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. 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. 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. 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 temporal patterns earlier.
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 methods22 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
Table: Important pathogen threats for introduction into new regions and range extensions within endemic regions, and probable sources and pathways for introduction

<table>
<thead>
<tr>
<th>Pathways for introduction*</th>
<th>Regions at risk</th>
<th>Endemic region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected livestock</td>
<td>Americas</td>
<td>Asia</td>
</tr>
<tr>
<td>Infected livestock</td>
<td>Americas, southern Europe</td>
<td>Africa, Asia</td>
</tr>
<tr>
<td>Infected livestock</td>
<td>Europe, Asia, Africa</td>
<td>Americas</td>
</tr>
<tr>
<td>Infected people</td>
<td>Europe, Americas, Australia</td>
<td>Africa, Asia</td>
</tr>
<tr>
<td>Infected people</td>
<td>Africa, Asia, Europe</td>
<td>South America</td>
</tr>
<tr>
<td>Infected people</td>
<td>Europe, Americas</td>
<td>Africa, Asia</td>
</tr>
<tr>
<td>Infected livestock</td>
<td>North Africa, east Asia, central and western Europe</td>
<td>Africa, Asia, Europe</td>
</tr>
<tr>
<td>Infected livestock</td>
<td>Southern Europe</td>
<td>Southern hemisphere</td>
</tr>
<tr>
<td>Migratory or dispersing birds</td>
<td>Africa, Asia</td>
<td>Australia</td>
</tr>
<tr>
<td>Migratory or dispersing birds</td>
<td>Northern Europe</td>
<td>Africa, Asia, Australia</td>
</tr>
</tbody>
</table>

*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.*

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. 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.

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 in people, including yellow fever virus and dengue virus, to reach other continents within the few days that hosts are infectious, and even during the latent period for some diseases. Several of these pathogens were also aided by the 20th century introductions of another key vector, *Aedes albopictus*. 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*<sub>b</sub>) of the pathogen, and if the host population is immunologically naïve to the introduced pathogen, as is usually the case, then the effective pathogen reproduction number (*R*<sub>e</sub>) is close to the maximum *R*<sub>b</sub>. This high *R*<sub>e</sub> 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, as the fraction of the population that is immune to infection rises. 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 or socioeconomic conditions, 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. 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. 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. 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 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.

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. The case fatality rate (5%) in Turkey has been
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
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,\textsuperscript{59} Lyme disease in Canada,\textsuperscript{24} and tick-borne encephalitis at increasing altitude in Slovakia.\textsuperscript{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).\textsuperscript{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.\textsuperscript{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.\textsuperscript{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) after being introduced to new locations and encountering new anthrophiophilic vectors. The original genotype of West Nile virus (NY99) was replaced by another (WN02) that differs by three consensus nucleotide changes and exhibits increased transmission efficiency in C. pipiens and Culex tarsalis mosquitoes. 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. 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. 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.

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. 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. Vaccines for wildlife hosts—in development for West Nile virus—and field tested at a small scale for Lyme borreliosis—offer some reasons for optimism, but substantial work remains
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.75 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), 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.36,77 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.76 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.78,79 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.80 Additionally, new techniques to develop vectors resistant to pathogens by infecting them with naturally occurring intracellular insect parasites (eg, Wolbachia) offer some promise.81

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.82 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.83 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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