Invited review

Drivers for the emergence and re-emergence of vector-borne protozoal and bacterial diseases

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Abstract

In recent years, vector-borne parasitic and bacterial diseases have emerged or re-emerged in many geographical regions causing global health and economic problems that involve humans, livestock, companion animals and wild life. The ecology and epidemiology of vector-borne diseases are affected by the interrelations between three major factors comprising the pathogen, the host (human, animal or vector) and the environment. Important drivers for the emergence and spread of vector-borne parasites include habitat changes, alterations in water storage and irrigation habits, atmospheric and climate changes, immunosuppression by HIV, pollution, development of insecticide and drug resistance, globalization and the significant increase in international trade, tourism and travel. War and civil unrest, and governmental or global management failure are also major contributors to the spread of infectious diseases. The improvement of epidemic understanding and planning together with the development of new diagnostic molecular techniques in the last few decades have allowed researchers to better diagnose and trace pathogens, their origin and routes of infection, and to develop preventive public health and intervention programs. Health care workers, physicians, veterinarians and biosecurity officers should play a key role in future prevention of vector-borne diseases. A coordinated global approach for the prevention of vector-borne diseases should be implemented by international organizations and governmental agencies in collaboration with research institutions.
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1. Introduction

Diseases transmitted by arthropod vectors are of major importance to the health of humans and animals globally. A wide number of infectious agents, hosts and vectors are involved with these diseases and their epidemiology. Disease patterns differ from one geographic zone to another, and may change over time due to a plethora of factors. The objective of this review is to evaluate the different causes responsible for the emergence and re-emergence of vector-borne protozoal and bacterial diseases and describe how major drivers affect the patterns of their local and global distributions.

Emerging pathogens include infectious agents that have been described in other regions and imported into areas, where they were previously not known; agents that were constantly present in the affected area on a low level or in a different host and due to some change have become more widely spread in the population under concern; or organisms that were previously not recognized and have been identified and associated with a new disease or an illness with a previously unknown etiology. Accidental importation of disease vectors such as tick species or mosquitoes from one area to another could ultimately be responsible for the spread of diseases to new regions. Conversely, transmission of naive domestic or wildlife animals into an endemic region for disease such as piroplasmosis has resulted countless times in epidemic outbreaks (Caracappa, 1999; Hofle et al., 2004). The advances in molecular biology during the last two decades have led to the discovery of new vector-borne pathogenic organisms. Most of the *Bartonella* species were not known until 10–15 years ago. These arthropod-transmitted bacteria were associated with disease

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syndromes, such as cat scratch disease, bacillary angiomatosis, peliosis hepatis and endocarditis (Breitschwerdt and Kordick, 2000). Lyme disease, the most prevalent vector-borne disease in North America emerged just over 20 years ago as a new disease with a recognized borrelial causative agent (Benach et al., 1983). However, molecular detection of historical specimens indicated that this infection has been circulating in North America and Eurasia for centuries prior to the recognition of the disease as a major pathogen of humans and dogs (Marshall et al., 1994; Matuschka et al., 1996; Hubbard et al., 1998).

Newly described and older ehrlichial organisms have been recently reclassified within the family *Anaplasmataceae* on the basis of phylogenetic analysis of gene sequences (Dumler et al., 2001). The expansion of the *Anaplamataceae* family has included several zoonotic emerging ehrlichial pathogens recognized only in the last two decades. The tick-borne *Ehrlichia ewingii* and *Ehrlichia chaffeensis* were described in humans and dogs in North America (Anderson et al., 1991; Buller et al., 1999). These newly described pathogens appear to be restricted in their geographic spread by the presence of appropriate vector ticks. *Anaplasma phagocytophilum* (previously *Ehrlichia phagocytophilum/Ehrlichia equi*) has a wider known geographic spectrum and is associated with disease in several animal species including dogs, horses, ruminants, and recently also in cats (Bjoersdorff et al., 1999). It emerged in the last decade as a human pathogen in North America, Europe and some parts of Asia, and is frequently associated with the presence of rodent reservoir hosts (Chen et al., 1994; Parola, 2004).

Vector-borne infections transmitted from wildlife reservoir species to domestic animals or humans are of major concern. New pathogens that may jump the species barrier and be transmitted from one host to another are a constant threat to human and animal welfare. *Borrelia burgdorferi*, *Babesia microti* and *A. phagocytophilum* are zoonotic pathogens which are clearly associated with sylvatic cycles of infection involving wild rodents and ticks. These pathogens may be found concomitantly in mammalian hosts or ticks (Krause et al., 2002; Adelson et al., 2004). A less well known tick-transmitted organism which emerged as a pathogen of cats during the 1970s is the piroplasm *Cytauxzoon felis*. It infects bobcats (*Lynx rufus*) asymptomatically in North America, while causing a violent and frequently fatal hemolytic disease when infecting domestic cats (Wagner, 1975; Glenn et al., 1983; Meinkoth et al., 2000).

Re-emerging pathogens are those organisms that have re-appeared in locations from which they have previously disappeared or radically decreased in prevalence. The re-emergence of vector-borne pathogens is often related to changes in the environment, the pathogen, or the host. For instance, the phenomenon of malaria re-emergence is frequently related to changes that affect the spread of the mosquito vectors (Tyagi, 2004), the development of drug-resistant parasites (Sharma, 1996), or human migration (Marques, 1987). The epidemiology of vector-borne diseases is often associated with other events affecting the populations that are exposed to the infectious organisms. Visceral leishmaniasis caused by *Leishmania infantum* in the Mediterranean basin was traditionally predominantly a disease of young children. The name of the causative agent of this disease reflects the predilection to infants. However, immunosuppressed adults are apparently highly susceptible to the development of clinical visceral leishmaniasis. With the spread of HIV into Europe during the last 25 years, a current major risk group for visceral leishmaniasis in southern Europe is HIV-positive people (Desjeux and Alvar, 2003).

Some outbreaks of protozoal vector-borne diseases appear mysterious at this time and require further research for elucidation and basic understanding of their transmission mechanisms, epidemiology and environmental drivers responsible for their emergence. The recent detection of cutaneous leishmaniasis in red kangaroos in Australia's Northern territory is posing a potential threat to humans and animals (Rose et al., 2004). Australia has previously been considered free of endemic *Leishmania* species and also of suitable sand fly vectors for the transmission of leishmaniasis (Stein and Dyce, 2002; Rose et al., 2004). A somewhat comparable puzzling situation is present in the eastern USA, where kennel dogs infected with zoonotic *L. infantum* have been found in several states without known vectors or autochthonous human cases, which are usually present, where active transmission of visceral leishmaniasis occurs (Gaskin et al., 2002; Rosypal et al., 2003). The vector-competence of a local sand fly species is currently being investigated (Ostfeld et al., 2004).

The following sections will discuss the major impacts of vector-borne zoonotic, human and veterinary diseases and the drivers for their emergence and re-emergence. A cause and effect approach will be utilized to analyze the impact of the different drivers on the occurrence and spread of infections responsible for some of the world's most common causes of mortality, such as malaria, or economic losses with diseases leading to human disability or severe livestock production losses (Fig. 1).

2. Major impacts of vector-borne diseases

The costs incurred due to bacterial and protozoal vector-borne infectious diseases are numerous and diverse. They range from economic losses related to production of farm animals to disability and loss of work years and most severely to the loss of human lives. The drivers influencing vector-borne diseases, can therefore, have devastating effects upon the lives of people of every nationality or socioeconomic class.
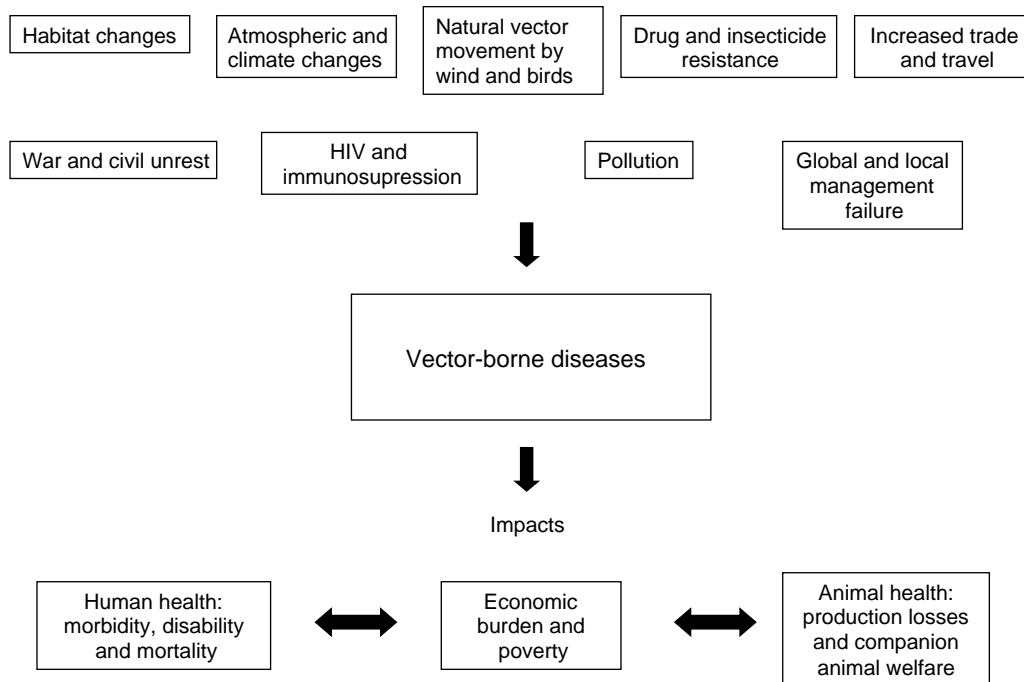
Fig. 1. Major forces associated with the emergence, re-emergence and spread of vector-borne protozoal and bacterial pathogens, and their impacts.

2.1. Human health

Infectious and parasitic diseases are responsible for more than 25% of the global human disease toll (Hoetz et al., 2004). The UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases (TDR) lists 10 priority infections out of which eight are vector-borne (Table 1). These diseases are responsible for a large number of disability adjusted life years (DALYs), a measure of the number of healthy years of life lost due to premature death and disability (WHO, 2002). Malaria is the most deadly of these diseases with a total of 1–3 million malaria annual deaths and 1–5 billion annual febrile episodes in malarious areas (Breman, 2001). The majority of malaria cases occur in sub-Saharan African countries, which are also some of the worlds' poorest countries. The direct costs of malaria include the costs of prevention and treatment, which according to some studies range from 2 to 3% of the household income in these countries (Chima et al., 2003; Russel, 2004). When the direct costs are combined with other direct household illness costs they produce a greater expense. For instance, in Nigeria, the total mean direct cost burden of malaria and other illness amounts to 7% of the household monthly income (Onwujekwe et al., 2000). But, it is the indirect costs of malaria that inflict the most severe economic losses and are responsible for more than 75% of the total household malaria costs in Africa (Russel, 2004). Sick African adults were reported to loose one to five working days per malaria episode (Chima et al., 2003). Similar findings were also reported from other continents. Patients with uncomplicated malaria from Myanmar were

mostly male and head of families. The main financial burden of disease was due to absence from work, equivalent to 4.2 days per capita economic output per episode (Gatton and Cho-Min-Naing, 2004). The addition of disease costs to the household expenses can often push low-income families into further poverty and starvation. A study from Malawi has shown that the average total cost burden for Malaria was 7.2% of the annual income, but for the very poor socioeconomic group it constituted a disastrous 32% (Ettling et al., 1994).

In contrast to the deadly malaria, Lyme disease in the USA is rarely fatal, but it is a widely spread and frequently reported infection. The mean annual incidence of Lyme disease in the USA during 1993–1996 was 4.73 cases per

Table 1

Vector-borne diseases included in the current portfolio of the UNDP/World Bank/WHO special program for research and training in tropical diseases (TDR)

Annual deaths (thousands)	Disease burden in DALYs[a] (thousands)	Disease
1124	42,280	Malaria
0	5644	Lymphatic filariasis
59	2357	Leishmaniasis
15	1760	Schistosomiasis
50	1598	African trypanosomiasis
0	987	Onchocerciasis
21	653	Dengue
13	649	Chagas disease

Information derived from the WHO 2002 World Health Report (WHO, 2002).

[a] DALYs—disability adjusted life years (the number of healthy years of life lost due to premature death and disability).

100,000 population and the expected national expenditure over 5 years for therapeutic interventions to prevent Lyme disease sequelae was estimated to be 2.5 billion dollars (Maes et al., 1998).

Chagas disease (American trypanomiasis) in South and Central America is an infection with a reported decreasing health and economic impacts due to a successful multi-national control program that involved the interruption of vectorial and transfusional transmission (Dias et al., 2002; Moncayo, 2003; Hoetz et al., 2004). In Brazil, $USD 516 million were invested in the Chagas disease control program between 1975 and 1995, of which 78% were spent on vector control. Prevention of 277,000 infections and 85,000 deaths translated into savings of 1,620,000 DALYs, 41% from averted deaths and 59% from disabilities prevented. The control program was reported to be cost-effective with each one dollar spent on vector control resulting in $USD2.01 of savings (Hoetz et al., 2004). Unlike the progress in the control of American trypanomaisis, the reported prevalence of African trypanosomiasis (sleeping sickness) has dramatically increased in several countries in Central Africa during the previous decade (Remme et al., 2002; Stich et al., 2003; Hoetz et al., 2004). The drugs available for treatment of sleeping sickness are only partially effective and may have severe side effects that endanger the patients. Furthermore, reaching the target population for prevention and treatment is difficult because of civil unrest in some of the countries, where infection is most prevalent.

2.2. Animal health and economic burden

Domestic animals serve as companions to humans, a means of transportation or work in many countries and a source of food for a world with a rapidly growing human population (Schillhorn van Veen, 1999; Melendez, 2000). Domesticated animals have been associated with human society for thousands of years, and it is difficult to think of human enterprise throughout history without the contribution of animals. In addition, wild life animals are just as important in maintaining balance in nature and preservation of ecosystems. Vector-borne diseases are extremely harmful to animals and cause severe losses. In the late 1980s, it was estimated that just hemoparasitic diseases of cattle were responsible for annual global economic losses of $USD 7 billion (Duncan Brown, 1997). Losses are not only the result of animal mortality, but also due to morbidity causing a decrease in productivity such as meat production, milk yield or egg laying, and cost of control measures.

Of the estimated 250 million cattle in Central and South America in the early 1990s, approximately 175 million (70%) were in tick infested regions (Montenegro-James, 1992). Tick-borne bovine babesiosis and anaplasmosis were responsible for an economic loss of $USD 875–1365 million/year just in Latin America, the world's largest producer of beef meat (Montenegro-James, 1992; Duncan Brown, 1997). Anaplasmosis is a major pathogen of cattle responsible for heavy losses also in some parts of North America (Morley and Hugh-Jones, 1989).

The production of farm animals in Africa is severely affected by tick and fly-borne bacterial and protozoal pathogens. Tick-transmitted heartwater disease (cowdriosis) was estimated to cause an annual national loss of $USD 5.6 million in Zimbabwe, with the greatest component being the acaricide cost, followed by the milk loss and treatment costs (Mukhebi et al., 1999). However, maintaining enzootic stability for ruminant tick-borne diseases in Zimbabwe with minimal acaricidal control might be more economic than an intensive prevention regimen (Meltzer et al., 1995; Chamboko et al., 1999). A different experience was found in Burkina Faso with prevention of African animal trypanosomiasis in cattle by insecticides against the tsetse vectors of this disease. The prevention effort improved the overall health of cattle and resulted in a resumption of fertility and milk production (Bauer et al., 1999).

3. Major drivers for the emergence and re-emergence of vector-borne protozoal and bacterial organisms

The ecology and epidemiology of vector-borne diseases are affected by the 'disease triangle' comprising three major factors. These include the pathogen, the host (human, animal or vector) and the environment consisting of physical, biological and socioeconomic aspects. The interrelations between these three factors depend on the sensitivity of each factor and the rate of exposure to the other two factors (Sutherst, 2004). In this section, a simplistic approach was carried out to describe the major forces involved in the emergence and re-emergence of vector-borne diseases (Fig. 1), each driver as a single entity. However, it has to be realized that the biological ecosystems are complex and driven by multiple factors simultaneously.

3.1. Habitat change, deforestation and urbanization

Habitat change, in the form of deforestation, extensive land use, agricultural development and alterations in water storage and irrigation habits, provide new niches for vectors (Gubler, 1998; Patz et al., 2000; Sutherst, 2004). Deforestation and transformation of forests to grazing land, agricultural areas, human settlements or open areas, result in significant alterations in the environment and changes in the composition of vectors, and therefore, the introduction of new pathogens (Patz et al., 2000). Upsurges of malaria were co-incident with deforestation and changes in land use in Africa, Asia and Latin America (Patz et al., 2000). Cleared forests are usually more sunlit and prone to the formation of neutral pH puddles, which may favor specific anopheline larvae (Patz et al., 2000). The construction of dams and irrigation canals may be associated with alterations in water acidity and salinity as well as introduction of new vectors

such as snails and mosquitoes, their larvae and their parasites (Patz et al., 2000). For example, the construction of the dam at Diama, Senegal, was aimed at preventing the intrusion of seawater into the river. This resulted in the reduction in salinity and increased water pH, increased fecundity and growth of freshwater snails and introduction of *Schistosoma mansoni* to humans in the lower and middle valleys of the Senegal River Basin (Southgate, 1997). Another example is the spread and establishment of *Anopheles culicifacies* and the emergence of *Plasmodium falciparum* malaria in the Thar Desert in north-western India following the construction of irrigation canals (Tyagi, 2004).

The world is undergoing human population growth and massive urbanization. These processes are associated with displacement of people from rural areas to urban centers, creating new contacts and interactions in the new densely populated environment (Patz et al., 2000). The newcomers are usually more vulnerable to the endemic diseases to which they may not be immune. On the other hand they may introduce new pathogens and vectors to the new environment. Under these conditions, the chances for exchange and transmission of vectors and parasites increase (Patz et al., 2000). Unplanned and uncontrolled urbanization in developing countries usually results in the deterioration of public health infrastructure, sanitation, water, sewage and waste management systems (Sutherst, 2004). In addition, the construction of new roads provides means of vector and host transportation. These alterations produce ideal conditions for the transmission of vector-borne diseases to large populations (Gubler, 1998; Patz et al., 2000).

3.2. Atmospheric and climate changes

Changes in climate and temperatures affect the distribution of vectors and the effectiveness of pathogen transmission by vectors (Gubler et al., 2001; Hunter, 2003; Patz and Sari Kovats, 2005). The atmospheric composition changes constantly as a result of human activities, particularly combustion of fossil fuels. This results in the significant increase of atmospheric carbon dioxide concentrations and reduced plant water loss through evapotranspiration. Therefore, plants produce more foliage with the same amount of water, increasing the density of plant foliage for extended periods in the year and providing more favorable microclimates for insect vectors (Ramirez and Finnerty, 1996). The increase in atmospheric carbon dioxide concentrations together with emission of carbon monoxide, volatile organic compounds, methane and halogenated compounds are thought to destroy the stratospheric ozone layer and increase the greenhouse effect (WHO, 2002; Patz et al., 2000). Global surface temperatures increased about 0.3–0.6 °C during the 20th century (Zell, 2004). As warm air can hold more moisture, the hydrological cycle has changed in response to the increased global temperature and so did the waterborne disease vectors (Patz et al., 2000). Mosquitoes and ticks are extremely sensitive to temperature

and climate changes. Their feeding activity, reproduction and mortality rates are usually directly correlated with the ambient temperature (Zell, 2004). Global warming was suggested to result in the spread of habitats of tropical insects into more northern and southern latitudes as well as higher elevations (Shope, 1991; Zell, 2004).

Major climate events such as El Nino trigger the emergence of disease outbreaks. The warm El Nino events were associated with increased precipitation in South America, United States and East Africa and caused drought in South Africa, India, Southeast Asia and Australia (Boumma et al., 1997; Zell, 2004). Increased rainfall favors the growth of mosquito population resulting in an increased incidence of mosquito-borne diseases. It was associated with the epidemics of Rift Valley fever during the 1997–1998 El Nino event. Increased precipitation was also associated with malaria outbreaks in Pakistan, Peru and Rwanda (Zell, 2004).

3.3. Pollution

Satellite data have shown that urban and industrial air pollution suppresses precipitation. Measurements obtained by the Tropical Rainfall Measuring Mission satellite revealed that both cloud droplet coalescence and ice precipitation formation were inhibited in polluted clouds (Rosenfeld, 2000). A recent study has shown that heavy smoke from forest fires in the Amazon reduced cloud droplet size and delayed the onset of precipitation from 1.5 km above cloud base in pristine clouds to more than 5 km in polluted clouds and more than 7 km in pyro-clouds (Andreae et al., 2004). Pollution associated alterations in rainfall may alter vector habitats, and therefore, the distribution of associated pathogens.

3.4. Development of insecticide and drug-resistance

The basis for the development of insecticide- and drug-resistance is complex. Major factors involved include selection, the development of genetic mutations, and extensive and improper drug use. Population and vector movement, among other factors, are involved in the emergence of drug-resistant vectors and pathogens. Insecticide and drug resistance of vectors and parasites are powerful drivers for the re-emergence and upsurgence of diseases. The following reports exemplify the role of resistance in the spread of Malaria. Chloroquine-resistant *P. falciparum* cerebral malaria causing a high mortality rate was recently reported from Saudi Arabia, where malaria was previously considered chloroquine-susceptible (Alrajhi et al., 1999). A significant increase of malaria-specific mortality in Senegal, Malawi and Zaire has also been associated with the increase in chloroquine resistance (Talisuna et al., 2004). In Chindwara in central India, where an outbreak of malaria has taken place during the previous decade, DDT-resistant *A. culicifacies* was found to be the dominant mosquito species (Neeru Singh et al., 2003).

3.5. Globalization and increased trade, travel and human movement

Globalization and the associated 'open borders' policy caused a remarkable expansion of trade and human movement. These are two major drivers for the emergence and spread of vector-borne diseases. Large quantities of goods are transported daily around the world allowing invasion of vectors through airplanes, ships, containers, luggage and by other means (Gubler, 1998; Sutherst, 2004). The second-hand tire industry has been reported to contribute to the increased geographic dispersion of *Anopheles* species who lay their eggs in used tires (Reiter and Sprenger, 1987). Livestock, pet and exotic animal international transportation are also important factors in the spread of infectious agents and vectors.

Recently, a Pet Travel Scheme has facilitated the movement of pets to the United Kingdom from specified countries in Europe, rabies-free islands, the USA and Canada. During a period of 4 months in 2002, 17 dogs out of 53 that entered under the scheme were found to be infected with exotic pathogens (*Leishmania* species, *Babesia canis canis*, *Babesia gibsoni* and *Ehrlichia canis*) (Shaw et al., 2003). A significant rise in international trade of reptiles and tortoises occurred in recent years. In 2002 only, 87,000 reptiles were imported to the United Kingdom through Heathrow airport alone. This has resulted in the transport of several disease-vectors and pathogens carried by these reptiles (Kenny et al., 2004). In a shipment from Zambia to Florida, 15 of 38 *Amblyomma sparsum* ticks collected from leopard tortoises (*Geochelone pardalis*) were found to carry *Ehrlichia ruminantium* (previously *Cowdria ruminantium*) (Burridge et al., 2000), the agent of heartwater disease in ruminants, a disease with a great economic impact. The two latter reports suggest that trade of exotic animals may pose a threat to animals and humans by the introduction of new vectors and pathogens.

Tourism and international travel are additional important drivers. The amount of international travel is increasing each year. About 1 million people travel internationally each day, and about 50 million passengers travel annually from developed to developing countries and vice versa. To emphasize this point, 20 million people visit malarious endemic areas, and 10,000 malaria cases were estimated to be imported annually to the European community (Sutherst, 2004). In 2001, 7223 imported malaria cases were reported in France alone (*P. falciparum*—83%; *P. ovale*—6.3%; *P. vivax*—6.0%; *P. malariae*—1.3%). These cases were imported from tropical Africa (95%), Latin America (2.7%) and Asia (2.2%) (Danis et al., 2002). Local vectors can become infected with imported pathogens and may result eventually in autochthonous cases. Such an example is believed to be the outbreak of *P. vivax* malaria in 10 adult people who stayed in a camp in North Queensland, Australia, 1 month after a man with imported *P. vivax*-malaria visited the camp (Hanna et al., 2004).

Proximity to international airports appears to be a risk factor for infection with vector-borne pathogens. One example is the locally acquired *P. vivax*-malaria cases which occurred in 2003 in Palm Beach County, Florida, USA. Epidemiological investigation revealed that all seven patients lived within 10 miles from the Palm Beach International Airport (Center for Disease Control, 2003). Another example is an autochthonous infection with *P. ovale* in a 75-year-old woman from Alcalá Spain, who had never traveled abroad and never received blood transfusions or blood derivates. The woman lived near an international airport (Cuadros et al., 2002). The two latter reports have suggested that the route of malaria introduction was via airplanes.

In recent years, many travelers are accompanied by their pets, and these may serve as transport hosts for vectors and for a variety of infectious agents. In this way a vacation to a sunny holiday resort may result in infection with endemic pathogens. This phenomenon was demonstrated in a study performed at Utrecht University in the Netherlands, where most of 75 dogs diagnosed with a *B. canis* and/or an *E. canis* infection had visited an endemic area, most often the Mediterranean region or the Dutch Antilles (Zandvliet et al., 2004).

3.6. The effect of HIV and the use of immunosuppressive drugs

Suppression of the immune system, whether acquired by natural infection with immunospressive pathogens such as HIV, or induced by therapy as in the case of cancer or organ transplant, may change the distribution and spread of infectious diseases. Cellular immunity is most important in defense against protozoa and some bacteria, and its impairment may induce extreme susceptibility to a new infection, or allow reactivation of dormant and otherwise asymptomatic previous infection. Reactivation of Chagas disease caused by *Trypanosoma cruzi* in South and Central America, is a major problem in these areas (Ferreira and Borges, 2002). As with other opportunistic infections, reactivation of Chagas disease is associated with low CD4 T-lymphocyte counts (Ferreira et al., 1997). The geographical overlapping of visceral leishmaniasis and HIV has been described as a deadly gridlock with co-infection reported from more than 34 countries, and leishmaniasis becoming an important cause of mortality in AIDS patients in some of these countries (Desjeux, 1998, 2004). HIV has altered the spectrum of *Leishmania* parasites found to infect humans. Some zymodemes of *L. infantum* that cause only cutaneous manifestations in immunocompetent people were found to cause a visceral disease in HIV-positive patients. Other zymodemes are found exclusively in *Leishmania/* HIV co-infection. In addition, lower monoxenous trypanosomatids different to the *Leishmania* and *Trypanosoma* species known to infect humans have been found in HIV-positive patients (Chicharro and Alvar, 2003).

Some vector-borne bacterial infections have also been associated with HIV infection. HIV-coinfection with the emerging tick-transmitted human ehrlichioses caused by *A. phagocytophilum and E. chaffeensis* is particularly life-threatening (Paddock et al., 2001), and louse-transmitted *Bartonella quintana* appears to be a frequent infection in homeless and HIV-positive patients with fever (Raoult and Roux, 1999; Koehler et al., 2003).

Transmission of diseases by contaminated needles and blood transfusions, rather than by their natural vectors, may also affect the distribution patterns of bacterial and protozoal infectious agents. Transfusion malaria occurs all over the world and is frequently reported from non-endemic areas due to blood donations made by donors who have traveled or immigrated from malarious countries (Guerrero et al., 1983). *Babesia* of different species and *Leishmania* species have been transmitted to humans and dogs by contaminated blood products (Singh et al., 1996; Pedrizet et al., 2000; Owens et al., 2001; Stegeman et al., 2003). A high proportion of needles from intravenous drug users in Madrid have been found to be positive for *Leishmania* DNA by PCR, and it is likely that this infection is transmitted by sharing needles and syringes among drug users, who are often also HIV-positive (Cruz et al., 2002; Molina et al., 2003).

Transplantation of solid organs is frequently associated with infection due to the immuno-suppressive therapy administered to the recipients, contaminated blood transfusions or contaminated donated grafts. Infection with vector-borne pathogens in organ recipients who have a depressed immune system is often fatal despite specific therapy. Malaria transmission via the graft with *P. falciparum* or *P. vivax* has been documented in liver, kidney and heart recipients (Fischer et al., 1999). Similarly, visceral leishmaniasis has been documented in recipients of the same organs following transplant surgery (Hernanadez-Perez et al., 1999). Therefore, strict evaluation of donors' tissues for infectious agents prior to surgery is essential.

3.7. War and civil unrest

It is estimated that there are more than 14 million refugees globally. Refugees due to armed conflicts, natural disasters or poverty are found in different parts of the world mainly in Africa, South and Central Asia, the Pacific, and the Americas (Sutherst, 2004). War as well as civil unrest prevent active intervention and proper public health measures for disease prevention (e.g. vector control, vaccination and access to health services). Civil unrest was associated with the recent resurgence of trypanosomiasis and leishmaniasis in Eritrea, Sudan and Ethiopia (Molyneux, 2001). Concurrent infection with HIV and poverty in these countries further complicate the situation as the population has no financial capabilities to obtain professional medical aid and medications.

3.8. Movement of vectors by wind and migrating birds

The global spread of infectious agents by vectors is affected by natural factors such as movement of vectors by wind, carriage on transport hosts like migrating birds, and by means of transportation (e.g. flying, walking) (Sutherst, 2004). For example, during the spring of 1996, an estimated 581,000 *A. phagocytophilum*-infected *Ixodes ricinus* ticks were imported into Sweden by migrating birds suggesting that birds play an important role in dispersing *I. ricinus*-borne pathogens between countries and continents (Bjoersdorff et al., 2001). Another example is the wind-borne movement of *Simulium sirbanum* and *Simulium damnosum*, the principal vectors of onchocerciasis in West Africa, causing human blindness. These flies have been shown to spread and carry *Onchocerca* infection for hundreds of km with the monsoon winds in the rainy season (Baker et al., 1990).

3.9. Global and governmental management failure

Incorrect global and governmental management is associated with the emergence and re-emergence of diseases. This includes an imbalanced distribution of resources, lack of sound public health policy, emphasis on emergency response rather than prevention, and shortage of experts trained to respond effectively to emerging and re-emerging infections (Molyneux, 2001; Sutherst, 2004).

4. Scientific advances, conclusions and future prospects

The complex association between disease drivers such as changes in weather, pollution or global travel, and their health and financial impacts is gradually being elucidated by research. Epidemiologic tools and techniques for the research of infectious diseases have improved significantly in the last few decades. The use of risk analyses, geographic information systems (GIS), remote-sensing technologies and climate models in research has provided tools for the expansion of epidemic knowledge, epidemic prediction, and the planning of effective control and policy analysis (Molyneux, 2001). In addition, the development of sophisticated diagnostic methods for vector-borne pathogens and especially the introduction of molecular techniques, mainly the development of the polymerase chain reaction and nucleotide sequencing, have allowed rapid, sensitive and specific diagnoses, which in turn facilitate accurate treatment and timely prevention efforts.

Reversing the trend of emergence and re-emergence of vector-borne diseases is the ultimate challenge. The development of new chemotherapeutics, vaccines, insecticides, repellants and biological products against the major vector-borne diseases is crucial for achieving control or eradication. The greatest effort should undoubtedly be directed to the battle against malaria as it is the major

vector-borne killer in the developing countries. Multi-drug therapies (combination therapies) or rotational therapy should be employed against parasites and vectors in order to prevent the development of drug-resistance. There is a vital need for insecticides and repellants that are safe for the environment, and for the development of alternative preventative approaches such as biological pest control, e.g., the use of entomopathogenic fungi, nematodes, wasps and birds in the control of ticks and other vectors (Gubler, 1998; Samish and Rehacek, 1999).

Multi-national eradication and control programs have proven successful in the battle against several vector-borne diseases including Chagas disease in Latin America and River blindness in western Africa (Kerr, 2003; Moncayo, 2003). The involvement of global organizations such as the Untied Nations' agencies including the WHO and World Bank has played an important part in the funding and coordination of such programs. Private pharmaceutical companies, public organizations and philanthropic trusts and societies have also made their significant contributions. Sustainability studies and risk evaluations to forecast future outbreaks and appreciate the effect of global changes upon the environment and the transmission of diseases have been published. Such studies have been helpful by making recommendations for policies and intervention efforts (Patz et al., 2004; Ezzati et al., 2005). In the future, more global resources should be allocated to the development of prediction and prevention programs to eradicate or minimize vector-borne diseases in developing countries (Gubler et al., 2001; Molyneux, 2001). There is further need for greater involvement of international non-governmental development and aid organizations (Molyneux, 2001). It is vital that a coordinated global rather than a governmental approach should be implemented in vector-borne disease prevention.

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