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CHAPTER 6

Ecoepidemiology of Alphaviruses and Flaviviruses

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INTRODUCTION

The arboviruses (arthropod-borne virus) are viruses that require the hematophagous action of an arthropod vector for transmission to hosts (vertebrates). Arboviruses infect humans directly via enzootic or spillover cycles. However, dengue (DENV), chikungunya (CHIKV), and yellow fever viruses (YFV) in their cycles of urban transmission require competent vectors to cause major epidemics. Culicidae mosquitoes (Diptera: Culicidae) occupy a preferential position due to their obligate hematophagy, maximum adaptability to multiple environments at different latitudes and altitudes, and a great variability of preferred hosts from which they can feed and in which they can spread the virus. Infectious diseases caused by viruses are one of the greatest concerns for public health worldwide (Bueno and Jiménez, 2010). The arboviruses comprise...
viruses of the families Togaviridae (genus *Alphavirus*), Flaviviridae (genus *Flavivirus*), and Bunyaviridae (genus *Orthobunyavirus*). The natural cycle of transmission of these viruses mainly involves mosquitoes of the genera *Culex, Aedes, Anopheles, Psorophora,* and *Haemagogus.* Birds and rodents are among the main reservoirs of these viruses (Parra-Henao and Suárez, 2012). The major arboviruses that affect humans are DENV, YFV, West Nile virus (WNV), Eastern equine encephalitis virus (EEEV), Western equine encephalitis virus (WEEV), Mayaro virus (MAYV), St. Louis encephalitis virus (SLEV) and La Crosse encephalitis virus (Bunyaviridae family), and Oropouche virus (OROV, Bunyaviridae family).

Human cases of *arboviruses* occur when populations of infected female mosquitoes bite to feed (hematophagy). While people of all ages can suffer from the disease, children being the most susceptible to illness and death and people over 50 years of age are the ones with the most severe cases of illness. As all mosquitoes do not carry viruses, people will not always get sick out of their bites, only an annoyance similar to influenza can occur, which can be resolved in a few days. In serious cases, the symptoms occur between 4 and 10 days after being bitten by mosquitoes. The disease can start with fever, skin rash, headache, muscle pain, nausea, or vomiting, then it can progress to paralysis, coma, and possibility of death. People who survive can suffer permanent effects on health such as memory loss, paralysis, and changes in personality (Sarwar, 2016a).

The faunistic, bioecological, and distribution data of the culicids allow us to distinguish between species with the capacity to maintain the enzootic stage of some of these arboviruses of others that can act as vectors of the virus to the human being. The study of bioecology and the population dynamics of mosquito vectors is important to predict local transmission scenarios and determine which species should be controlled according to their possible participation in both the enzootic cycle of the disease and its arrival, and even maintenance in the human being.

The objective of this chapter is to discuss the factors that contribute to the ecoepidemiology of diseases caused by several main arboviruses.

## Factors That Favor Zoonoses and Diseases Transmitted by Vectors

The confluence of several factors in recent years has allowed the dissemination of some tropical viruses that were previously confined to certain specific geographic areas. Perhaps the biggest determinants have been climatic changes, the population increase, the displacements of human populations, global trade, air travel that shortens distances, human
invasion of wild areas, and therefore interaction between humans and wild or domestic animals (Plowright et al., 2015; Jones et al., 2008).

Also influencing zoonotic diseases in which the human is an accidental host that temporarily or permanently maintains the disease such as the Ebola virus (Filoviridae) and the severe acute respiratory syndrome virus (SARS–Coronaviridae) (Plowright et al., 2015; O’Shea et al., 2014). The presence of vectors such as arthropods easily mobilizes infection in humans such as Leishmania, Plasmodium, Ehrlichia, chikungunya, dengue, and encephalitis (Bender and Shulman, 2004; Parrish et al., 2008).

On the other hand, the displacements of pathogens or vectors through wild fauna, such as migrations of birds, also have an influence (Monsalve et al., 2009). Human activities, such as the increase of international trade, displacement of great distances in short periods of time, have spread pathogens, vectors, and animal reservoirs, for example, Ebola, WNV by Culex, SARS, and monkey pox virus (Daszak et al., 2001; Bengis et al., 2004). Nor should we forget the mutations and natural genetic recombination of viruses (Monsalve et al., 2009).

**Arbovirus Cycles**

The transmission cycle of arboviruses is considered complex due to the necessary interaction between the hosts and the vectors of the disease. The basic transmission cycle of arboviruses is through an adult mosquito that feeds on an infected host. The mosquito then transports the infective viral particles in their salivary glands and then, in a secondary feeding, transmits the virus to another susceptible host. For viral transmission to be successful, a competent vector is necessary. The competent vector is the ability of an insect to receive, transport, and transmit virus from one host to another. There are many factors that affect vector competition, such as temperature (Dohm et al., 2002), population dynamics (Sardelis et al., 2001; Baqar et al., 1993), and the concentration of viral particles in the blood (Komar et al., 1999; Chamberlain, 1958). The interaction between a vector and a host is an important element to determine vector capacity. The vector capacity is determined by the density of vectors, the competition of the vector species, the ability to successfully feed on a viremic host, the incubation time necessary for an infectious vector to infect another host, and the survival rate (Unnasch et al., 2007). The competences of arbovirus vectors differ from each other and are based on geographic locations and virus strains. This interaction between vectors, reservoirs, and hosts is what contributes to the existence and maintenance of arboviruses.

Most arboviruses with the exception of DENV are kept within a jungle cycle, where bloodsucking insects act as vectors and wild vertebrates
are involved as hosts. Although in the Americas, the jungle cycle for DENV has not been verified, in a tropical forest in northeastern Brazil, an amplicon of DENV-1 was detected in a *Haemagogus leucocelaenus* and DENV-3 infecting larvae of *Aedes albopictus* with transovarian transmission. This suggests that this virus could be involved in a sylvatic cycle (De Figueiredo et al., 2010). *Haemagogus* have food and flight adaptability; in certain scenarios, they can fly at ground level by stinging humans and wild animals when they enter their ecological niche (Maestre et al., 2008; Muñoz-Rodríguez et al., 2010), they can not only fly in open areas, distances between 250 and 350 m, but also distances close to 11 km, and in extreme conditions they can even fly 50 km or more in search of food (Forshey et al., 2010; Moraes, 2007). Some studies have reported that the collection of these species in the vicinity of rural dwellings adjacent to forest areas (Maestre et al., 2008; Muñoz-Rodríguez et al., 2010) increases the probability of contact with humans and domestic animals (Muñoz-Rodríguez et al., 2010) (Fig. 6.1).

**Vectors**

Mosquitoes are found throughout the world, and many species can transmit pathogens that can cause viral diseases. These viruses normally infect birds and small mammals. During these infections the level of the virus can increase in these infected animals, thus facilitating transmission to humans by mosquitoes. During the last decades there was an
emergence of new diseases and new categories of pathogens, emerging and reemerging pathogens; most of them are emerging zoonotic viruses, which means that they can infect animals and humans. The international catalog of arboviruses has registered approximately 1400 arboviruses that affect domestic animals, humans, and some of these arboviruses cause subclinical infection detected by the presence of antibodies (Pfeffer and Dobler 2010; Bueno and Jiménez, 2010).

The transmission of DENV by mosquitoes could be limited in wild ecosystems, where urban species of Aedes aegypti or A. albopictus; for example, in canopy forests (Mexico), other mosquito species inhabit the blood of bats, birds, and other wild animals (Abundes-Gallegos et al., 2018). Recently, DENV was also found in Desmodus, as well as in ectoparasites of the order Diptera Streblidae, Strebla wiedemanni, and Trichobius parasiticus; it is an interesting finding since flies could also be involved in the maintenance of DENV in nature (Abundes-Gallegos et al., 2018).

Recently, Zika virus was detected in the salivary glands in female Culex mosquitoes, coronator, Culex tarsalis, and Aedes vexans captured in wild Mexican forests, suggesting that all mosquito species could easily transmit arboviruses to bats and humans and that strains could be amplified naturally in Chiroptera and other vertebrates (Elizondo-Quiroga et al., 2018). While the urban cycle of DENV is maintained between humans and A. aegypti, the mechanisms for maintaining DENV in the jungle cycle are still unknown, despite the fact that DENV has been detected by molecular methods in wildlife in different countries.

Influence of Environmental, Social, and Plant Coverage Variables in Arbovirosis

The distribution of A. aegypti and A. albopictus is known to be influenced by environmental factors such as temperature and demographic factors such as urbanization (Lounibos et al., 2002; Brown et al., 2011). The survival of A. aegypti and A. albopictus is highly dependent on temperature and water availability (Luz et al., 2008). The greenery index of vegetation canopy can be used as a substitute to indirectly know soil moisture at the surface level. The coverings of vegetation near ground level have been used to associate them with the larval development capacity in these sites (Estallo et al., 2008; Nihei et al., 2014). Eggs and adults require moisture to survive in the dry season; drought levels affect adult mortality (Sota and Mogi, 1992; Russell et al., 2001). The protection of vegetation acts as a cover reduces evaporation and wind speed in the secondary canopy, which protects the development
of the mosquito in those places (Linthicum, 1999; Fuller et al., 2009; Hahn et al., 2014).

Temperature

The increase in temperature can increase the range of action of the different reservoirs and vectors of communicable diseases, among which there are rodents, mosquitoes, and ticks. Some mosquito genera can reproduce exponentially and arise at higher latitudes, propagating geographically with the consequent risk (Gorodner, 2016). High temperatures increase the metabolism of insects and increase egg production and the need to feed, which causes an indirect effect on the longevity of the vector (Patz and Kovats, 2002). The greatest development of *Aedes* in Buenos Aires (Argentina) occurred several months later with temperatures above 20°C and accumulated rainfall exceeding 150 mm; a marked decrease was registered below 16.5°C, and there was no development below 14.8°C (Vezzani et al., 2004).

Precipitation

The principal habitats for the main vector species of arboviruses, *A. aegypti* and *A. Albopictus*, are manmade, containers or water tanks that are used for the storage of rainwater (Morrison et al., 2004). Some local studies show that there is a relationship between precipitation and the abundance of vectors (Scott et al., 2000; Romero-Vivas and Falconar, 2005). The increase in humidity favors a habitat for the development of mosquito vectors; floods can cause catastrophic effects on nature by decreasing food sources, as deforestation favors the movement of insects to areas inhabited by humans (Patz and Kovats, 2002).

Altitude

Climate changes are causing alterations in the behavior of hosts and vectors that favor the spread of zoonoses including arboviruses (Monsalve et al., 2009), for example, the adaptation of the *Aedes* that has been observed in Colombia since 1981 where it was thought that the species did not live above 1585 masl but was captured at 1600 masl and later at 2200 masl in Malaga–Santander (Suárez and Nelson, 1981). Cases of dengue associated with the presence of *A. aegypti* at 1746 masl were reported in Caqueza, Colombia (Rodriguez and De la Hoz, 2005), and the National System of Surveillance in Public Health (SIVIGILA) between 1999 and 2010 recorded 628,016 cases of dengue, of which 2801 cases were presented in 53 municipalities located above 1800 masl.
(Padilla et al., 2013). In 2016 the presence of *A. aegypti* was confirmed at 2302 masl and infection with the DENV at 1984 masl; this being the highest recorded altitude for this vector and infection reported in Colombia (Ruiz-López et al., 2016). The same situation has been recognized in Cochabamba (Bolivia), where colonies of *A. aegypti* are completing their biological cycle at 2450 masl but the DENV transmission at these altitudes is unknown (Aquino et al., 2016). Thanks to the adaptation of the vector, arboviruses constitute a risk and threat of epidemics in populations that live at higher altitudes.

**Social Factors, Urbanization, Displacement, Travel, and Vector Increase**

*A. aegypti* are highly domesticated mosquitoes and apparently feed exclusively on humans (Bargielowski et al., 2013); larvae preferentially develop in artificial containers in close relationship with human habitation (Powell and Tabachnick, 2013). *A. albopictus* is more common to find in semiurban and rural areas feeding on a variety of mammals and birds. Although the development of the larvae has similar behavior to that of *A. Aegypti*, they also are able to develop in an artificial container (Reiter, 2001; Gratz, 2004; Juliano and Philip Lounibos, 2005; Li et al., 2014).

The indiscriminate anthropic action within an ecosystem produces instability, which has caused, over the years, the emergence of several arboviruses and other viral diseases with the findings of new reservoirs. The abovementioned factors can be related to the following facts: between 1954 and 2006, the isolation of at least 196 different types of arboviruses was possible, of which 160 were isolated for the first time in the Brazilian Amazon with at least 100 new types for the world (Vasconcelos et al., 1992). In Brazil, about 36 arboviruses have been associated with the human disease, some even causing serious conditions that can lead to death (Vasconcelos et al., 1992; Pinheiro et al., 1997; Vasconcelos et al., 2001, 1992). Of these, five are of great importance in terms of public health, as they are associated with epidemics, which are DENV, OROV (Bunyaviridae family), MAYV (Togaviridae family), Rocio virus, and YFV. DENVs and Rocio virus are associated with epidemics in urban areas, while MAYV and YFV are associated with human disease in wild areas (Vasconcelos et al., 1984). In Rio Grande do Sul, 55 mosquitoes species were identified, of which 22 were registered for the first time and the main arboviruses that circulate in the neotropical region belong to the *Flavivirus* genus such as SLEV, YFV, and Ilhéus virus among other arboviruses (Cardoso et al., 2010).
The epidemiological role of *A. serratus* in natural conditions was also determined to be infected with Saint Louis and Oropouche encephalitis virus in the Brazilian Amazon (Vasconcelos et al., 1991; Vasconcelos and Travassos-da-Rosa, 1998), Aura virus in Pará and in the province of Misiones, Argentina (Travassos-da-Rosa, 1998; Sabattini et al., 1998), and Trocara virus in Tucuruí, Pará in the Peruvian Amazon (Travassos-da-Rosa et al., 2001; Turell et al., 2005) and is considered secondary vector of the Ilhéus virus, acting in the maintenance of the wild cycle of the virus (Shope et al., 1966). Despite intensive studies, very little is known about most of these viruses, except for general information, isolation method, and ability to infect laboratory animals.

Trips that have shortened the long distances in turn have contributed to the expansion of vectors to nonendemic areas, producing the appearance of epidemics in nonendemic areas. *A. albopictus*, since its introduction in Europe in 2004, has spread from northern Italy to many countries of the European Union (Schaffner and Karch, 2000) and on August 2010 in southeastern France, an endemic area for *A. albopictus*, the first index case of an acute febrile syndrome was reported in a 7-year-old girl (patient 1), 1 day after returning from Rajasthan (India), serum was positive for CHIKV infection by polymerase chain reaction (PCR); 3 weeks later the index case, another girl appeared (patient 2), who experienced clinical symptoms similar to febrile syndrome, the patient had no history of travel to endemic areas of CHIKV and resided at 2.5 km from the index case; the serum sample was positive for CHIKV. The doctor of patient 2 reported that another girl (patient 3), a close friend of patient 2, showed clinical symptoms compatible with CHIKV infection; patient 3 lived near patient 1 and on September 15, she was invited by patient 2 to her home; the two girls presented with numerous mosquito bites and the serum sample of patient 3 had high specific anti-CHIKV IgM titers and a weak signal by reverse-transcriptase-polymerase chain reaction (RT-PCR). Given that patients 2 and 3 did not report any recent travel to endemic areas of CHIKV; their clinical episodes were classified as autochthonous cases of CHIKV infection. The phylogenetic analysis showed that these viral strains belong to a group that is closely related to the strains of India; the CHIKV isolate of patient 2 could be derived from an Indian strain introduced by patient 1 (Grandadam et al., 2011). Likewise, in 2010 coinfections with DENV and CHIKV occurred in this region (La Ruche et al., 2010).

It is known that *A. albopictus* is currently present in Albania, Croatia, Bosnia and Herzegovina, France, Germany, Greece, Italy, Montenegro, the Netherlands, Portugal (Madeira Island), Slovenia, Spain, and Switzerland. In some of the aforementioned countries, imported cases have been reported. Given the amplitude of arboviruses, high viremias in
humans, and the global distribution of *A. aegypti* and *A. albopictus*, it can be stated that there is a high risk for the import of the virus into new areas by infected travelers (Torres and Navarro Suay, 2014).

It should also be recognized that the risk of acquiring and transmitting arbovirosis depends on factors such as geographical area, geographical destination, route, duration, type of trip, season of the year, and class of travelers (cooperators, missionaries, guides, or adventure travelers) who visit endemic areas of infectious diseases and maintain close contact with natives who are high-risk factors and low-risk travelers (diplomats, businesses, hostesses, or tour operators) who have little contact with native people and their visit to endemic areas is limited (Fig. 6.2).

**Pathophysiology of Arboviruses**

The arboviruses are transmitted by the bite of mosquitoes, which become infected when feeding from reservoirs that contain high levels of viremia. In this process of infection, a dissemination is also generated that affects the salivary glands of the mosquito, which allows the passage to new reservoirs of the virus during the feeding of the vector, the saliva of the mosquito is initially deposited in the extravascular space of
the affected vertebrate. Then after getting mediated by the interaction of
the envelope protein and receptors on the surface of the host cell, they
enter the cell by endocytosis and the low pH releases from the com-
ponents of the virus, and they are taken to the cytoplasm through pores;
the nucleocapsid is disassembled in the cytoplasm, giving rise to the
replication of the virus (Kuno et al., 2017).

ECOPIDEMIOLOGY OF FLAVIVIRUS

Generalities of Flavivirus

They are enveloped RNA viruses, not segmented single chain and icosa-
hedral symmetry, which are part of the Flaviviridae family. Flaviviruses
are arboviruses transmitted to vertebrate hosts by a vector arthropod (ticks
and mosquitoes). Some flaviviruses, such as DENV, YFV, WNV, SLEV,
Japanese encephalitis virus (JEV), or encephalitis virus transmitted by ticks
(TBEV), cause diseases in humans, and the signs can vary from a nonspe-
cific febrile syndrome, encephalitis, hemorrhagic fever, and death (Calisher
and Gould, 2003; Hall et al., 2017; Feitoza et al., 2017). The DENV is mainly
transmitted by female mosquitoes of the genus A. aegypti and A. albopictus,
distributed in all tropical and subtropical countries, both species consid-
ered invasive (Rey and Lounibo, 2015). In Table 6.1, a list including flavivi-
rus, its abbreviation, and its vector is shown.

The DENV remains in nature in two cycles: urban and wild (Weaver
and Vasilakis, 2009). A. aegypti is the main vector of the urban cycle and
involves only humans, and the sylvatic cycle involves nonhuman pri-
mates. Wild DENV cycles have been well documented in West Africa
and Southeast Asia, but not in the Americas (Vasilakis et al., 2011). The
majority of the Colombian territory is considered endemic for DENV as
74% of the municipal capitals are below 1800 masl and have climatic
conditions with temperatures ranging between 15°C and 40°C, with an
average of 27°C, relative humidity of moderate to high and variable
rainfall (Chaparro-Narváez et al., 2016). In the Cordoba Department
(Colombia), temperature and humidity, as well as the state of vegeta-
tion, were significantly related to the appearance of DENV (Meza-
Ballesta and Gónima, 2014). Likewise, this department is endemic to
DENV, and 89.7% of the cases reported between 2001 and 2010 were
concentrated on 43% of its municipalities (Meza-Ballesta and Gónima,
2014). The average incidence of DENV between 2003 and 2010 was 36.5
cases/100,000 inhabitants, and the average mortality was 0.3 cases/
100,000 inhabitants (Alvis et al., 2015).

It has recently been reported that undifferentiated tropical febrile dis-
ease is endemic (Mattar et al., 2017). In Córdoba and Uraba (Colombia),
mosquitoes of the several genera have been captured, such as Aedes,
| Species                        | Abbreviation | Vector | Species                      | Abbreviation | Vector |
|-------------------------------|--------------|--------|------------------------------|--------------|--------|
| Gadgets Gully virus           | GGYV         | Ticks  | Ntaya virus                  | NTAV         | Mosquitoes |
| Kadam virus                   | KADV         | Ticks  | Tembusu virus                | TMUV         | Mosquitoes |
| Kyasanur virus                | KFDV         | Ticks  | Spondweni virus              | SPOV         | Mosquitoes |
| Langat virus                  | LGTV         | Ticks  | Zika virus                   | ZIKV         | Mosquitoes |
| Omsk virus                    | OHFV         | Ticks  | Banzi virus                  | BANV         | Mosquitoes |
| Powassan virus                | POWV         | Ticks  | Boubou virus                 | BOUV         | Mosquitoes |
| Royal Farm virus              | RFV          | Ticks  | Edge Hill virus              | EHV          | Mosquitoes |
| Tick encephalitis virus       | TBEV         | Ticks  | Jugra virus                  | JUGV         | Mosquitoes |
| Louping-III virus             | LIV          | Ticks  | Saboya virus                 | SABV         | Mosquitoes |
| Meaban virus                  | MEAV         | Ticks  | Sepik virus                  | SEPV         | Mosquitoes |
| Saumarez Reef virus           | SREV         | Ticks  | Uganda S virus               | UGSV         | Mosquitoes |
| Tyuleniy virus                | TYUV         | Ticks  | Wesselsbron virus            | WESSV        | Mosquitoes |
| Aroa virus                    | AROAV        | Mosquitoes | Yellow fever virus          | YFV        | Mosquitoes |
| Dengue virus                  | DENV         | Mosquitoes | Entebbe bat virus          | ENTV        | Unknown |
| Kedougou virus                | KEDV         | Mosquitoes | Yokobe virus               | YOKV        | Unknown |
| Cacipacore virus              | CPCV         | Mosquitoes | Apoi virus                 | APOIV        | Unknown |
| Koutango virus                | KOUV         | Mosquitoes | Cowbone Ridge virus        | CRV          | Unknown |

(Continued)
| Species                                      | Abbreviation | Vector   | Species                        | Abbreviation | Vector     |
|----------------------------------------------|--------------|----------|--------------------------------|--------------|------------|
| Japanese encephalitis virus                 | JEV          | Mosquitoes| Jutiapa virus                  | JUTV         | Unknown    |
| Murray Valley encephalitis virus            | MVEV         | Mosquitoes| Modoc virus                    | MODV         | Unknown    |
| Saint Louis encephalitis virus              | SLEV         | Mosquitoes| Sal Veja virus                 | SVV          | Unknown    |
| Usutu virus                                 | USUV         | Mosquitoes| San Perlita virus              | SPV          | Unknown    |
| West Nile virus                             | WNV          | Mosquitoes| Bukalasa bat virus             | BBV          | Unknown    |
| Yaoundé virus                               | YAOV         | Mosquitoes| Islas Carey virus              | CIV          | Unknown    |
| Kokobera virus                              | KOKV         | Mosquitoes| Dakar bat virus                | DBV          | Unknown    |
| Bagazza virus                               | BAGV         | Mosquitoes| Montana myotis leukoencephalitis virus | MMLV     | Unknown    |
| Ilheus virus                                | ILHV         | Mosquitoes| Phom Penh bat virus            | PPBV         | Unknown    |
| Israel Turkey meningoencephalitis virus      | ITMV         | Mosquitoes| Rio Bravo virus                | RBV          | Unknown    |
| Ecuador Paraiso Escondido virus              | EPEV         | Dipterous |                              |              |            |
Culex, Anopheles, Culiseta, Mansonia, Coquillettidia, Psorophora, Armigeres, Myzorhynchus, and Taeniopygus (Jaramillo et al., 2005; Parra-Henao and Suárez, 2012). In the year 2016 in Cordoba (Colombia), by means of RT-PCR-nested the flavivirus circulation was confirmed: DENV-2 in A. aegypti, YFV in Haemagogus splendens, SLEV in Mansonia titillans, Culex spp., and WNV in Culex spp. (Hoyos-López et al., 2016). It is also known that Culex quinquefasciatus, A. aegypti, A. Vexans, and A. albopictus bite humans and bats (Kimpel and Mehlhorn, 2013). In addition, there are different serological or molecular evidences on DENV in wild bats, in brains and bat sera in Hainan, China (Zhang et al., 1998), antibodies DENV-1, -2, and -3 in Costa Rica and Ecuador (Platt et al., 2000), and antibodies against flaviviruses in Glossohaga soricina, Artibeus jamaicensis, and Artibeus lituratus in the Yucatan Peninsula of Mexico (Machain et al., 2013). The same serotype was evidenced in intestines and in blood, and phylogenetic analyses showed a spillover effect of humans toward bats in Costa Rica (Vicente-Santos et al., 2017). No molecular evidence was detected in liver, spleen, and serology in wild bats from Campeche and Morelos (Mexico); what has suggested that probably in America, bats are not amplifiers of DENV, and isolation studies should be implemented to determine their role as reservoirs of DENV (Cabrera-Romo et al., 2016). Sequences of DENV have been reported in bats; for example, a sequence of DENV-1 was obtained in a Carollia perspicillata in French Guiana (Lavergne et al., 2009; De Thoisy et al., 2009); for DENV-2, they have been reported in A. jamaicensis, Carollia brevicauda, and Myotis nigricans in the Gulf of Mexico and the Pacific coast (Aguilar et al., 2008) and in G. soricina, A. jamaicensis, A. lituratus in Campeche and Chiapas Mexico (Sotomayor et al., 2014).

In a C. perspicillata captured in Ayapel and a Phyllostomus discolor captured in San Carlos, municipalities of the department of Córdoba (Colombia), amplicons of a size of 143 bp of the NS5 gene were determined in brain, lung, and liver samples that when sequenced corresponded to serotype 2 of the DENV. The consensus sequence of these amplicons was 100 bp and presented high homologies of DENV-2 sequences registered in GenBank. The amplicons were registered in GenBank with MGO11655.1 sequences obtained from C. perspicillata (CIIBT-106-2) and with MGO11656.1 sequences from P. discolor (CIIBT-193-2). It is becoming known and proposing that bats may be involved with viruses that affect human health.

ECOEPIDEMIOLOGY OF ALPHAVIRUS

Generalities of Alphaviruses

They are enveloped RNA viruses, not segmented of single chain and positive sense, of the alphavirus family Togaviridae genus. They are
transmitted mainly by arthropods (arboviruses) and also by a wide variety of small mammals and birds. Viruses belonging to this genus are classified as new or old world, depending on the geographical location from which they were originally isolated (Strauss and Strauss, 1994). New world alphaviruses include EEEV, Venezuelan equine encephalitis virus (VEEV), and WEEV, which cause encephalitis in humans and other mammals, while old world alphaviruses, such as CHIKV, o’nyong-nyong virus (VONN), Ross River virus (VRR), Semliki Forest virus, and Sindbis virus (SINV), cause fever, rash, and arthralgia; this syndrome rarely causes mortality (Ryman and Klimstra, 2008). In South America the MAYV is considered arthrogenic. The reemergence of CHIKV reiterates the potential threat posed by alphaviruses to human health, and the need to understand mechanisms involved in their biology (Simon et al., 2006; Ferro et al., 2015). Many of these viruses circulate permanently in an enzootic cycle that involves wild animals that live in nearby environments where anthropic activities take place. Tropical alphaviruses have special tropism for osteoarticular tissue, patients develop chronic rheumatologic conditions similar to rheumatoid arthritis and ankylosing spondylitis. The example is the CHIKV, although other viruses less known in our environment, such as Sindbis, VRR, MAYV, VONN, and Barmah Forest, have a potential to spread through vectors and cause chronic rheumatological disorders. With the exception of the Eilat alphavirus whose range of hosts is restricted to insects only (Hermanns et al., 2017) (Fig. 6.3).

The reservoirs of these viruses are usually wild animals, although humans can become reservoirs, the transmission is by mosquitoes and the nonvector from person to person is exceptional.

Evidence of Alphaviruses in Bats of America

In 1970 in Oaxaca (Mexico) a vampire bat Desmodus rotundus was found infected with an epidemic strain of VEEV (Correa et al., 1972). In Guatemala a serological study on 939 neotropical bats of 22 species of an enzootic focus of Venezuelan equine encephalitis was carried out during 1971–75, in which VEEV antibodies were found in seven bat species, three belonging to the genus Artibeus, and the virus was isolated from a Uroderma bilobatum. This study suggested that the genus Artibeus is regularly infected with the virus and possibly serves as an alternative host for virus maintenance (Seymour et al., 1978).

In Trinidad Island, a seroprevalence study was conducted against antibodies selected from flavivirus and alphavirus in a sample of 384 bats (10 genera and 14 species). The sera were analyzed by the Enzyme-Linked-Immunosorbent-Assay (ELISA) technique using antibodies specific
FIGURE 6.3 Timeline: behavior of equine encephalitis in America from 1930 to 2017. *EEEV*, Eastern equine encephalitis virus; *VEEV*, Venezuelan equine encephalitis virus; *WEEV*, Western equine encephalitis virus.
to WNV, VEEV, EEEV. About 2.9% of the sample (11/384) were sero-positive against VEEV-specific antibodies, none of the sera were sero-positive against antibodies to the VWN and EEEV viruses (Thompson et al., 2015). In the departments of Córdoba and Sucre (Colombia), a study was conducted in which 24 bats species were captured, and a natural infection of the VEEV of bats was detected in the species *Artibeus planirostris* (frugivore) and *Sturnira lilium* (frugivore). A fragment of the nsP4 nonstructural protein of the alphaviruses corresponding to 195 bp was amplified. The positive samples were reamplified, and the amplicons were sequenced. The obtained consensus sequence of 154 kb presented a 97.7% similarity with sequences of the gene that codes for the precursor of the nonstructural and structural protein of VEEV registered in the Genbank.

Table 6.2 shows some arboviruses of the families Flaviridae and Togaviridae, with epidemiological characteristics and their distribution.

MAYV was originally isolated in Trinidad in 1954 from the serum of febrile patients. MAYV affects people who work or reside in contact with the natural environment. However, outbreaks have also been reported in large cities. The disease caused by MAYV takes 3–5 days and includes fever, headache, myalgia, rash, and arthralgia of large joints, and occasionally, arthritis; the convalescence of this disease could require several weeks. MAYV remains in the wild as a zoonosis of primates that are infected by the bite of *Haemagogus* mosquitoes that live in the canopies. A study of 335 blood samples from indigenous communities in the Rio Negro region, Brazil, indicated that 41.5% had antibodies against MAYV, which shows that it is a common infection in this region. During 2007, cases of Mayaro fever have also been presented in large cities such as Manaus, the capital of the state of Amazonas. In that city, IgM antibodies against MAYV were detected by immunoassay in the serum of 33 patients, the MAYV genome was identified in one of these sera. The patients had fever, headache, arthralgia, eye pain, and rash. Evidence of the migration of MAYV to other parts of Brazil has also been reported. In 2000 three patients who had Mayaro fever and most likely acquired it in the city of Camapuã, located in the center-west of the country, traveled to the city of São Paulo, where they were diagnosed. Therefore MAYV is an emerging virus that affects humans, including individuals who live in the large cities of the Amazon region. This virus could spread to other regions of Brazil, as well as other tropical countries of America, as it is introduced by sick travelers or migratory birds. MAYV and CHIKV could also be transmitted by *A. aegypti*. This background makes it possible to imagine a future scenario in which MAYV, after adapting to the urban cycle, could be the cause of major epidemics (Garcia and Moraes, 2014).
TABLE 6.2  Main Zoonotic Arboviruses Transmitted by Mosquitoes

| Family   | Virus       | Vector                  | Host                      | Transmission cycles | Human diseases | Geographical distribution                  |
|----------|-------------|-------------------------|---------------------------|--------------------|---------------|--------------------------------------------|
| Flaviridae |             |                         |                           |                    |               |                                            |
|          | DENV        | *Aedes*                 | Humans, primates          | U,S,R              | FS, FH        | World (tropics)                            |
|          | YFV         | *Aedes*                 | Humans, primates          | R,S,U              | FS, FH        | Africa and South America                   |
|          | WNV         | *Aedes, Anopheles, Culex, Coquillettidia, and Ochlerotatus* | Birds, pigs             | R,S,U              | FS, ME        | Africa, Asia, Europe, and North America    |
|          | JEV         | *Culex*                 | Birds                     | R                  | S FS, ME      | Asia, Pacific                              |
|          | SLEV        | *Culex*                 | Birds                     | R,S,U              | FS, ME        | America                                    |
|          | MVEV        | *Culex*                 | Birds                     | R                  | FS, ME        | Australia                                  |
|          | USUV        | *Aedes, Culex, and Culiseta* | Birds                    | R                  | FS           | Africa, Europe                             |
| Togaviridae |             |                         |                           |                    |               |                                            |
|          | CHIKV       | *Aedes*                 | Humans, primates          | U,S,R              | FS            | Africa, Asia, and Australia                |
|          | RRV         | *Aedes*                 | Humans, marsupials        | R,S,U              | FS            | Australia, South Pacific                   |
|          | Mayaro      | *Aedes*                 | Birds                     | R                  | FS            | South America                              |
|          | VONN        | *Anopheles*             | Unknown                   | R,S,U              | FS            | Africa                                     |
|          | VSIN        | *Aedes, Culex, and Culiseta* | Birds                    | R                  | FS            | Africa, Asia, Australia, and Europe        |
|          | EEEV        | *Aedes, Coquillettidia, Culex, and Culiseta* | Birds                    | R                  | FS, ME        | America                                    |
|          | EEOV        | *Aedes, Culex*          | Birds                     | R                  | FS, ME        | America                                    |
|          | VEEV        | *Aedes, Anopheles, and Culex* | Rodents                  | R                  | FS, ME        | America                                    |

*CHIKV*, Chikungunya virus; *DENV*, dengue virus; *EEEV*, virus de la Encefalitis del Este; *EEOV*, virus de la Encefalitis del Oeste; *FH*, hemorrhagic fever; *FS*, systemic fever; *JEV*, Japanese encephalitis virus; *ME*, meningoencephalitis; *MVEV*, Murray Valley encephalitis virus; *R*, rural; *RRV*, Ross River virus; *S*, suburban; *SINV*, Sindbis virus; *SLEV*, Saint Louis encephalitis virus; *U*, urban; *USUV*, Usutu virus; *VEEV*, Venezuelan equine encephalitis virus; *VONN*, o’nyong-nyong virus; *WNV*, West Nile virus; *YFV*, Yellow fever virus.
SURVEILLANCE MODE

The main objective of surveillance is to detect infection cases of arboviruses in an opportune manner. Early detection will allow an adequate response and characterization of the outbreak, as well as the identification of circulating viral strains. Multiple surveillance models can be considered to detect the introduction of arboviruses in an area; you can also track the disease once it is introduced or follow up on the disease when it is already established. A study conducted on domestic herbivorous animals in the Brazilian Amazon demonstrated susceptibility to alphaviruses using antibodies to inhibit hemagglutinins. Prevalences by animal species indicated that there were significant differences between horses and water buffaloes and between cattle and sheep. Horses showed high prevalence of antibodies in cross-reactions between four alphavirus antibodies used. These results show that domestic species could serve as sentinels to detect arbovirus circulation in the Brazilian Amazon (Casseb et al., 2012).

TREATMENT

There is no specific antiviral drug treatment for most arboviruses. Symptomatic treatment is recommended after ruling out other diseases. Control of the spread of arthropod-transmitted viruses in the Americas has not been very successful. Dengue continues to cause chaos in many areas of the Americas, extending from the United States to Argentina. During the first years of the 21st century, several outbreaks of dengue occurred in several regions of Asia, Africa, and Americas recently with an unprecedented magnitude, especially in Central America and the Caribbean. For some arboviruses causing large outbreaks such as DENV and CHIKV, there is no specific treatment or commercially available vaccine to prevent infection. Until a vaccine is developed, the only effective means of prevention is to protect individuals against mosquito bites. It should be noted, however, that the only method available to prevent transmission is vector control, although experience indicates that this has rarely been achieved. The resulting large outbreaks could collapse existing health-care systems and public health infrastructure in countries of Central South America and the Caribbean and potentially hinder some aspects of social organization.

Control Measures for Arboviruses

The World Health Organization has identified *Aedes* mosquitoes, for example, *A. aegypti* as the main vector of arbovirosis, which has adapted
to environmental changes such as the increase of urbanizations. Unfortunately, the reduction of mosquito control programs that occurred during the 1960s did not have more resources, generating loss of expertise and infrastructure. With the epidemics of ZIKA and CHIKV reactive reactions, such as the use of spray and fumigations, have been presented, but these strategies are not sustainable, causing long-term resistances to many insecticides (Rabaan et al., 2017).

The continuous applications of insecticides cause the development of resistance in vector species, increase of toxic effects in the food chain, as well as adverse effects on the quality of the environment, which ultimately affect humans and animals. The application of plant extracts with active molecules is an alternative strategy for the control of mosquitoes. Extracts of several plants, such as neem (Azadirachta indica), piperita (Mentha piperata), lemon eucalyptus (Corymbia citriodora), and basil (Ocimum basilicum), have good repellent effectiveness against some mosquito species (Nicoletti et al., 2014; Sarwar, 2016b).

Historically, biological control uses predatory species and pathogenic microorganisms to reduce the population of mosquito species that act as disease vectors. This control strategy for mosquito-borne arboviruses, which do not normally have specific antiviral therapies available, is important because the resources used are typically biodegradable and ecological. During the last decade the advance of molecular biology has allowed the optimization of genetic materials associated with biological control agents. A significant advance has been the discovery of the cytoplasmic incompatibility induced by the Wolbachia bacterium, which has improved replacement programs and the introduction of dominant lethal genes into local mosquito populations by releasing genetically modified mosquitoes (Huang et al., 2017).

**CONCLUSION**

The ecoepidemiological studies are important for the solution of public health problems related to zoonotic diseases. The ecoepidemiological studies that involve biological, ecological, and geographical aspects related to the transmission cycle allow the development of adequate strategies for the prevention and control of vector-borne diseases. The relationship between the emergence of infectious diseases and the climatic variations associated with human behavior and that of vectors is also important; this demonstrates the need to address public health problems from complex and multidisciplinary perspectives.
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