24. Invasions of vector-borne diseases driven by transportation and climate change

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Abstract

Biological invasions are as old as life itself but have become increasingly frequent due to the globalisation of travel and transportation. During the latest decades, climate change has become an additional driver. Vector-borne diseases, too, are invading more frequently, following an invasion of a vector, a pathogen, a reservoir host or a combination of these. In the past, such invasions have had dramatic effects on public health (e.g. the plague in Europe), livestock health (e.g. bluetongue in southern Europe) or wildlife (e.g. avian malaria on Hawaii). As the volume and speed of travel and transportation increase and climate change continues, more invasions of vector-borne diseases are to be expected, also in Europe. Recent arrivals include the West-Nile, Usutu and bluetongue viruses and the mosquito vector *Aedes albopictus* (Skuse). Around 12 arboviruses are potential candidates for invasion in Europe in the next decades as well as at least one rickettsia, one bacterium and two protozoa. However, the likelihood of such invasions is small in most cases. The main vectors involved are ticks and *Aedes* and *Culex* mosquitoes. Two serious threats are invasions of the Chikungunya and dengue viruses in southern Europe, where the competent vector *Ae. albopictus* has already become established. In fact, at the time of writing this article (August 2007) an outbreak of Chikungunya occurred in Italy (see Chapter 10). An increasingly important risk route for disease introductions is that between East Asia and Europe. Whilst most climate-driven invasions cannot be prevented, many transportation-driven invasions can be. This requires a precautionary approach based on risk analyses, preventive measures in the country of origin, intensive surveillance, early warning and interception. High-risk trade flows for pathogens, such as live animals, and for mosquitoes, such as used tyres and water-filled containers, should be strictly regulated or even reduced. If, however, an introduced vector or pathogen has inadvertedly become established, it should be eradicated as soon as possible. Mosquito invaders can be eradicated by draining water pools, application of insecticides, or use of biological larvicides. Pathogens can be eradicated by vector control, vaccination of infected people or livestock and isolation and treatment of infected hosts. Culling of infected livestock is another option. International agreements such as the Convention on Biodiversity and the International Health Regulations encourage preventive measures, and the world trade regulations allow restrictions on trade if and when the health of humans and animals is at stake. The ultimate policy goal would be to replace free trade by safe trade.

Keywords: biological globalisation, bio-invasion, eradication, pathogen, prevention, regulation

Introduction

The world is globalising and nature is no exception. More and more species are expanding their ranges across ancient distribution barriers. The overall result has been termed 'biological globalisation' (e.g. Bright 1998, Van der Weijden *et al.* 2007).

Biological invasion is by no means a recent phenomenon. In fact, it is as old as life itself. Every species tends to expand its range. Some can even cross thousands of kilometres moving on air or ocean currents alone, while others can do so by flying and still others by hitchhiking on the latter. For example, the Sindbis virus is carried annually between South Africa and Scandinavia by migrating birds (Gould *et al.* 2006). The process was accelerated after *Homo sapiens* spread out of Africa. Humans introduced plant, animal and microbe species in Asia, Europe, Australia and the Americas, both deliberately and accidentally. A next 'quantum leap' was made after Columbus had 'discovered' America in AD 1492. Three decades later, the Pacific was crossed as well[16]. These two events paved the way for increasing transoceanic trade and travel and associated species introductions, leading to genuine biological globalisation (Crosby 1972, 1986). The most recent 'quantum leap' was the introduction of the aircraft. Species can today move further, faster and in greater numbers than ever before.

In this chapter we discuss:
- the main drivers of bio-invasion;
- some bio-invasions from the past that had a major impact;
- some historical examples of vector-borne disease invasion and their impact;
- categories of vector-borne disease invasion;
- recent invasions of vector-borne disease in Europe and candidates for future invasion;
- priorities for prevention and control;
- an overall strategy for prevention and control of vector-borne disease in Europe;
- technical and legal opportunities for prevention and control;
- guidelines for action.

Bio-invasion and its drivers

Bio-invasions are a universal phenomenon. Invasions have taken place in species of every major taxon and every trophic level into virtually every terrestrial and aquatic habitat and every continent including Antarctica. Box 1 gives some basic definitions from invasion biology.

Bio-invasions have several drivers. The main drivers are:
- international travel and transportation;
- climate change;
- habitat transformation.

Habitat transformation can facilitate bio-invasion in two different ways. Firstly, it can remove distribution barriers between distinct biotas that were long or always separated. For example, in AD 1869 the Suez Canal connected the Mediterranean Sea and the Red Sea/Indian Ocean, leading to frequent species interchange. Secondly, habitat transformation can help species that were already introduced across a barrier, to establish and spread in its new area. Even though all habitats appear to be invasible (Willamson 1997), some are more invasible than others. For example, soils that are physically disturbed and/or highly enriched with nutrients are often used by introduced plant species (Lake and Leishman 2004) and may form bridgeheads for invasion.

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[16] Columbus was certainly not the first visitor from the Old World since the original immigration waves from Asia. Five hundred years earlier, the Vikings had reached the northeast coast of North America. However, that did not generate substantial exchange of terrestrial species. Three reasons can be mentioned for this. The northern colder zones of the Old World and New World host fewer species than the warmer zones; a higher proportion of these species was already shared; and the traffic volumes involved were relatively small. As for the Pacific, there is evidence that before AD 1492 Polynesians visited the west coast of South America and from there introduced the sweet potato in Oceania (Ballard *et al.* 2005).

Some invasions are caused by two or three drivers acting in combination. For example, over the latest decades many plant species from warmer and rocky areas have invaded urban areas in the Netherlands (Tamis 2005)[17]. Somewhat simplified: habitat transformation (i.e. urbanisation in the past) created a suitable environment, climate change raised the local temperature and international travel and transportation introduced the seeds.

Box 1. Some definitions in invasion biology, epidemiology and biogeography.
Invasion biology is a young branch of biology. It is only 50 years old, as young as e.g. DNA biology, and much younger than medical and veterinary epidemiology. Although Charles Darwin laid some of the foundations, the real starting point was Charles Elton's groundbreaking *The ecology of invasions by animals and plants* (1958). There still is confusion as to some basic definitions and concepts. Here we apply the following definitions:

Alien (species): A species that does not naturally occur in an area where it is found at a particular moment. Synonyms: *exotic, non-indigenous* and *non-native species*.

Biological globalisation (biotic globalisation, bio-globalisation): The process of increasing connections between the separate biotas of the world, leading to biotic homogenisation and numerous new ecological interactions. Insofar as this process is facilitated by man – through transportation, travel, breakdown of distribution barriers, and man-made climate change – it can be named *anthropogenic bio-globalisation*.

Counter-invasion: Invasion following the deliberate introduction of a natural enemy of an invasive pest species.

Endemic disease (in epidemiology): A disease that occurs continuously in a certain area, at a more or less constant level.

Endemic species (in biogeography): A species occurring exclusively in a certain area.

Enzootic disease: Endemic disease among animals.

Import cases: Cases of infectious diseases that have been brought into a country by infected patients or animals.

Introduction: The transportation of a species into an area where it does not yet occur. This can be done intentionally, accidentally and unconsciously, or accidentally but consciously.

Invasion: The settlement and subsequent spreading of a species in a new area.

Invasive species: A species that colonises a new area, maintains itself, reproduces and spreads actively. (Many authors confine 'invasive' to those species causing ecological, medical or economic damage).

Native species: A species that for at least millennia occurs in a particular area. Synonym: *indigenous species.*

Impacts of bio-invasions in history

The impacts of bio-invasions on nature and the human society are often negligible, at times beneficial and sometimes harmful or even devastating. The best example of a beneficial impact, at least for human nutrition, has been the introduction of crop and livestock species from the

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[17] Change of *micro*climates can be an important driver as well. For example, the construction of heated greenhouses and buildings in temperate climates has created suitable conditions for subtropical insects such as the Mediterranean fruit fly *Ceratitis capitata* and the Pharao ant. Such species rarely spread beyond their artificial environment, but this will happen more frequently as climate changes continues.

Old World into the New World and vice versa. This so-called 'Columbian Exchange' (Crosby 1972) provided opportunities for more diverse crops and higher yields in most regions in the world[18]. Likewise, the exchange of livestock species – mainly from Old World to New World – gave a major boost to the previously marginal livestock production in the New World.

By contrast, species introductions have also caused disasters, accidental introductions not less than deliberate ones. For example, the Columbian Exchange also included the exchange of pathogens, pests and weeds, mainly from the Old Word to the New World. We mention seven examples of harmful species introductions, which include a virus, a fungus, several mammals, a fish and a mollusc. We present them in roughly chronological order:

- European colonisers accidentally introduced the smallpox virus and several other Old World pathogens in the Americas in the 16th and 17th century. This caused mass mortality among indigenous Americans, decimating their populations. It was a decisive factor in the shift of power from the Amerindians to the European colonisers.
- After the introduction of the potato in the 16th century from South or Central America century in Europe, a deadly pathogen followed three centuries later: the potato blight fungus *Phytophthora infestans* (Mont.) de Bary[19]. Originating in Central Mexico, it was probably introduced in 1843 or 1844 from South America or the USA (Andrivon 1996). In 1845 it devastated the potato crop in western Europe. Ireland was hit hardest. In 1845, 1846 and 1848 a third to three quarters of the crop failed. By 1851 about 2.5 million persons were lost, with an estimated 1 million having emigrated and 1.5 million having died from the effects of the famine (The History Place 2000).
- In 1859 British colonisers in Australia introduced the European rabbit for hunting purposes. The species spread widely and quickly became a pest, competing with sheep livestock and indigenous fauna (Williamson 1997). By 1997, the costs in agricultural damage still amounted to some $600 million annually, plus $20 million in control costs (Bomford and Hart 2002).
- Species introductions have also caused the extinction of many indigenous species. This rarely happened on continents and in oceans, but frequently on islands and in lakes. On islands, most damage was done by introduced predators such as rats and cats, as well as by herbivores such as goats and rabbits. (Williamson 1997, Quammen 1996). The process started several millennia ago and become global since the 15th century. As for lakes, a recent example is the predatory Nile perch *Lates nilotica* L. in Lake Victoria. Introduced for fishing in 1954, it remained little noticed until it exploded in the 1980s. While spreading it eradicated about two hundred endemic cichlid fish species (Goldschmidt 1998).
- In 1905 the muskrat *Ondatra zibethicus* L. was introduced from North America in Bohemia, Central Europe, for fur production. In the 1920s muskrats were released or escaped in Russia, Finland, France and the British Isles, and started undermining banks, dams and riverside trees (Williamson 1997). In the Netherlands they undermine dikes since 1946, creating risks of flooding. Six hundred people are needed permanently to catch muskrats in order to prevent disaster and reduce damage to dikes (LCCM 2004).
- In 1986 the zebra mussel *Dreissena polymorpha* Pallas, native to Europe, was found in North-American lakes, probably introduced in the ballast water of a ship. The species quickly started its invasion, which still continues. By swamping it causes major damage to the indigenous freshwater fauna and covers and clogs intakes and outlets of power plants and factories. Along

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[18] Most introduced crop and many livestock species hardly spread spontaneously, so whether the term 'invasion' is appropriate is a matter of definition.

[19] *Phytophthora* is today classified as an oomycote.

with the quagga mussel *D. rostriformis bugensis* Andrusov, also introduced from Europe, the zebra mussel causes an estimated one billion dollar per year in damage and control costs (Pimentel *et al.* 2005).

These cases illustrate that deliberate introductions (rabbit, Nile perch and muskrat) are not less harmful than accidental introductions. They also illustrate that, next to the damage inflicted on nature, bio-invasions can damage multiple sectors of society, ranging from public health, agriculture, forestry and fisheries to industry, energy supply, housing, water infrastructure and tourism. The economic costs are an estimated 120 billion dollar per year in the USA alone (Pimentel *et al.* 2005).

What makes many harmful invasions even more harmful is that they are irreversible (although there are exceptions such as goats and rats introduced on smaller islands that can be eradicated). For example, potato blight still occurs in Europe. In the Netherlands it is even a main target of pesticide use.

Historical cases of invasions of vector-borne disease

Plague in the Old World and beyond

Invasions of vector-borne[20] diseases, too, can be devastating. Perhaps the most devastating invasive vector in history was the oriental rat flea *Xenopsylla cheopis* Rothschild. It can carry and transmit the bacterium *Yersinia pestis* that causes bubonic and pneumonic plague and has its natural reservoirs in burrowing rodents. The black rat *Rattus rattus* L. is a temporary host but before dying can transmit the bacterium to a vector, usually the rat flea (Benedictow 2004). The distributional history of the trio bacterium/flea/rat is closely associated with the development of the global shipping network. Hence the three plague pandemics were of an increasingly global scale (McNeill 1998).

Perhaps in the 1st or 2nd century AD, the flea travelled with black rats aboard ships from India to the Middle East and thence, probably with rats and camels to the Black Sea and Mediterranean Sea areas. This later facilitated the first plague pandemic (AD 541-810) that started in Central Africa, India or Arabia, and ranged from Arabia east to China and west to Southern Europe.

The second pandemic (AD 1346-1720) followed after the fleas had travelled north, again with ship rats, to western and northern Europe. Hence the initial wave, the Black Death[21] (AD 1346-1353) that started in the Crimea, could hit almost the whole of Europe, killing between 25% and 60% of the population (Benedictow 2006). On land, the spread of the disease was accelerated by people fleeing from the plague while carrying the bacterium with them in their blood and/or in infected fleas. Many waves followed, covering almost four centuries until the last major outbreak in Marseille in 1720.

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[20] We apply the term 'vector' to invertebrates that can carry and transmit a pathogen from a reservoir host to humans or (feral or domesticated) animals. We exclude animals such as dogs, rodents and bats that are a permanent or temporary host to a pathogen and can directly transmit it to humans.

[21] Several scholars have provided evidence that other pathogens such as anthrax or a viral hemorrhagia may have played an additional or even dominant role in the Black Death. See Scott and Duncan (2004) for a review. This debate has not yet been concluded.

The third pandemic (AD 1855-1959) started in China and became truly global. After reaching the seaports of Hong Kong and Canton, *Yersinia pestis* could travel with ship rats to southern Asia, Africa and the Americas, facilitated by the global network of steamships that had developed. The bacterium developed reservoirs in mammals (usually burrowing rodents) in new areas, including western North America, where it colonised prairie dogs. Plague is becoming a re-emerging concern due to increased incidence and antibiotic resistance (Tatem *et al.* 2006a).

Yellow fever in the New World

Another historical example of vector-borne disease invasion is the introduction of the yellow fever virus and its vector *Aedes aegypti* L. in the New World. The most commonly cited hypothesis is that the virus was introduced from Africa, along with *Ae. aegypti*, in the bilges of sailing vessels during the slave trade. The timing and African origin of the invasion were recently supported by molecular gene sequence analysis (Bryant *et al.* 2007). There is circumstantial evidence that Dutch slave ships were involved (Van der Weijden *et al.* 2007).

In 1647 the first outbreak was reported on the Caribbean island of Barbados (Childs Kohn 2001). Vector and virus spread across the Caribbean and beyond, causing mass mortality. Amerindians and Europeans were hit much harder than African slaves, who were more or less immune to the virus. This affected the balance of power in the Caribbean. The virus became a powerful ally of African rebels in Haiti revolting against the French army and thus generated a 'biological Waterloo' for Napoleon. Haiti owed its independence in 1804 not least to an earlier introduced vector-borne disease.

From 1881 to 1884, yellow fever as well as malaria frustrated French attempts to construct the Panama Canal (Spielman and D'Antonio 2001). *Plasmodium falciparum, P. malariae* and *P. vivax* had been introduced in the previous centuries, probably with infected African slaves and European contract labourers. The USA was more successful from 1906 after the discovery of the key role of mosquitoes in the transmission of yellow fever and malaria. Once again, the French were beaten by mosquito-borne diseases introduced much earlier by their fellow-Europeans. This time they had to yield maritime power to the USA (Spielman and D'Antonio 2001).

This case also makes clear that understanding vector-borne disease can be a key success factor in public healthcare, the economy and politics. Today, this may still be the case, considering such devastating diseases as malaria, bilharziasis, yellow fever, dengue and sleeping sickness.

Other cases

In recent history, the most devastating vector invasion was that of the malaria mosquito *Anopheles gambiae* Giles in South America. Native to Africa, the mosquito was introduced in 1930 from Dakar, Senegal, into northeast Brazil, either by aircraft or by a rapid passenger ship (Lounibos 2002). Although *Plasmodium falciparum* had already become endemic, the greater vectorial capacity of *An. gambiae*, as compared to local mosquitoes, sparked severe malaria epidemics costing 16,000 lives (Soper and Wilson 1943). Even though the mosquito had already spread widely covering 54,000 km^2, it was eradicated in 1940 as a result of the remarkable large-scale, army-style campaign that included larviciding of all potential habitats with crude oil, Paris green and pyrethrum, as well as drainage of pools (Soper and Wilson 1943, Childs Kohn 2001, Killeen 2003).

Vector invasions can also severely hit faunas. A classical example is the introduction of the southern house mosquito *Culex pipiens fatigans* (now: *Culex quinquefasciatus*) Wiedemann in the Hawaiian island of Maui in 1826 (Quammen 1996, Lowe *et al.* 2001). Eggs and larvae of the mosquito were introduced in the water storage jars of a British ship sailing from Mexico. The avian-pox virus and *Plasmodium relictum*, which can cause avian malaria, had been introduced earlier with poultry by settlers. However, the parasite and the virus lacked a competent vector. Once established, the mosquito quickly started transmitting both pathogens from poultry to indigenous birds, including members of the endemic family of honeycreepers (Drepanididae), regarded by many as one of the most magnificent bird families in the world. As the mosquito spread to other islands, the impact became dramatic. Before the close of the 19th century, 16 endemic bird species and subspecies had suffered extinction (see Chapter 4).

Just before the close of the millennium, the West-Nile virus invaded North America, probably from the Mediterranean (see Chapter 8). It probably arrived by ship or aircraft from the Mediterranean with infected imported birds, mammals, stowaway mosquitoes or travellers. But it may also have arrived with infected migratory birds. The virus found competent indigenous reservoir hosts (birds) as well as vectors (mosquitoes). The first outbreak was in New York in 1999. Many outbreaks followed as the virus quickly spread across North America. In 2006 alone, 4,269 people in 44 states of the USA were reported ill, including 177 fatalities (CDC 2007). In addition, there were thousands of fatalities among horses and wild birds (see Chapter 8).

Tick invasions so far have not caused dramatic effects. In Europe, one probably invaded species that has caused damage is the brown dog tick *Rhipicephalus sanguineus* Latreille. It probably originated in Africa (Garben *et al.* 1980) and subsequently invaded southern Europe, but how and when that happened is not clear. *R. sanguineus* is unusual among ticks, in that it can complete its entire life cycle indoors (Lord 2001). It attaches to the armpits and groins of dogs, its preferred host, as they walk through high grass or low scrub. Cattle, cats and sheep can also serve as host, as can humans. If dogs are no longer available (or made unattractive by application of a repellent), ticks can take a blood meal on humans. Thus they can transmit Lyme disease as well as rickettsias, mainly *Rickettsia conorii*, which causes Mediterranean spotted fever (Parola 2004). Damage may increase in the future as the tick has spread North, mainly with infected dogs of tourists. In the Netherlands it was first observed in 1962 and later became established, though it can probably only survive indoors. Control may become more difficult as the tick is developing resistance against acaricides (Estrada-Peña 2003).

More harm is known from some cases where the pathogen itself rather than its tick host invades a new area. Lyme disease in North America is a possible example. The causative pathogen is the spirochaete bacterium *Borrelia burgdorferi*, which may have originated in Eurasia[22]. With approximately 20,000 new cases reported each year, Lyme disease has become the most common vector-borne disease in the USA (CDC 2007).

Invasions of non-arthropod vectors can be devastating as well. For example, the flatworm *Schistosoma mansoni* Randall is one of the causal agents of intestinal schistosomiasis (bilharziasis) in Africa. The damage inflicted on human health became even greater after it was introduced,

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[22] A Eurasian origin of *Borrelia burgdorferi* is likely since the genetic diversity within the *B. burgdorferi* complex is much higher in Eurasia than in America. How and when the species invaded North America is not yet clear. It may have been introduced by infected humans, animals or ticks. Alternatively, migratory birds can have introduced the bacterium. Several bird species are competent reservoirs of the bacterium (Ginsberg *et al.* 2005).

probably with the slave trade, in the American tropics, where it found a competent intermediate host in the freshwater snail *Biomphalaria glabrata* Say. Today, 83 million people host *S. mansoni* (DeJong *et al.* 2001).

In the next paragraphs we narrow our focus to arthropod vectors of human and animal diseases, leaving aside plant diseases and non-arthropod vectors. We further focus on invasions into Europe (not specifically the EU), disregarding invasions into other continents and from one part of Europe to another. In addition, we focus on (possibly) successful bio-invasions, disregarding the numerous airport cases and import-linked cases of exotic diseases, although these can start an invasion in exceptional cases.

Vector-borne disease invasion in Europe

The plague was not the last arthropod-borne disease to invade Europe. It was followed by *Plasmodium falciparum* malaria, introduced from West Africa. Several other diseases followed, mainly in the 20th century, driven by the globalisation of travel and transportation. Table 1 lists three vectors and four vector-borne pathogens that have invaded Europe[23].

Aedes albopictus

The Asian tiger mosquito *Ae. albopictus* is a subtropical mosquito, native to Asia, that breeds in natural or artificial containers with stagnant water, such as used tyres and tins, with which it is often transferred, even overseas. From Asia it spread to southern Europe (1979), North America (1985), South America (1986), Africa (1991) and islands in the Indian and Pacific Oceans. In the laboratory *Ae. albopictus* can transmit c. 22 arboviruses, including those causing dengue fever, West-Nile disease, yellow fever, Cache Valley disease, Eastern equine encephalitis and Chikungunya. Some of these viruses are actually circulating in Europe, while others only arise as imported viruses (Gould *et al.* 2006). However, as for the USA, Moore and Mitchell (2000) state that in terms of its role as an arbovirus vector, evidence is lacking to incriminate *Ae. albopictus* as the vector of even a single case of human disease. It has even replaced *Ae. aegypti* in large areas in the USA (Lounibos 2002). *Ae. albopictus* seems to be a threat only in areas where *Ae. aegypti* is absent. For example, in 2005/06 it caused heavy epidemics of Chikungunya on La Réunion and other islands in the Indian Ocean. More than 250,000 people became infected and an estimated 260 died from the disease, implying a case-fatality rate of 1/1000 (Josseran *et al.* 2006).

Unlike *Ae. aegypti, Ae. albopictus* is capable of colonising temperate areas permanently. Records of the mosquito in Europe have been associated with imports of used tyres (Italy, France, Belgium) and ornamental plants (the Netherlands; see Chapter 14). In Italy it is now a dominant pest mosquito, which is probably partly due to the fact that the infestation derives from several successive introductions, each with large numbers of individuals and added genetic variation

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[23] The table does not include the rat flea, which invaded long before AD 1500, as probably did the brown dog tick, which is also excluded. Neither does the table include allergies induced by the presence or behaviour of arthropods, such as the allergic reactions caused by bed bugs (*Cimex spp.,* Hemiptera) and asthma related to alien cockroaches (e.g. *Periplaneta spp.,* Dictyoptera), nor dermatoses caused by insects and arachnids. Diseases where both the pathogen and its vector are supposedly native to Europe have also been left out. One example is Lyme disease, caused by the bacterium *Borrelia burgdorferi* and spread by the sheep tick *Ixodes ricinus*. Another example is the Toscana virus (TOSV) that was first isolated in 1971 in central Italy from the sandfly *Phlebotomus perniciosus* (Charrel *et al.* 2005), which ranges from France, Portugal and Spain to Greece and Turkey.

Table 1. Three arthropods vectors and four arthropod-borne pathogens invaded in Europe since AD 1500.

Vector	Pathogen(s) transmitted	Native area of vector or pathogen	First record in Europe	Pathway of vector or pathogen
*Aedes albopictus** Asian tiger mosquito	In laboratory: c. 22 arboviruses In field: Chikungunya, dengue, West-Nile WNV*	Vector: Southeast Asia	Vector: 1979 Albania. Pathogen WNV: *see below*	Vector: ship-borne, used tyres and ornamental plants. Pathogen WNV: *see below*
Native *Anopheles* spp. Malaria mosquitoes	*Plasmodium falciparum**†	Tropical Africa	Pathogen: 16th century Spain, Portugal. Eradicated after WW II	Pathogen: slave ships?
Native *Culex spp.* and other mosquitoes	West-Nile virus*, Usutu virus*	WNV: Africa, Middle East. Usutu: Africa	WNV: 1962 France (horses), 1996 Romania (humans), Usutu: 2001 Austria (birds)	Viruses: migratory and/or imported birds?
Culicoides spp. (biting midges) Native *C. obsoletus, C. pulicaris, C. scoticus* Invaded *C. imicola**	Bluetongue virus*	Pathogen: Subtropics, Tropics	Pathogen: 1956 Spain/ Portugal. Vector *C. imicola*: 1982 Iberian peninsula	Pathogen: ship-borne cattle? Vector *C.imicola*: probably ship-borne cattle or wind-borne across Mediterranean
*Monomorium pharaonis** Pharao ant	(Native) bacteria incl.: *Salmonella, Pseudomonas, Staphylococcus, Streptococcus, Clostridium*	Vector: Africa	Vector: probably some centuries ago	??

* = invaded.
†= eradicated after WW II in Europe.

Box 2. Five categories of invasion of vector-borne disease.

A vector-borne disease requires at least three species: a pathogen, a reservoir host and a vector. Obviously, an invasion of such a disease can be successful only after each of the three species is present in the new area. Thus we can distinguish five categories of invasion:

1. Competent vector and reservoir host species present, pathogen invades (P > V/R).
   This probably happened when *Plasmodium falciparum* was introduced in the New World, probably with slave shipments. The parasites found a competent reservoir host (humans) as well as competent vectors among indigenous anopheline species[1]. Note here that pathogens are often introduced with an infected reservoir host, but if that host species already lives in the new area, this is not an invasion of the host species, not even if individuals spread and interbreed with indigenous individuals.
2. Pathogen and competent reservoir species present, vector invades (V > P/R).
   This was, to some extent, the case when *Anopheles gambiae* was introduced in Brazil in or some time before 1930. *P. falciparum* had already become endemic and a reservoir species (humans) was present. Even indigenous vectors were present, but *An. gambiae* is a much more efficient vector.
3. Competent vector present, pathogen and reservoir host invade (P/R > V).
   Such invasions may occur either simultaneously or shortly after one another. One example is the introduction of the European rabbit in Australia in 1859, where it quickly spread and became a pest. To control the rabbit, attempts were made from 1936 onward to introduce the myxoma virus, native to South America. Success had to wait until 1950, when *Aedes* and *Culex* mosquitoes had also become infected (Williamson 1997).
4. Competent reservoir host present, pathogen and vector invade (P/V > R).
   These invasions, too, may occur either simultaneously or one shortly after one another. This was probably the case when the yellow fever virus and its vector *Ae. aegypti* were introduced from Africa in the New World in the 17th century. Suitable reservoir species were humans, monkeys and several forest mosquito species.
5. Pathogen, vector and reservoir host invade (P/V/R >).
   These invasions may occur either simultaneously or one shortly after one another.
   This happened on Hawaii in the early 19th century, when poultry infected with avian malaria and avian pox were introduced first and a competent mosquito vector a few decades later (Quammen 1996).

In theory, two additional categories should be mentioned: (R/V > P) and (R > P/V).
This can happen only if the pathogen already survived in an indigenous reservoir host. But if it already caused a similar disease in that host, we cannot speak of a disease invasion. So these categories are relevant only in those rare cases where the (potential) pathogen was already present without causing a similar disease.

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[1] Coatney *et al.* (1971) took the view that all South-American *Plasmodium* species, including those hosted by monkeys, were introduced with slave trade from Africa. Accordingly, Escalante *et al.* (1995) provided evidence from protein analysis that *P. brasilianum* and *P. simium*, parasites of South-American monkeys, are more or less identical to the human parasites *P. malariae* and *P. vivax,* respectively.

(Gratz 2004, Urbanelli *et al.* 2000). As recently as August 2007, a local outbreak of Chikungunya virus occurred in Italy, vectored by *Ae. albopictus* (see Chapter 10). An additional risk is that indigenous mosquitoes take over the vectorial role of *Ae. albopictus*. A Dutch report concluded that - apart from *Ae. albopictus* - five out of the 35 mosquito species in the Netherlands are potential vectors of WNV, including *Culex pipiens* (Reusken and Takken 2006).

Anopheles spp.

Anopheles mosquitoes can transmit *Plasmodium* and some can transmit the most vicious species *P. falciparum*, which causes malaria tropica. Its most efficient vector is *An. gambiae*, native to tropical Africa. *P. falciparum* may have travelled with infected African slaves[24] or crew members, as anopheline mosquitoes developed from larvae in water storage jars and transmitted the parasite from infected to non-infected individuals. Once arrived, the parasite found competent vectors among European *Anopheles* species and spread across southern Europe. Thereby this invasion falls in the 1st category of Box 2 (P > V/R).

Malaria was eradicated from the whole of Europe by the early 1970s. However, it has recently re-emerged as a matter of growing concern in Europe (see Chapters 2 and 3). Massive epidemics of autochthonous malaria occurred in adjacent Azerbaijan and the Asian part of Turkey. In addition, imported malaria is a growing issue, especially import into western Europe, with a majority of cases caused by *P. falciparum* (Sabatinelli *et al.* 2001).

Culex and other mosquitoes

The West-Nile virus was first isolated in Uganda in 1937. After being found in Egypt and Israel, it was first isolated in Europe in the 1960s, from horses in southern France. The first major human outbreak came in 1996 in Romania (see Chapter 8). The virus has an exceptionally wide range of hosts as well as vectors. It has been found in many bird, mammal and even alligator species, though it has its reservoirs among birds. It can be transmitted by many mosquito and tick species, often *Culex pipiens*.

The virus was probably introduced in Europe by infected migratory or imported birds. Its permanent presence in Europe is partially sustained by repeated introductions. So far, the damage inflicted on human and animal health has been much smaller in Europe than in the USA, perhaps because repeated infection has generated a higher degree of immunity in European humans and animals (see Chapter 8).

The Usutu virus is another virus that was probably introduced in (Central) Europe with infected migratory or imported birds. The current knowledge is summarised by Weissenböck *et al.* in Chapter 9. The virus is transmitted by *Culex* and other mosquito species. So far it has not been associated with severe or fatal diseases in humans.

Since seasonal migration is not considered a species invasion, both virus invasions are examples of the 1st category in Box 2 (P > V/R).

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[24] At the time, African slaves were also held in Spain and Portugal.

Culicoides spp.

The epidemics and recent outbreaks of bluetongue in Europe illustrate the 1st category mentioned in Box 2 (P > V/R). However, the virus is not only transmitted by the indigenous biting midges including *Culicoides obsoletus* Kieffer, *C. pulicaris* L. and *C. scoticus* Downes and Kettle, but also by *C. imicola* Kieffer, a probably recent invader from Africa into Europe. The latter invasion fits in the 2nd category (V > P/R) and is still limited to southern Europe.

The virus may have originated in the Mediterranean. It was first described in South Africa after merino sheep were introduced from Europe in the late 18th century (Gould *et al.* 2006). The virus subsequently spread globally. It affects ruminants, not humans. It is enzootic in South Africa, Australia, the Americas and parts of Asia, and has hit Europe several times. In the 1956-1960 epidemic in Spain and Portugal, 180,000 sheep died. In 1979-1980 an epidemic occurred on the Greek islands of Rhodes and Lesbos. The virus appears to have established itself in southern Europe (Elbers 2003).

In August 2006 the virus was first found north of the Alps in an area encompassing parts of the Germany, the Netherlands, Belgium, France and Luxemburg (see Chapter 7). The serotype involved was nr. 8. This was identified earlier in Africa and the Americas and suspected in India, but not in Europe so it was a new invasion in Europe from some of these regions. The virus possibly arrived with infected animals. Its invasion coincided with the warmest July on record in the Netherlands. After a mild winter and a warm spring, new outbreaks took place in July 2007, indicating that the virus may become enzootic in North-West Europe (see Chapters 6 and 7).

Monomorium pharaonis L.

Another example of the 2nd invasion category (V > P/R) is the introduction of the pharaoh ant. It is the oldest and most widespread invasive pest among ant species. Probably native to Africa, it has successfully invaded areas on every continent except Antarctica. Due to its ability to transmit some bacterial human pathogens, its presence in hospitals is of great concern (Erdos and Koncz 1977). It is concentrated in tropical regions but is also commonly found in temperate zones within suitable human infrastructure, including climate-controlled buildings.

In the Netherlands it was first reported in 1900 in the post office of the town of Leeuwarden, where it probably arrived by mail. Due to the introduction of central heating, the houses in the Netherlands became warmer since 1950, coinciding with the advance of the ant (Van der Weijden *et al.* 2007). Even though the abundance of this ant in cold climates will be restricted, its continued presence suggests a potential to spread to locations more suitable for ant colonisation (Holway *et al.* 2002).

Summarising, the invasions listed in Table 1 represent only three of the five categories listed in Box 2: 1, 2 and 4. Perhaps categories 3 and 5 did not yet occur in Europe. Category 5 will remain unlikely since it requires invasions of three matching species. Category 3 is more conceivable. For example, an alien bird or mammal species infected with an alien virus might be introduced from North America or East Asia, and subsequently be vectored by an indigenous mosquito or tick.

Candidates for vector-borne disease invasion

Predicting specific new arthropod-borne invasions, even on the short term, is hardly possible, for various reasons:

- How far and how fast vectors and pathogens spread in time and space is difficult to predict for most species.
- Many factors and complex interactions are involved.
- The processes involved are often poorly understood.
- Quantitative data are often lacking.

Table 2 presents a list of arthropod-borne diseases that can be regarded as potential candidates for invading Europe. This list is not prioritised, nor does it indicate the likelihood of an invasion and outbreaks in European. The list is based on expert consultation and literature review by Van der Giessen *et al*. (2004), supplemented with a literature review by Van Lier *et al*. (2007) and a study by Gould *et al.* (2006). Those arthropod-borne diseases already mentioned in Table 1 have been excluded. For primary sources we refer to the three articles just mentioned.

Combining Tables 1 and 2, we find that around 12 pathogenic viruses are potential candidates to invade (parts of) Europe, as well as one rickettsia, one bacterium and two protozoa. However, most of these invasions are unlikely to happen in the near future. To illustrate this, between 1969 and 1999, 87 suspected cases of 'airport malaria' were reported in Europe, almost all caused by *P. falciparum*-infected anopheline mosquitoes transported from Africa. None of these caused a mosquito or *Plasmodium* invasion. African anopheline vectors can survive in Europe only during 2-4 months a year. In addition, 52,000 imported malaria cases have been reported since 1953, but none of these has led to a secondary case (Tatem *et al*. 2006b). The return of malaria seems a small risk under the present climate and the present quality of healthcare.

As illustrated by Table 1, most vector-borne disease invasions in Europe resulted from transportation, and a few from bird migration. Climate change has not yet been a main driver. However, it may have played a role in the invasion and subsequent spread of bluetongue in North-West Europe in the warm summer of 2006 (see Chapter 7). In a global review, Sutherst (2004) found very few publications that unambiguously predict a change in the range of a vector-borne disease in response to climate change. One example was dengue, which is expected to expand its range. However, there can be little doubt that if climate change continues, it will become a major driver of vector-borne disease invasion. In an analysis of the potential arbovirus emergence in the UK, Gould *et al.* (2006) even stated that climate change is probably the most important requirement for the emergence of arthropod-borne diseases such as dengue fever, Rift Valley fever, Japanese encephalitis, bluetongue and African horse sickness.

In addition, unpredicted invasions will inevitably take place. As pointed out by Takken *et al*. (Chapter 7), a bluetongue virus outbreak as far north in Europe as in 2006 was considered impossible by several experts. West-Nile virus in North America was another surprise. Furthermore, emerging diseases may come from unknown pathogens and hosts. Over the last 40 years alone, at least 39 new pathogens have been identified (WHO 2007), including HIV, Marburg, Ebola, SARS and BSE / new variant CJ, all of them zoonoses. New species and variants will continue to emerge and vector-borne pathogens, their vectors and their hosts will be no exception. With over a million insect species described, estimates for the total number of insect species range from 2 tot 20 million.

Even not yet existing varieties will pose hazards, such as multiple resistant vectors and pathogens. Evolution never stops and will continue to take us by surprise.

Table 2. Arthropod-borne diseases that are potential candidates for invasion in Europe.

Pathogen	Disease	Reservoir host ( ): not in Europe	Vector ( ): not in Europe	Geographical range of disease
Bunyaviridae				
Phlebo virus	Rift Valley fever	sheep, goat	*Aedes* spp. *Culex* spp.	Africa, Middle East
La Crosse virus	California encephalitis	several mammals incl. red fox, (gray squirrel), (Eastern chipmunk)	*(Ae. triseriatus)*, *Ae. albopictus*	North America
Flaviviridae				
	Dengue fever	humans, (monkeys)	*Aedes* spp.	Tropical Africa, Central America, Southeast Asia
	Japanese encephalitis	birds, pigs	*Ae. albopictus, Culex* spp.	Asia, Australia
	Kyasanur Forest disease/Alkhurma	sheep	ticks	India, Arabic Peninsula
Togaviridae				
	Equine encephalitis (Eastern, Western, Venezuelan)	horses, wild birds	*Aedes* spp., *Culex* spp.	America, Asia
	Ross River virus	various animals	mosquitoes	Australia, South Pacific
Reoviridae				
Coltivirus	Colorado tick fever	rodents	*(Dermacentor andersoni)*	North America
Rickettsiales and Bartonellaceae				
Ehrlichia chaffeensis	Human monocytic ehrlichiosis	deer, raccoon	ticks	America
Gram-negative rods				
Yersinia pestis	Bubonic and pneumonic plague	rodents	fleas	America, Asia, Tropical Africa
Protozoa				
*Plasmodium vivax**, *Plasmodium falciparum**	Benign tertian malaria, Malaria tropica (= Malignant tertian malaria)	humans	Native: *Anopheles* spp. incl. *An. atroparvus,* Alien: *An. quadriannulatus*	Africa, Asia, America. Vector *An. quadriannulatus:* Southern Africa

*Eradicated after WW II in Europe, but re-invasion is not impossible.

Priorities

It is obviously impossible to check every ship, airplane, person and cargo for any possible pathogen or vector species. Therefore it is necessary to identify high-risk vectors, regions, pathways, vehicles and habitats.

Roughly speaking, high-risk *vector groups* for Europe are Culicidae (*Culex* and *Aedes)* and ticks, as indicated in Tables 1 and 2. Some species can transmit several diseases and some can find suitable rural or urban environments in Europe. In addition, some have indigenous relatives that can join them as vectors. Perhaps the most important immediate threats are invasions of the Chikungunya and dengue viruses, which can be transmitted by *Ae. albopictus,* already established in southern Europe.

As for high-risk *regions* for invasions of arthropod-borne diseases in Europe, Tables 1 and 2 make clear that such diseases can come from any continent except Antarctica. But obviously, we first have to look at regions with more or less similar climates. These are not found in the tropics but in the subtropical and temperate zones: East Asia, North America, southern South America, southern Africa, Australia and New Zealand. Among these, we should focus on two subsets:

- Regions with a high biodiversity, which can be expected to have a high diversity of pathogens and vectors as well: East Asia, North America, southern Africa and perhaps Australia.
- Regions with which Europe has most trade and travel, including tourism. These are mainly North America, Japan and increasingly China.

Tatem and Hay (2007) found that North America and East Asia are most similar in climate to central and western Europe. Combining all this, the main risk regions for central and western Europe seem to be North America and East Asia (mainly Japan and China), whilst for southern Europe, southern Africa and Australia should be added.

High-risk *pathways* are ship and air traffic rather than car and train traffic, since Europe has no car and train traffic with North America, Australia and South Africa, and little car and train traffic with East Asia. However, cars, trains and inland navigation can play a key role in the secondary spreading of species from airports and seaports.

High-risk *vehicles* for mosquito vectors are water-filled containers on ships, mainly tyres and plant-containers. Not-disinfected aircraft cabins are an additional risk. As for pathogens, high-risk vehicles are infected humans and live animals, including livestock, pets and associated arthropods. The numerous imported cases of human vector-borne diseases have not yet sparked outbreaks in Europe (Tatem 2006a), but the recent invasion of bluetongue in Northwest Europe may have started from an imported infected animal (see Chapter 7).

We cannot entirely exclude the possibility of terrorists deliberately introducing arthropod-borne pathogens. However, bio-terrorists would probably prefer much more effective weapons such as anthrax, Marburg fever and smallpox. And if livestock would be the target, the foot-and-mouth disease virus is a much more powerful weapon than is the bluetongue virus.

Finally, high-risk *habitats* for mosquito invasion include wetlands, freshwater as well as brackish ones, and water containers (including tiny ones) in urban environments. Heated buildings are also at risk, particularly from subtropical mosquitoes and ticks, as do greenhouses close to seaports and airports, such as those found in the Netherlands.

Strategy for prevention and containment

Two types of invasion

What strategies are feasible if we wish to prevent invasions of vector-borne diseases? This depends on the type of invasion involved: climate-driven or transportation-driven.

Climate-driven invasions cannot be stopped in many cases since they often take place along a broad front. From a conservation point of view, it may not even be wise to stop such invasions, since species need space to adjust their ranges to the changing climate. On the contrary, it may be wise to facilitate such invasions, for example by creating ecological networks. Fortunately, the risk that climate-driven populations will explode is limited by the fact that they will often be accompanied by their natural enemies.

But, of course, nobody will advocate facilitating invasions of human and animal pathogens and their vectors. Next to causing health problems, they could spark habitat destruction from drainage of wetlands. If such species can be contained or eradicated, it should be done. Fortunately, there are few vector-borne diseases likely to invade Europe in response to climate change alone in the next decades.

Transportation-driven invasions, by contrast, can be stopped in many cases, since they often have to pass a narrow entry point (bottleneck) such as a seaport or airport. The risk of population explosions is much greater in such cases, since these species will have lost most of their natural enemies. Here it seems wise to apply the Precautionary Principle for three reasons:

- The damage from an introduction is unpredictable but may be large and widespread.
- The introduction may well be irreversible and the damage permanent.
- Even if eradication, containment or control is possible, prevention is often less costly and less harmful to the environment.

The favoured options are: prevention > eradication > containment > control.

Preventing introduction

The practical opportunities for prevention of invasions depend on the type of vector or pathogen, technical opportunities for detection and identification, and opportunities for eradication.

Mosquitoes are introduced mainly by ship-borne transportation of eggs and larvae in tyres (Tatem *et al.* 2006). Another ship-borne vehicle are ornamental plants such as Bromeliads that carry water in their axils (Lounibos 2002), and *Dracaena sanderiana* plants placed in water or gel (Scholte *et al.* 2007a). There are no confirmed examples of vector establishment from air travel, although there is circumstantial evidence that this has occurred (Tatem *et al.* 2006). This difference is probably due to the fact that airplanes carry small numbers of adult mosquitoes, whilst water jars in ships can carry large numbers of eggs and larvae (Lounibos 2002).

Eggs and larvae can be eradicated by removing water from tyres and applying larvicides in plant containers. Introduction of adult mosquitoes can be prevented by spraying aircraft cabins with insecticides, whilst avoiding health risks. The absence of *Ae. albopictus* from New Zealand, in spite of intensive trade with Japan, may well be the result of strict preventive measures (Tatem *et al.* 2006). In Australia, however, *Ae. albopictus* is a frequent visitor, mostly from the Torres Strait (Ritchie *et al.* 2006).

Introduction of pathogens can be prevented most effectively by avoiding import of infected animals. This requires intensive surveillance and - in case of doubt - quarantine measures. In case of doubt, quarantine should be applied. Another effective measure is minimising transport of vectors, as mentioned. Infected travellers should be taken to hospital as soon as possible and treated in a mosquito-free room.

Surveillance is expensive, so it is necessary to set priorities. Instead of searching for needles in the haystacks of all different travel and trade routes, it is much more efficient to identify high-risk routes and traffic. The focus would be on transportation between distant seaports and airports sharing a similar climate but not a similar fauna, focusing on those routes with most travel and trade. Tatem *et al.* (2006) have recently done innovate research in this field. They found that the present distribution of *Ae. albopictus* can largely be explained by two factors: climatic similarity and traffic volume. They used this to calculate the likelihood of further introductions of *Ae. albopictus* and of malarious *Anopheles* species escaping from Africa.

As for *Ae. albopictus*, Tatem *et al.* (2006 and 2006a) calculated that out of >6,000 possible air travel routes, 8 of the top 10 risk routes depart from Japanese airports, one from a South-Korean and one from a Taiwanese airport. None of these routes have a European destination. However, out of >25,000 possible shipping routes, the top 20 all depart from Japanese seaports and 5 of these have a European destination: Genoa. This was one of the earliest European cities to report *Ae. albopictus*, which was established there in 1990.

As for *Anopheles*, Tatem *et al.* (2006) calculated the likelihood of four principal members of the *An. gambiae* complex, effective vectors of *P. falciparum,* escaping from Africa. One conclusion is that *An. gambiae sensu stricto* can be introduced in tropical Asia and America, but very unlikely in Europe. The southern species *An. quadriannulatus* Theobald is a more serious candidate for introduction in (Mediterranean) Europe, particularly by sea traffic. However, it is a less efficient malaria vector because it rarely bites humans (Takken *et al.* 1999).

Finally, Tatem and Hay (2007) calculated how the climate similarities between airports across the globe change with the seasons. One conclusion was that central and western Europe is climatically most similar to Japan and China in January, but to the eastern USA in July.

Such sophisticated analyses can greatly help to prioritise monitoring, inspection and quarantine efforts. Predictably, the fast-growing economy of China will figure more and more in such analyses.

Eradication

There are various ways to prevent species from spreading following introduction. One is to minimise the area of suitable habitat for such species (e.g. wetlands in the case of mosquitoes) in the vicinity of seaports and airports. But once a vector or a pathogen, or both, have already started to spread, quick eradication becomes crucial. Various methods are available.

For eradicating vectors, at least mosquito vectors, classic methods are drainage of artificial and natural water pools and spreading of (acceptable) insecticides, particularly larvicides. Biological control by natural enemies, though sometimes very effective in controlling an established species, is rarely appropriate to eradicate it or to prevent it from spreading. Introduction of sterilised or genetically modified males may be more effective. For example, the New-World screwworm fly *Cochliomyia hominivorax* (not a vector but a parasite) was eradicated in North Africa in 1991, soon after its establishment, by the introduction of sterilised males (Kouba 2004). However, this technique has been less successful in the case of mosquito or tick control.

Once a vector has spread, eradication becomes much more difficult, but it may still be feasible if the species has an Achilles heel, such as slow dispersal or a narrow range of hosts or habitats. A classic example is the eradication of *An. gambiae* in Brazil. The mosquito had spread widely in the northeast of the country from 1930. The large-scale eradication campaign that was launched could be successful only because the mosquito mainly bred in small pools, borrow pits, and shallow wells dug for drinking water near houses, not in forests. Furthermore, the mosquito did not fly long distances (Elton 1958, Lounibos 2002, Killeen 2003).

If a pathogen has spread, eradication methods include vector control, vaccination of infected people or livestock (provided an appropriate vaccine is available) and isolation and treatment of infected people or livestock with drugs. In the case of livestock, culling of (suspected) infected animals is an additional option.

The most spectacular eradication success story is the worldwide eradication of the smallpox virus, completed in 1977, applying mass vaccination, case finding (supported by local people) and isolation of infected persons (Fenner *et al.* 1988). However, this campaign could be successful only because the smallpox virus has no other reservoir hosts than humans.

One success story involving a vector-borne pathogen was the eradication of malaria from vast non-tropical regions in North America, Australia, Asia and Europe after World War II. This was achieved through campaigns that combined patient treatment with mosquito control using drainage or spraying of water pools. *Plasmodium vivax* and *P. falciparum* vanished from the whole of Europe (but see Chapter 3). But again, these *Plasmodium* species have no other reservoir hosts than humans, at least not in Europe. Eradicating a pathogen that has a broader host and reservoir range is much more difficult.

If the species has spread and cannot be eradicated at reasonable costs, further spread can in some cases be prevented by containment, applying the same methods as mentioned above. In severe cases the creation of distribution barriers, comparable to fire-lanes in forests, would be considered, such as zones of dry land where mosquitoes cannot breed, or fences that stop big mammal vector species[25]. However, effective barriers will be feasible in few cases.

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[25] One extreme example of containment of an animal is the long fence established in Australia in the early 20th century to contain the dingo, a notorious sheep killer. The fence is 5614 km long, three times as long as the Great Wall of China (Bomford and Hart 2002). Such fences can perhaps contain an introduced reservoir host species in exceptional cases, but not a pathogen or a vector.

If containment is not an option or fails, the last resort is control. Effective control should be integrated, combining ecological, biological and chemical methods with social strategy, as advocated by Spielman and D'Antonio (2001) and Utzinger *et al.* (2002) for malaria. In some cases, an organised counter-invasion by a natural enemy introduced from the native area of the vector species can be effective, though no success stories involving mosquitoes are known to us.

International regulations

Even though preventive measures are to be preferred, it is precisely such measures that can easily come into conflict with international trade and thereby with economic interests. There is a basic contradiction between free trade and the protection of humans, animals, plants and ecosystems from introduced pathogens, vectors and pests. Some advocates of free trade therefore argue that such risks are a fact of life in a globalising world and should be accepted in view of the benefits of free trade to the economy and human welfare. However, this viewpoint seems to be one-sided and short-sighted and is not justified by present trading rules.

When the first global system of trading rules, the General Agreement on Tariffs and Trade (GATT) was developed and implemented in 1948, the risk of spreading diseases and pests was recognised and provisions were included to reduce such risks. Contracting parties were allowed, under certain conditions, to close their borders for those imports representing a proven risk of introducing diseases.

Several other multilateral agreements were adopted that specifically aim at the protection of human, animal and plant health and biodiversity.

Protecting biodiversity

The most comprehensive international agreement on the subject of introducing alien species is the Convention on Biological Diversity (CBD), agreed in Rio de Janeiro in 1992. It states that each contracting party shall, as far as possible and appropriate, prevent the introduction of, or control or eradicate those alien species that threaten ecosystems, habitats or species (IAS).

A key principle is the precautionary approach: a state should take appropriate action even if there is lack of scientific certainty. A state should give priority to prevention of introduction of IAS above eradication, containment and control.

Protecting human health

A second relevant multilateral agreement is the new International Health Regulations. The regulations aim to provide a legal framework for the prevention, detection and containment of public health risks at source, before they spread across borders, through the collaborative actions of states parties and the World Health Organisation.

Protecting animal health

The need to control (communicable) animal diseases at global level led to the creation of the Office International des Epizooties (OIE; World Organisation for Animal Health) in 1924. Each member country reports the (communicable) animal diseases that it detects on its territory. The OIE then disseminates the information to other countries, which can take the necessary preventive action. This information also includes diseases transmissible to humans as well as intentional introduction of pathogens. The OIE develops normative documents relating to rules that member countries can use to protect themselves from the introduction of diseases and pathogens, without setting up unjustified sanitary barriers.

Trade rules

Relevant World Trade Organisation agreements on the subject of diseases are the Agreement on Technical Barriers to Trade (TBT) and the Agreement on the application of Sanitary and Phytosanitary Measures (SPS).

Under the TBT legitimate objectives to regulate the import of goods include:
- protection of human health or safety;
- animal or plant life or health;
- the environment.

For example, based on the TBT, the Dutch government issued a covenant for the import of Lucky Bamboo *Dracaena sanderiana*. The interest to be protected was public health (http://www.bis.org.in/sf/feb2007/gtbtn07NLD73.doc, accessed 10 September 2007). This was not specified in more detail, but in 2005 *Ae. albopictus* was discovered in containers with lucky bamboo imported from China (Scholte *et al.* 2007a,b).

Under the SPS, measures can be taken to protect animal or plant life or health from risks arising from the entry, establishment or spread of pests, diseases, disease-carrying organisms or disease-causing organisms.

Clearly, both TBT and SPS allow restrictions on imports of human, animal and plant pathogens as well as their vectors. This includes imports of car tires and plants carrying a high risk of containing vectors.

However, a state may not regulate the import of goods with the effect of creating unnecessary obstacles to international trade. For this purpose, regulations shall not be more trade-restrictive than necessary to fulfil a legitimate objective.

Gaps in multilateral regulations

Specific gaps in the international regulatory frameworks persist, notably in relation to species that are invasive, but do not qualify as plant pests under the international agreements, with regard to a number of pathways. These include:
- Unintentional introductions of invasive alien species through international assistance and humanitarian programmes, tourism, military, scientific research, cultural and other activities.
- Intentional introductions of alien species for non-food purposes, including certain aspects of horticulture and trade in pets and aquarium species.

One surprising gap in the European regulatory framework is that the EU can intervene in case of an invasion that threatens livestock or crops, but not in case of an invasion that threatens public health.

Summarising, whilst the global transportation network, the trade volumes and the number of trade-related invasions are growing, the legal framework for preventing trade-related bio-invasions is developing as well, even though there are major gaps to be filled.

Suggested guidelines

The frequency of invasion of vectors and their pathogens is likely to increase further in the course of this century, as the three main drivers continue to operate:

- Global travel and transportation will continue to grow. Species will move even faster, further and in greater numbers than today.
- Habitat transformation will also continue, including the creation of disturbed habitats that are often used as bridgeheads by invasive species. In Europe, the restoration of freshwater and saline wetlands may provide new habitat for introduced mosquitoes. And the creation of habitat networks such as Natura 2000 of the European Union (EU) may facilitate the spread of some introduced species, including ticks, with their reservoir hosts.
- Climate change has become an additional driver of bio-invasion and will continue as well, making some regions less, and others more suitable for pathogens, their reservoir hosts and their vectors. As vector-borne diseases mainly occur in the tropics and subtropics, Europe may see more of such diseases invading.

Since climate-driven invasions are much more difficult to stop than transportation-driven invasions, it seems wise to concentrate prevention and control efforts on the latter. We suggest applying the following guidelines[26]:

1. Put prevention first. Apply the Precautionary Principle to all transportation-driven invasions. As for climate-driven invasions, confine application to high-risk invasions.
2. Effective prevention should include:
    - Prepare risk analyses for a wide range of candidate invasive pathogens and vectors, for Europe at large as well as for individual states. Culicid mosquitoes and ticks deserve particular attention. These analyses would include the likelihood of invasion for various species/pathway combinations, expected impacts, methods of prevention, eradication and control as well as the costs involved. For a few pathogens the possibility of deliberate introductions by bio-terrorists would be taken into account as well.
    - Identify high-risk travel and trade flows. For pathogens, these include: live animals as well as humans travelling from regions where harmful vbds are endemic. For mosquito vectors: air in airplanes as well as water and gel in containers on ships. For ticks: live animals.
    - Identify high-risk travel and transportation routes. Focus on high volume transportation between distant seaports and airports having a similar climate but not a similar fauna, using models such as those developed by Tatem *et al.* (2006).
    - Identify high-risk habitats for invasion and minimise such habitats in the vicinity of seaports and airports. Or, alternatively, minimise specific high-risk transportation volumes to specific seaports or airports.
    - Prepare contingency plans for a wide range of risk species invasions, similar to the current plans for outbreaks of highly contagious human and veterinary diseases. Make sure that appropriate insecticide, vaccine and drug stockpiles as well as skilled manpower will be available within a matter of days.

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[26] Many of these recommendations were taken from Wittenberg and Cock (2001) and Van der Weijden *et al.* (2007).

- Try and prevent deliberate or accidental introduction of every species considered a risk, or for which no risk-analysis is available. This requires at-source measures in exporting countries, including surveillance, interception or disinfection of contaminated cargo, and disinfection of airplanes, ships and risk cargo. Supplement this in importing countries by strict border checks, interception and quarantine measures at seaports and airports.

3. When, in spite of such measures, a risky alien pathogen or vector or pest is found, or a species for which no risk analysis is available, try and eradicate it as soon as possible. Mosquitoes can be eradicated by drainage of natural and artificial water containers and by using pesticides and sterilised males. Many pathogens can be eradicated by rapid isolation and treatment of infected persons or animals, vaccination, and – if necessary - culling of infected animals.
4. If the species has nevertheless spread and cannot be eradicated at reasonable costs, try and contain its range, applying the same methods as mentioned under 3. In severe cases the creation of distribution barriers can be considered.
5. Raise awareness of the risks of bio-invasions among tourists, exporters, transporters, importers, customs-officers and other stakeholders.
6. Develop and promote best preventive practices for the travel and trade business. 'Global hygiene' in travel and trade should become as generally accepted as hygiene has become in private and social life.
7. The present EU system of individual identification and registration of livestock is a powerful tool in tracking and tracing infected animals in case of an outbreak and controlling that outbreak. The system is less relevant for vector-borne disease, since vectors can move unchecked. But in the early stages of an invasion of a pathogen or tick vector species, the system can help to eradicate that species.
8. Introduce a legal obligation to report emerging alien harmful species, while compensating the reporting party for the cost in case of isolation and eradication.
9. Make importing firms and persons legally liable for the economic damage from species introductions.
10. Improve coordination between (or merge) specialised agencies responsible for bio-invasions harming public health, animal health, plant protection, fisheries, gardening and nature. For example, the West-Nile virus is hosted by many bird and mammal species including humans and transmitted by many mosquito species. That renders an ecological and integrated approach inevitable.
11. Enhance multidisciplinary research on vector-borne diseases, including experts in entomology, ornithology, ecology, epidemiology, virology, climatology, logistics, economy and law.
12. One challenge is the development of predictive models for the various stages of bio-invasion. For example, models to predict the likelihood of species *A* being introduced in seaport *B* from seaport *C* with cargo type *D*.
13. Improve international coordination, both at the European and global level. Introduce an obligation for EU members to mutually inform and consult each other on bio-invasions and measures taken, and to provide assistance in prevention, eradication and control efforts. Mandate the EU to intervene in case of an invasion that threatens public health and can affect other member states. In addition, mandate the EU to build up strategic stocks of vaccines and pesticides. Comply with present 'safe trade' agreements (SPS and TBT). Negotiate more specific agreements with high-risk countries such as Japan and China. And where necessary, fill the gaps in the global regulations.

More generally speaking, so far as trade is concerned, the ultimate goal would be to detach biological from economic globalisation and to replace free trade with safe trade.

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