Zoonotic aspects of vector-borne infections

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Summary
Vector-borne diseases are principally zoonotic diseases transmitted to humans by animals. Pathogens such as bacteria, parasites and viruses are primarily maintained within an enzootic cycle between populations of non-human primates or other mammals and largely non-anthropophilic vectors. This ‘wild’ cycle sometimes spills over in the form of occasional infections of humans and domestic animals. Lifestyle changes, incursions by humans into natural habitats and changes in agropastoral practices create opportunities that make the borders between wildlife and humans more permeable. Some vector-borne diseases have dispensed with the need for amplification in wild or domestic animals and they can now be directly transmitted to humans. This applies to some viruses (dengue and chikungunya) that have caused major epidemics. Bacteria of the genus Bartonella have reduced their transmission cycle to the minimum, with humans acting as reservoir, amplifier and disseminator. The design of control strategies for vector-borne diseases should be guided by research into emergence mechanisms in order to understand how a wild cycle can produce a pathogen that goes on to cause devastating urban epidemics.

Keywords

Introduction: from enzootic cycle to epidemic cycle, from epidemic cycle to urban cycle

Vector-borne diseases are responsible for 22.8% of emerging infectious diseases and 28.8% of those that have emerged over the past decade (1). This resurgence has coincided with climate change, which supports the hypothesis that the climate is influencing the emergence of vector-borne diseases, as vectors are sensitive to environmental conditions (rainfall, temperature, etc.). These diseases are among the leading causes of morbidity and mortality in both humans and animals. For example, dengue fever infects between 50 and 100 million people each year, with a mortality rate of up to 2.5% (2). Rift Valley fever was responsible for massive epizootic outbreaks among domestic animals, killing 3,500 lambs and 1,200 ewes in Kenya in 1930 (3). West Nile fever decimated part of the bird population on the North American continent and infected 40,000 people, with nearly 1,700 deaths between 1999 and 2013. The tick-borne encephalitis virus is responsible for the most important neuroinvasive disease transmitted by ticks in Europe and Asia, with several thousand human cases a year and mortality of up to 35% depending on the subtype concerned (4). Their common feature is that they have an etiological agent of viral origin. There are more than 500 arthropod-borne viruses, one-quarter of which cause human diseases, such as haemorrhagic fever and meningoencephalitis, which can result in death (5).

Mosquitoes are the leading vector for human infectious agents, followed by ticks (6). Globally, ticks are the vectors that transmit the greatest variety of infectious agents (bacteria, parasites and viruses) to both humans and
animals. It is important to note that no ticks are specific to humans, who always become infected accidentally. As they transmit an enormous number of bacteria, parasites and viruses, ticks are the main vectors for the majority of zoonoses worldwide. For example, Lyme disease, which is associated with bacteria of the tick-borne genus *Borrelia*, has become widespread in temperate regions, especially in the United States, with nearly 300,000 new cases each year, compared with only 60,000 in Europe.

Vector-borne pathogens (bacteria, parasites and viruses) are transmitted between vertebrate hosts by an arthropod vector that ensures biological transmission. These pathogens include arboviruses, which are responsible for zoonoses that originally existed solely in highly complex forest and rural ecosystems. These zoonoses involve many vector species (mainly zoophilic) that infect a wide variety of non-human hosts. Viral emergence coincides with the uptake of a wild virus by an anthropozaophilic arthropod (which bites both humans and animals), thereby initiating a human-to-human transmission cycle in which humans become the main amplifier host. Anthropozaophilic mosquitoes mainly occur in an urban environment where a single vector species and a single (human) vertebrate host ensure transmission. Arboviruses such as dengue fever or chikungunya have now dispersed with the need for a sylvatic cycle to produce epidemics. They have succeeded in exploiting the human environment by taking advantage of the strong anthropophilic tendency of vectors that feed on human blood and by expanding into breeding sites created by humans. Tick-borne pathogens include many bacteria, parasites and viruses that circulate mainly in forest areas as part of a cycle involving ticks and wild animals (rodents, rabbits, ungulates and birds). Humans are only infected accidentally when they enter forest habitats. Some bacteria or parasites circulate mainly in domestic animals and, in this case too, humans are only infected occasionally. Just as arboviruses infect mainly humans, certain bacteria carried by fleas or sandflies are transmitted from human to human without the need for a mammal as an amplifier host.

**Enzootic cycle with accidental infection of humans**

Arboviruses circulate primarily in a forest cycle in which the virus is transmitted between populations of vertebrates (such as monkeys and rodents), with zoophilic arthropods acting as vectors. Humans are only infected accidentally. Rift Valley fever, transmitted by mosquitoes, is a zoonotic disease that primarily occurs in epizootic outbreaks when environmental conditions exacerbate the proliferation of vectors. Similarly, Venezuelan equine encephalitis, transmitted by mosquitoes and endemic in the Americas, caused the death of hundreds of thousands of horses in the 1960s, with many human cases. Finally, Crimean-Congo haemorrhagic fever, transmitted by ticks, causes outbreaks of viral haemorrhagic fever with extremely rapid multiplication of the virus in animals (cattle, sheep and goats, but with no clinical signs), resulting in human infection with a very high mortality rate. Tick-borne pathogens include many viruses, bacteria and parasites that circulate mainly in forest zones where ticks live alongside wild animals (rodents, rabbits, ungulates and birds). Humans are only infected accidentally when they enter forest environments. This applies to the bacteria that cause Lyme disease, with thousands of new cases reported each year in Europe and the United States. Similarly, the tick-borne encephalitis virus is responsible for the most important neuroinvasive disease transmitted by ticks in Europe and Asia, with several thousand human cases a year.

**Examples of viruses transmitted by mosquitoes/ticks**

**Rift Valley fever virus**

The Rift Valley fever virus, described for the first time in 1931 in Kenya’s Rift Valley (3), belongs to the family *Bunyaviridae* and the genus *Phlebovirus*. It is responsible for epizootic outbreaks affecting mainly domestic ruminants (cattle, sheep, goats, buffalo), causing abortions and high mortality rates in young animals. Before 1977, Rift Valley fever was confined to sub-Saharan Africa, where it mainly caused epizootic outbreaks; human cases were rare and not serious. In 1977, there were widespread epizootic outbreaks in the Nile delta where many human fatalities were reported (7). The virus also struck the island of Madagascar in 1990/1991 (8). In 2000, it occurred outside the African continent, simultaneously in Yemen and Saudi Arabia (9). Human infection usually presents as flu-like symptoms with possible complications, such as encephalitis and hepatitis, accompanied by haemorrhagic fever, often leading to death. Unlike with other arboviruses, contact with the tissue of infected animals or the inhalation of aerosols can lead to infection. A live attenuated Smithburn vaccine is available, which is administered mainly to cattle. In Africa, nearly 30 species of mosquito belonging to the genera *Aedes*, *Culex*, *Anopheles*, *Eretmapodites* and *Mansonia* have been found naturally infected by Rift Valley fever virus. It has also been isolated in other insects such as biting midges, black flies and ticks. Rift Valley fever virus also has an extremely wide range of vertebrate hosts. Factors known to have increased the epidemic risk in the past include the heavy rainfall that accompanied El Niño in East Africa in 1997 and 1998, the construction of the Aswan and Diama dams in Egypt in 1977 and water impoundment along the Senegal River in 1987. Rift Valley fever virus has very high epidemic potential; the arrival of an infected human or animal in the viraemic phase would probably be sufficient to trigger vector-borne transmission because of the wide range of hosts that the virus is capable of infecting.
Venezuelan equine encephalitis virus

The Venezuelan equine encephalitis virus, which is an alphavirus of the family Togaviridae, is endemic in the New World. It was isolated for the first time in 1938 (10). The zoonotic cycle in tropical forest involves rodents as reservoir hosts and mosquitoes of the sub-genus Culex (Melanoconion) as vectors. The virus is transmitted to humans and horses by mosquitoes of the genera Psorophora (P. conifinis, P. columbanae) and Ochlerotatus (O. taeniorhynchus, O. sollicitans). The substitution of certain amino acids in the virus envelope (E2) of certain enzootic strains would seem to have intensified viraemia in horses, allowing infection of mosquitoes. Humans are only accidentally infected and develop a highly debilitating dengue-like fever that can sometimes degenerate into fatal encephalitis.

Crimean-Congo haemorrhagic fever virus

Crimean-Congo haemorrhagic fever (CCHF) is caused by a nairovirus of the family Bunyaviridae, causing severe haemorrhagic fever in humans, with a mortality rate of 10–40%. The virus was isolated for the first time in the Democratic Republic of Congo in 1944 (11) and is found in Africa, Europe, the Middle East and Asia. The virus is transmitted mainly by ticks of the genera Hyalomma (H. marginatum or H. anatolicum), Rhipicephalus, Ornithodoros, Boophilus, Dermacentor and Ixodes. The vertebrate hosts are wild mammals (including buffalo, wild boar and mountain sheep) or domestic mammals (cattle, goats, sheep, horses, camels); these animals become infected with no apparent clinical signs (12). Only humans appear to show pathological signs when infected by the virus, which means that circulation of the virus can be detected only from human cases among livestock or crop farmers or veterinarians. Humans become infected by tick bites or by direct contact with infected tissue or blood (13). There is no vaccine for either humans or animals. Environmental changes associated with human activities (war, new agropastoral practices, etc.) appear to be the major factors disrupting the zoonotic cycle and creating conditions conducive to the emergence of epidemics. Of all the tick-borne viruses infecting humans, CCHF is the one with the widest geographic distribution, raising fears of an upsurge of the disease in temperate regions, especially Western Europe.

Tick-borne encephalitis virus

The tick-borne encephalitis virus belongs to the family Flaviviridae and the genus Flavivirus. It was described for the first time in 1931 in Austria, but the virus was not isolated until 1937 in Russia (18). In countries where the virus is present, reports of indigenous human cases and/or its detection in ticks collected in the field show that the virus foci are fairly stable. The wild cycle involves mainly tick populations that remain infected throughout their lifetime (19) (Ixodes ricinus in Western Europe and I. persulcatus in Eastern Europe and Asia) and wild small mammals (field mice, voles), which act as reservoirs (20). Several other wild and domestic species, as well as humans, are believed to be accidental hosts that develop little or no viraemia, rendering them unable to transmit the virus via the vector (21). They may nevertheless be used as sentinels for monitoring the risk of zoonosis (22).

Human infection is seasonal, peaking in the spring and summer, linked with the activity of the vector ticks. The human endemic area covers most of Eastern Europe, as well as Siberia and the Far East. These three areas correspond to the three different sub-types of the virus, with the geographic distribution of each virus more or less correlating with the geographic distribution of its vector. Human infection generally presents as flu-like symptoms with possible complications, such as meningoencephalitis of varying severity. Mortality is between 0.5% and 3% for the European and Siberian sub-types, but can be as high as 35% for the Far Eastern sub-type. Neurological sequelae occur in 10% of cases for the European sub-type but are higher for the other sub-types (23). Humans can also become infected by eating raw dairy products (cheese, milk) (24). An inactivated vaccine is available.

Examples of bacteria transmitted by ticks

Borrelia burgdorferi, sensu lato

Lyme disease is caused by spirochete bacteria belonging to the species Borrelia burgdorferi sensu lato. The natural cycle involves ticks of the genus Ixodes and a wide range of animal species that can act as reservoirs (rodents, rabbits, birds, lizards, etc.) (14, 15). The disease has a very wide range, which coincides with that of its various vectors, mainly in the northern hemisphere: I. scapularis and I. pacificus in North America (east and west coast respectively); I. ricinus in Western Europe; and I. persulcatus in Eastern Europe and Asia. The disease nevertheless appears to extend to the southern hemisphere, with human cases reported in Australia and South America. Animals and humans are both infected by the bites of infected ticks. Of the 19 species of Borrelia identified to date, just one – B. burgdorferi sensu stricto – is recognised as pathogenic for humans in North America, compared with five species in Europe: B. burgdorferi s.s., B. garinii, B. afzelii, B. spielmanii and B. bavariensis. Three other species are potentially pathogenic: B. bissetii, B. lusitaniae and B. valaisiana. In humans, the most common clinical sign is inflammation of the skin or erythema migrans. We also see arthritis, neuroborreliosis or even delayed cutaneous manifestations, depending on the Borrelia species involved (16, 17).
Epidemic cycle, from animals to humans

The emergence of a pathogen from a forest cycle involves the enzootic cycle coming into contact with humans and domestic animals. The trophic preferences of vectors therefore play a fundamental role in transmitting pathogens from animals to humans. Yellow fever, which originally operated in a forest cycle in which the virus moved between populations of monkeys and zoophilic mosquitoes in the forest canopy, underwent a process of urbanisation, mainly in Africa, where the virus is transmitted by a highly anthropophilic domestic mosquito, *Aedes aegypti*. Similarly, the West Nile virus formerly affected mainly migratory birds that acted as animal reservoirs. It has now become the second most widespread arbovirus in the world, after the dengue virus. It infects humans, who were previously only an accidental host, and over the past decade numerous fatalities have been reported in Europe (Greece) and the United States. Finally, Japanese encephalitis is one of the major viral diseases in rural areas of the Asian continent, where it once affected only wild birds and bats. This epidemiological profile was completely overturned with the introduction of intensive pig farming (pigs are the most effective amplifier host), facilitating transfer of the virus to humans living nearby. Certain tick-transmitted bacteria and parasites are capable of infecting many wild animals, as well as domestic animals, in which they cause serious disease. This is true of the bacterium *Anaplasma phagocytophilum*, which causes granulocytic anaplasmosis in animals and humans, as well as of parasites of the genus *Babesia*. Close contact with infected domestic animals is a source of human infection as it increases the chance of encounters between ticks and humans.

Examples of viruses transmitted by mosquitoes

Yellow fever virus

The yellow fever virus belongs to the genus *Flavivirus* of the family *Flaviviridae*. It was isolated in West Africa in 1927. To date, seven genotypes have been identified: five in Africa and two in the Americas (25). In Africa, the virus is transmitted in a forest cycle between non-human primates and zoophilic mosquitoes such as *Aedes africanus*. The virus was able to leave the forest with the help of mosquitoes capable of biting humans (*Ae. luteocephalus*, *Ae. furcifer*, *Ae. metallicus*, *Ae. apoh*, *Ae. taylori*, *Ae. vitattus* and members of the simpsoni complex). Urban yellow fever is found only in Africa, where human-to-human transmission is via the anthropophilic mosquito *Ae. aegypti*. The situation is completely different in the Americas, as only a forest cycle remains, in which the virus circulates between monkeys and sylvatic vectors of the genus *Haemagogus*. However, the steady spread of the vectors *Ae. aegypti* and *Ae. albopictus* is raising concern over the return of urban yellow fever epidemics in South America, as in the past. Although there is a safe and effective vaccine, vaccine 17D, it is not used extensively in the yellow fever-endemic region in Africa, which covers 34 countries with 500 million inhabitants.

West Nile virus

The West Nile virus provides an impressive example of the speed with which an arbovirus can invade five continents. This Flavivirus of the family *Flaviviridae*, isolated in Uganda in 1937, is maintained in nature in an enzootic cycle between *Culex* mosquitoes and several bird species. There are seven West Nile virus strains, with lineage 1 the most widely distributed in Africa, Europe and the Americas. In 1994, the West Nile virus became more active again in the Old World, with greater pathogenicity for humans and/or horses. In 1996, there was an epidemic in Bucharest (Romania) with more than 500 cases of encephalitis. In 1999, 40 deaths were reported in Russia and in 2000 eight deaths were reported in Israel. In 1999, the West Nile virus (genotype NY99) was introduced to New York, probably by an infected bird from the Middle East, and spread throughout the Americas. By 2002, a new genotype (WN02) had displaced it. WN02 has an amino acid substitution (V159A) in the envelope protein, which facilitated adaptation of the virus to mosquitoes of the genus *Culex* (26). This illustrates the plasticity of the viral genome, which can facilitate adaptation to other vectors, including anthropophilic vectors that play a key role in the emergence of epidemics. The West Nile virus has been isolated in more than 70 species of mosquito, mainly of the genus *Culex*, and in particular *Culex pipiens*, a sub-species of which (*C. p. molestus*) has a preference for biting mammals.

Japanese encephalitis virus

The Japanese encephalitis virus belongs to the family *Flaviviridae* and the genus *Flavivirus* and was first described in 1871 in Japan during an encephalitis epidemic in horses and humans. It is endemic in Asia, from the People’s Republic of China to Indonesia and from India to the Philippines. This virus has five strains: lineages 1, 2 and 3 are found in subtropical and temperate regions, and lineages 4 and 5 are confined to the Indonesian archipelago (27). More than 3 billion people worldwide live in areas at risk, with an estimated 30,000 to 50,000 cases each year. The geographic area where Japanese encephalitis is endemic has expanded over the past 70 years, with the virus spreading westwards. The Japanese encephalitis virus is transmitted in a zoonotic cycle between species of *Culex* (*Culex tritaeniorhynchus*) and pigs or birds. Humans are only accidentally infected and are considered a dead-end host for the parasite because of their low level of viraemia. Nevertheless, this is beginning to change owing to the growth in rice cultivation areas (where vectors proliferate) close to pig farms, where pigs amplify
the virus. For this reason, Japanese encephalitis should not be considered an exclusively rural disease, as it is starting to reach the outskirts of villages and even towns.

**Examples of bacteria and parasites transmitted by ticks**

*Anaplasma phagocytophilum*

Human or animal granulocytic anaplasmosis is caused by a small obligate intracellular gram-negative bacterium, *Anaplasma phagocytophilum*, of the family Anaplasmataceae (order Rickettsiales). Many tick species act as vectors for this bacterium: *I. ricinus* in Europe, *I. persulcatus* in Russia and Asia and *I. scapularis, I. pacificus* and *I. spinipalpis* in the United States (28). This disease, described for the first time in sheep in Scotland in 1932, has been reported in both animals and humans in Europe, Asia, the United States and Australia. Many wild mammals are naturally infected with this bacterium, including rodents, insectivores and wild ruminants such as roe deer (*Capreolus capreolus*) and red deer (*Cervus elaphus*). In the United States, it appears that domestic ruminants are not affected a great deal, but in Europe, ruminant livestock (cattle, sheep, goats), along with horses, are the animals most affected by this bacterium (29). The first human cases of granulocytic anaplasmosis were reported in the United States in the 1990s, and the number of cases has continued to grow since. Its current incidence is estimated at 6.1 cases per million inhabitants (30). In Europe, cases were first described in Slovenia in 1997, followed by many other countries, including Sweden, Greece, Spain, Russia and France. The real frequency of human infection is probably underestimated because of the high levels of seroprevalence detected, both in the United States (11–15%) (31) and in Europe (2–28%) (32). The clinical signs in domestic ruminants range from a high fever to a reduction in milk yield; in other mammals, the clinical signs can be very diverse, but the infection is often asymptomatic. In humans, the disease causes a high fever with chills, but, in general, anaplasmosis is not particularly serious. A small number of fatalities have been reported in both animals (domestic ruminants and wild animals) and humans (less than 1% of cases) (29).

*Babesia divergens, B. venatorum and B. microti*

Babesiosis is caused by obligate parasites (intracellular protozoa) that are transmitted by hard ticks and are capable of multiplying in many wild and domestic animals. However, only three species of *Babesia* are transmissible to humans: *B. divergens*, *B. venatorum* (EU1) and *B. microti*. Fifty or so human cases have been reported in Europe but this is probably an underestimate, because babesiosis takes many asymptomatic forms. *Babesia divergens* is a cattle parasite that can be transmitted to humans by the bite of the tick *I. ricinus*. This parasite is responsible for most of the human babesiosis cases in Europe (33); it is most widespread in temperate zones and its range continues to grow. This same parasite is also capable of infecting wild animals, including ungulates and some rodents (34, 35). *Babesia venatorum*, a species phylogenetically related to *B. divergens*, is also transmitted by the tick *I. ricinus*, and squirrels are strongly suspected of acting as reservoirs. It is increasingly being found in humans (36) and in ticks and wild ruminants in peri-urban forest areas (35). *Babesia microti* is a parasite of rodents transmitted by ticks of the genus *Ixodes*, including *I. ricinus* in Europe. Although it is responsible for several hundred human cases each year in the United States (37), only one human case has been reported in Europe to date (36).

**Urban cycle: the unique role of humans**

Some pathogens have dispensed with the need for amplification in wild or domestic animals and can now be transmitted directly to humans. The dengue and chikungunya viruses are prime examples of this: human hosts act simultaneously as the reservoir, amplifier and disseminator and the major vector is the strictly anthropophilic *Ae. aegypti*, which is found in urban areas that provide conditions conducive to their proliferation. Dengue is the leading arbovirosis in terms of human morbidity and mortality; this has been exacerbated in recent decades by the co-circulation of four dengue serotypes throughout virtually the entire inter-tropical convergence zone. Chikungunya tends to invade tropical regions, with incursions into temperate regions following the modification of an amino acid in the viral envelope that facilitates transmission by a vector which previously had only rarely been involved in transmission, *Ae. albopictus*. The bacteria *Bartonella bacilliformis*, transmitted by sandflies, and *Bartonella quintana*, transmitted by body lice, illustrate how bacteria are also able to dispense with an intermediate animal amplifier host; humans are considered to be the reservoir of both these pathogens.

**Examples of viruses transmitted by mosquitoes**

**Dengue virus**

The dengue virus, which is of the family *Flaviviridae* and the genus *Flavivirus*, is responsible for the most important arboviroses in terms of public health (38). There are four serotypes (DENV-1 to DENV-4), each of which is subdivided into five genotypes. Acquired immunity following infection by one of the serotypes confers protective immunity against the infecting serotype but not against the others. Ancestral forms of dengue virus formerly circulated in sylvatic cycles between populations of non-human primates and forest
canopy mosquitoes, which are relatively non-anthropophilic. These cycles have been described in Asia and Africa. Each of the dengue serotypes responsible for recent epidemics has evolved independently of the others from a sylvatic strain of the same serotype. Nowadays, human infections are caused by dengue virus strains which amplify only in humans, who become reservoir, amplifier and disseminator host. The clinical picture ranges from asymptomatic to classic dengue fever to dengue haemorrhagic fever, which can be fatal. Every year around 50–100 million people are infected, with a mortality rate of up to 2.5%. While classic dengue fever occurs practically everywhere in the range of the urban vector, *Ae. aegypti*, dengue haemorrhagic fever is more widespread in South-East Asia and tropical America. The dengue fever situation there is worsening, with a noticeable rise in the mortality rate. This appears to have coincided with degradation of the urban environment (rapid, uncontrolled urbanisation in developing towns and cities), increasing the number of potential breeding sites and promoting the proliferation of vectors. South-East Asia has become the major focus of dengue virus, with the co-circulation of four serotypes, resulting in a situation of hyperendemicity. Dengue haemorrhagic fever was first described in the Philippines in 1953–1954. In the absence of specific symptomatic treatments, Sanofi Pasteur is developing a tetravalent vaccine (phase III) against all four serotypes (39).

Chikungunya virus

The chikungunya virus, which was first isolated in Tanzania in 1952, belongs to the family Togaviridae and the genus Alphavirus. The name chikungunya derives from the Makonde word meaning ‘that which bends’, referring to the clinical signs of infected patients. Three genotypes have been described: East/Central/South African (ECSA), West African, and Asian. This virus, originally from Africa, is maintained within a forest cycle involving non-human primates and sylvatic mosquitoes of the genus *Aedes*, such as *Ae. furcifer, Ae. taylori, Ae. luteocephalus, Ae. dalzieli, Ae. vittatus* and *Ae. africanus* (40). Unlike in Africa, in Asia the chikungunya virus circulates in urban areas, where it is transmitted by house mosquitoes of the genus *Aedes* (Ae. *aegypti* and Ae. *albopictus*), with humans acting as the main amplifier host. Chikungunya symptoms include high fever, joint pain, headache, muscular pain and a rash. In 2004, the ECSA genotype of the chikungunya virus re-emerged in Kenya, from where it spread for the first time to the Indian Ocean region, causing unprecedented epidemics. In 2006, epidemics were reported in India and Africa (Cameroon, Gabon, Democratic Republic of Congo). Since 2008, strains of the ECSA genotype have circulated in South-East Asia (Malaysia, Singapore, Thailand, Indonesia, Myanmar and Cambodia). The first (exceptional) indigenous cases in Europe were reported in Italy in 2007 and in France in 2010. This re-emergence in waves is linked to the vector species *Ae. albopictus*. It has been demonstrated that a single change in the amino acids of the viral envelope glycoprotein E1 is responsible for this adaptation (41). Under experimental conditions, *Ae. albopictus* showed greater vector competence for the new chikungunya virus variant (42, 43). In October 2013, the first indigenous cases of chikungunya were reported in the Caribbean, where *Ae. aegypti* is the only vector present that is able to transmit the Asian-genotype chikungunya virus. Since then, this epidemic wave has affected around 40 countries in the Americas, including the United States and Brazil, causing over one million cases. Whether transmitted by *Ae. aegypti* or *Ae. albopictus*, both of which are highly anthropophilic, the Asian-genotype chikungunya virus will continue to spread. It is now rife in the South Pacific region (New Caledonia, Samoa, Tokelau, French Polynesia). Candidate vaccines are currently being studied: chimeric vaccines containing chikungunya virus structural proteins connected to the overall structure of another alphavirus; consensus-based envelope DNA vaccines; virus-like particles (i.e. viral particles with no genome) capable of triggering the production of neutralising antibodies; or a recombinant live attenuated measles vaccine expressing chikungunya virus-like particles.

Examples of bacteria transmitted by lice, fleas and sandflies

*Bartonella bacilliformis* and *B. quintana*

*Bartonella bacilliformis* causes Carrion’s disease (also known as Oroya fever or Peruvian wart) and *Bartonella quintana* causes trench fever. These gram-negative intracellular bacteria belong to sub-group α2 of the class Proteobacteria and the genus *Bartonella*. More than 30 species of *Bartonella* have been isolated to date in humans and in domestic and wild animals worldwide. A wide range of mammals act as reservoirs for the different species of *Bartonella*, but humans are the only known reservoir of *B. bacilliformis* and *B. quintana*. These two bacteria were discovered in 1909 and 1914 respectively (44). While trench fever is found throughout the world, the geographic distribution of Carrion’s disease is confined to its vector range, namely arid areas at altitudes of 500–3,000 metres in the Andes mountains (Peru, Ecuador, Colombia), as well as in Bolivia, Chile and Guatemala. *Bartonella bacilliformis* are transmitted to humans by sandflies of the species *Lutzomyia verrucarum*, and *B. quintana* are transmitted by body lice of the species *Pediculus humanus corporis*. In most cases the first infection is asymptomatic, but some patients develop Oroya fever or trench fever when the bacteria enter the erythrocytes. In some cases the bacteria can colonise secondary foci, such as the liver, the spleen; vascularised tissues of the heart, leading to endocarditis (*B. quintana*), or the endothelial cells of the skin, causing rashes (Peruvian wart in the chronic phase of *B. bacilliformis*) (45). Left untreated, infections...
with \textit{B. bacilliformis} can lead to death in about 40\% of cases. \textit{Bartonella quintana} was responsible for millions of human cases among soldiers and is now considered to be a re-emerging disease among the world’s homeless, with a high seroprevalence, and in its chronic forms it does not respond well to treatment with antibiotics (44).

\section*{Conclusions}

Vector transmission owes its effectiveness to each component in the vector-borne system – pathogen, vector insect and vertebrate host (reservoir, amplifier and disseminator hosts). But it also depends on the interactions of these components within their environment, the characteristics of which can affect the different actors directly or indirectly. The genotypes of the pathogen, vector insect and vertebrate hosts (broadly defined as vertebrates receptive to infection) are known to influence successful transmission. Not just any pathogen can be transmitted by any vector and be hosted by any animal or human host. The relationship between pathogen and vector can be measured in terms of vector competence (46). Nevertheless, vector competence does not stem solely from the cumulative effects of the genotypes of the vector and the pathogen – it also depends on the interactions between the two genotypes (47). Similarly, vertebrate populations are not all equal in the face of infection, because susceptibility varies depending on the species and geographic population. Environmental factors can affect transmission by aggravating or constraining it (e.g., developing weather conditions can be conducive or non-conducive to the proliferation of vectors or animals). The vector system is complex and the same goes for control strategies.

The greatest risk to human health comes from vector-borne diseases that are largely maintained within an urban cycle where high-density human populations create conditions conducive to the proliferation of mainly anthropophilic vectors. Recent epidemics of dengue fever or chikungunya remind us that it should be a priority to develop a vaccine. However, if we focus too heavily on humans and domestic animals, the sylvatic cycle continues unabated while remaining a source of infection for other cycles. Moreover, some pathogens are quick to adapt to anthropophilic vector-borne transmission; for example, a single change in the amino acids of a viral envelope protein can lead to devastating epidemics. In addition to studying the emergence mechanisms, combining field work with basic research, we need to: improve surveillance techniques by developing tools for rapid pathogen detection; find alternative means of prevention by testing vaccines against arthropod bites; and propose new control strategies, without neglecting to improve existing anti-vector control techniques.

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