mixed effects because feeding on additional alternative hosts sometimes results in increased vector densities which may result in higher transmission even if a smaller proportion feed on humans.^{60, 61} A more recent incarnation of this basic idea, termed the “dilution effect”, hypothesizes that naturally occurring biodiversity may, in some instances, play the same role.⁶² 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, due to the complexity of host-vector-pathogen interactions.^{63, 64} A more direct strategy, vector control targeted at larval mosquitoes (including elimination of larval habitat), can sometimes be more effective and has even resulted in the local eradication of a disease.⁶⁵ In addition, recent techniques to develop vectors resistant to pathogens by infecting them with naturally occurring intracellular insect parasites (e.g., *Wolbachia*) offer some promise.⁶⁶

In many cases the most effective public health strategies in the long term will combine efforts by clinicians and public health officials to treat and alter the behavior of patients to avoid infection with actions by others to reverse the ecological drivers of transmission. The

former is especially important at the leading edge of invading endemic or exotic pathogens where personal protective behaviors are often absent. Reversing ecological drivers of disease emergence requires identifying the causes of increases in incidence and targeting them with appropriate control measures, which requires integration between researchers, public health agencies, the government and the public. For example, risk related to specific types of land-use may be ameliorated by urban planning and by management of host and vector communities through landscaping, hunting, or restoration of ecological communities. Similarly, increases in incidence related to socio-economic changes may be reduced by prudent development and assistance following disasters and social upheaval. The vaccination campaign against TBE, for example, targeted at children in Latvia in response to the massive upsurge in incidence there in the early 1990s, 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% from 1999, with the greatest reductions seen in counties where incidence was previously highest.⁶⁷ Even modest changes in societal structure and socio-economic 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 because this is commonly an inevitable consequence of the globalization of trade and travel. History suggests that successful control requires prompt identification, swift action, and occasionally draconian social measures.

Conclusions

Vector-borne diseases currently impose an important global burden on public health, including widespread formerly zoonotic human diseases, such as malaria and dengue fever, as well as zoonotic diseases for which humans are dead end hosts, such as Lyme disease, WNV, and CCHF. Extensive land use change, the globalization of trade and travel, and social upheaval are driving the emergence of zoonotic VBPs including along local invasion fronts. Recognizing that a large fraction of the public health burden of both endemic and exotic VBPs comes from infection at the invading front enables prospective action to address both the ecological and sociological drivers of transmission. Financial and technological hurdles persist in developing countries, making diagnosis and control difficult where these diseases are stubbornly most prevalent, and limited knowledge hinders populations in developed countries from taking actions that would minimize their impact. Development projects that address disease can help in overcoming the above challenges and can combine with clinicians and public health professionals to play important roles in reducing the burden of vector-borne disease.

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Fig. 1.

Temporal patterns of reported cases (in thousands) for selected introduced vector-borne pathogens (red) and emerging endemic diseases (blue) on six continents. Introduced pathogens may cause striking epidemics followed by lower incidence (WNV in North America (<http://www.cdc.gov/ncidod/dvbid/westnile/index.htm>), CHIKV in Réunion⁷⁷), sporadic epidemics from repeated introductions and local transmission (dengue in Australia⁷⁸), or establishment and increased case burden (dengue in S. America¹⁴, <http://new.paho.org>). The incidence of some endemic zoonotic vector-borne diseases has increased markedly in the past several decades (Lyme disease in North America, <http://www.cdc.gov/lyme/stats/index.html>, plague in Africa⁷⁹), but may show different trajectories (plague in Africa vs. plague in Asia⁷⁹), even in neighboring regions (TBE in eastern (ex-communist) and western (historically free market) Europe) because of socioeconomic differences. CCHF is shown as endemic to Turkey because there is evidence of its presence there many years before its recent appearance in humans.

Fig. 2.

The global aviation network. Lines show direct links between airports, and the colour ramp indicates passenger capacity in persons per day (red = thousands; yellow = hundreds; blue = tens). Routes linking regions at similar latitudes (in the Northern or Southern hemisphere) represent pathways that pathogens are likely to move along to reach novel regions. Note the lack of high volume air traffic to most places in Africa, regions of South America, and parts of central Asia. If travel increases in these regions additional introductions of VBPs are likely. Adapted from ⁸⁰ with permission.

Fig. 3.

Interactions between economic status and disease risk, particularly applicable where contact with infectious agents is due largely to human activities outdoors, such as tick-borne diseases. Increased poverty increases reliance on subsistence activities that sometimes occur in vector-infested habitats. Increased income may be associated with increased recreation (especially in Europe and North America) that may also expose individuals to vectors of disease but also allow increased access to public health. Human activities take place against a backdrop of variable inherent risk from zoonotic vector-borne pathogens, measured as the density of host-seeking infected vectors such that the overall risk curve may rise or fall.

Fig. 4.

Seasonal patterns of tick-borne encephalitis (TBE) cases (columns) relative to abundance of questing nymphal ticks (*Ixodes ricinus*) (lines). The data for ticks are lagged by one month to account for the interval between a tick bite and diagnosis of TBE. In eastern European countries (Poland, Latvia and Lithuania), more TBE cases occur from late summer onwards, after the peak of tick activity, whereas in western Europe (Switzerland, Germany and Slovenia), TBE cases peak in mid summer. This is likely to reflect different principal purposes for human visits to forested tick habitats, either for collecting forest foods (more pronounced in eastern Europe) or for recreation.

Table 1

Significant pathogen threats for introduction into new regions and range extensions within known endemic regions, current endemic regions, and the likely source and pathways for introduction.

Pathogen	Regions at risk	Endemic Region	Pathways for introduction *
Japanese encephalitis virus	Americas	Asia	Infected livestock
Rift Valley Fever Virus	Americas, Mediterranean Europe	Africa, Asia	Infected livestock
Venezuelan equine encephalitis virus	Europe, Asia, Africa	Americas	Infected livestock
Chikungunya virus	Europe, Americas, Australia	Africa, Asia	Infected human
Mayaro virus	Africa, Asia, Europe	South America	Infected human?
Zika virus	Europe, Americas	Africa, Asia	Infected human
Crimean-Congo Haemorrhagic Fever	North Africa, Far East Asia, Central/ Western Europe	Africa, Asia, Europe	Infected livestock
Dengue virus	Southern Europe	Southern hemisphere	Infected humans
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 airplanes represent a potential pathway for all of these pathogens (except Crimean-Congo Haemorrhagic Fever which is tick-borne) in addition to those pathways listed.²³