# Overview of Selected Exotic Mosquito-Borne Viruses With Primary or Occasional Human Reservoirs

## Background

In addition to the arboviruses that are endemic to the United States, there are several exotic arboviruses of public health importance where humans act as the primary reservoir and are transmitted between people by mosquitoes. These viruses present a risk of introduction by an infected traveler or immigrant. Dengue fever, chikungunya fever, Zika fever, yellow fever, and Rift Valley fever are some examples of these exotic arboviruses. Although not all are nationally notifiable, cases of any of these diseases, whether imported or locally acquired, should be reported to the Department of Health (DOH) Bureau of Epidemiology as they are of urgent public health significance. Recognition of transmission in Florida requires an immediate response by local mosquito control personnel. Suspect cases should be immediately reported to the county health department, which will then immediately notify the State Arbovirus Coordinator and local mosquito control officials.

## Traveler Information

Mosquito-borne diseases have a worldwide distribution. Travelers should consult with their medical providers or specialty travel medical clinics about what diseases to be aware of and what precautions can be taken. This can include what vaccines and medicines they may need based on where they are going, how long they are staying, and what they will be doing.

Individuals traveling to locations where mosquitoes are active should take mosquito bite precautions while traveling. In some cases, travelers can be asymptomatically infected but still infectious to biting mosquitoes. Travelers can protect family members and prevent infection of local mosquitoes by avoiding mosquito bites for at least three weeks following return home. For more information on mosquito-borne disease prevention, please review the chapter on disease prevention and visit the following website: www.floridahealth.gov/%5C/diseases-and-conditions/mosquito-borne-diseases/prevention.html.

The CDC's travel website provides information about diseases, vaccination requirements, and disease prevention. Information is available by destination as well by disease. Links on how to find travel clinic locations are also provided. More information for travelers can be found at the CDC website: wwwnc.cdc.gov/travel/.

The *Yellow Book* is another good resource for travel health information and is published every two years by the CDC: wwwnc.cdc.gov/travel/page/yellowbook-home.

Health travel notices and alerts are important sources of information on current health issues related to specific destinations: wwwnc.cdc.gov/travel/notices.

## Dengue

**Epidemiology**: Dengue fever (DEN) and severe dengue (dengue hemorrhagic fever [DHF] and dengue shock syndrome [DSS]) are caused by any of four closely related dengue virus (DENV) serotypes (DENV 1–4). It is a painful, debilitating febrile disease, so-called "break-bone fever," that is rarely fatal. Unlike some related flaviviruses such as West Nile virus (WNV), humans are the only important vertebrate hosts of DENV. Dengue has become increasingly common in the Caribbean, Central America, the Pacific, and South America during the past two decades. Today, about 40% of the world's population lives in areas where there is a risk of dengue transmission. The World Health Organization estimates that 50 to 100 million infections occur annually, including 500,000 DHF cases and 22,000 deaths, which are mostly among children. There is no commercial vaccine currently available for DENV, so travelers to endemic areas should use measures to avoid mosquito bites.

Multiple imported dengue cases are reported in Florida each year involving individuals with recent travel history to a dengue-endemic country or territory. Dengue was historically present in Florida with periodic outbreaks in south and central Florida, and the last outbreak was reported in 1934–1935. The virus was eradicated following the advent of organized mosquito control programs, improvements in sanitation, and broad availability of window and door screens and air conditioning. In past Florida epidemics, the sole vector of DENV was *Aedes aegypti.* However, since that time, *Ae. albopictus* has become established in Florida, and this species is an important vector of DENV in Asia. Both species prefer to feed during the day, unlike most vectors associated with Florida endemic arboviruses. *Ae. aegypti* feeds most often on humans, is highly domesticated, and primarily utilizes artificial containers as larval habitats. In contrast, *Ae. albopictus* is an opportunistic feeder and fundamentally a treehole- and leaf axil-dwelling species that is secondarily an artificial container dweller. These mosquito species have a short flight range, so draining standing water around the home weekly is an important preventive action. Traditional CDC light traps, which are the standard mosquito traps used for most WNV, St. Louis encephalitis virus (SLEV), and Eastern equine encephalitis virus (EEEV) mosquito vector surveillance, are not optimal for these species. For more information on surveillance methods for these mosquito species, refer to the Dengue/Chikungunya Vector Management Plan in Urban Environments located in the List of Appendices.

During the summer of 2009, local dengue transmission involving DENV-1 was identified in Key West, Florida[1] and continued in 2010. Twenty-two cases were reported in 2009 and a subsequent serosurvey identified five additional individuals with dengue infections. Sixty-six cases of locally acquired DEN were identified in 2010. A single sporadic case of locally acquired DEN involving DENV-4 was identified in Key West in May 2016. No additional local cases have been identified since that time. In the summer of 2013, local dengue transmission was identified in Martin County, with 24 cases and four asymptomatic individuals identified. No additional cases have been identified since September 2013. In both the Key West and Martin County outbreaks, *Ae. aegypti* was identified as the vector. Twenty-four unrelated, sporadic introductions of locally transmitted dengue were also identified in central and south Florida counties in 2010 (2), 2011 (7), 2012 (3), 2013 (2), 2014 (5), 2015 (1), 2016 (3), and 2018 (1). No dengue introductions were identified in 2017.

[1] Radke et al., 2011.Dengue Outbreak in Key West, Florida, 2009. Emerg Infect Dis [serial on the Internet]. 2011 Jan [Accessed on 12/27/2011]. http://dx.doi.org/10.3201/eid1801.110130.

Table 1. Dengue Virus Introductions Reported in Florida, 2009–2018

| Year | County | Serotype |
|---|---|---|
| 2009 | Monroe | DENV-1 |
| 2010 | Monroe outbreak continued<br>Broward<br>Miami-Dade | DENV-1<br>DENV-3<br>DENV-1 |
| 2011 | Hillsborough<br>Martin<br>Miami-Dade (3)<br>Palm Beach (2) | DENV-1<br>Unknown<br>DENV-1; unknown (2)<br>DENV-1; unknown |
| 2012 | Miami-Dade (2)<br>Osceola | DENV-2; DENV-4<br>DENV-1 |
| 2013 | Martin<br>Miami-Dade (2) | DENV-1<br>DENV-1; DENV-4 |
| 2014 | Miami-Dade (5) | DENV-2 (2); DENV-3 (2); unknown |
| 2015 | Broward | DENV-3 |
| 2016 | Miami-Dade (2)<br>Monroe | DENV-2 (2)<br>DENV-4 |
| 2018 | Miami-Dade | DENV-2 |

**Incubation period**: The incubation period is 3 to 14 days in most cases. People can transmit the virus to other mosquitoes if bitten while viremic; the viremic stage usually begins the day before symptom onset and continues for approximately five days. It then takes 8 to 12 days for the mosquito to become infectious to previously uninfected people. A significant proportion (up to 50%) of people infected with dengue do not display symptoms but can still transmit the virus to mosquitoes.

**Clinical symptoms**: Symptoms generally last 3 to 10 days, although the febrile stage is usually seven days or less (range two to seven days). This illness is characterized by fever, myalgia, arthralgia, and retro-orbital pain. Up to 50% of infected persons may be asymptomatic but still infectious to mosquitoes. Others may experience a non-specific febrile illness rather than the classic break-bone fever. Severe dengue (DHF and DSS) is a group of severe symptoms that may include abnormal blood vessel permeability, hypovolemia, and abnormal blood clotting mechanisms. Signs of shock or bleeding starting near the end or immediately following the febrile period occur in a small percent of those infected. In those with severe disease, shock is the predominant sign. The DHF case fatality rate can be 10% or higher if untreated but is typically drastically lowered (<1%) with timely and appropriate fluid therapy. Acute liver failure and encephalitis are rare consequences of dengue infection. There is some indication that dengue may be transmitted in utero, particularly in the last trimester of pregnancy. In addition, severe dengue can occur during primary infection of infants born to dengue-immune mothers. Infection with one dengue serotype does not protect against the others. Those at greater risk for DHF and DSS include persons with previous dengue infection, pregnant women, infants, the elderly, and those with co-morbidities. However, severe illness can also occur in those without any of these risk factors.

For guidance on the investigation of DEN cases, please review the Guide for Surveillance and Investigation of Dengue/Chikungunya. A document with answers to frequently asked questions about DEN is included in the List of Appendices. A one-page document for medical providers,

"Dengue Fever – Information for Clinicians," can be found in the List of Appendices and should be paired with the "Chikungunya Fever – Information for Clinicians" document.

## Chikungunya

**Epidemiology**: Chikungunya fever (CHIK) is caused by infection with chikungunya virus (CHIKV), an alphavirus in the family *Togaviridae*. There is currently no vaccine available for CHIKV, so travelers to endemic areas should use measures to avoid mosquitoes. Prior to 2013, diagnosis in travelers was rare, but had occurred, particularly during epidemics in endemic countries. The virus was primarily found in parts of Africa and Asia; however, outbreaks have been documented in Europe. A 2007 outbreak in Italy was especially concerning as the country has a public health and vector control infrastructure similar to that of the U.S. The vector implicated in the outbreak was *Ae. albopictus*, a species with wide distribution in Florida. In December 2013, local transmission was identified on the Caribbean island of St. Martin. This marked the first time confirmed locally acquired CHIK cases had been identified in the Americas. Since the initial report, local transmission has been identified throughout the Caribbean islands, Mexico, and countries in South and Central America. In 2014, 12 cases of locally acquired CHIK were identified in Broward (1), Miami-Dade (2), Palm Beach (5), and St. Lucie (4) counties in Florida. In addition, 510 imported cases of CHIK were identified. No locally acquired cases have been identified since 2014 and the numbers of imported cases have decreased dramatically since 2014: 76 in 2015, 8 in 2016, and 5 in 2017.

CHIKV is transmitted by two main vectors: *Ae. aegypti* (primarily) and *Ae. albopictus*. These mosquitoes also serve as the vectors for dengue and both are common in Florida. Humans serve as the primary reservoir for CHIKV; however, other vertebrates such as non-human primates may also serve as potential hosts. Rare in utero transmission can occur, primarily in the second trimester, and intrapartum transmission has been documented. Rare infections acquired through needle sticks have been reported. Transfusion-acquired infections could theoretically occur but have not been documented to date.

**Incubation period**: After a mosquito bites a viremic host, on average it takes 10 days for the mosquito to become infectious to people (extrinsic incubation period). In humans, the incubation period is typically three to seven days from the time of the mosquito bite, but can range from 1 to 12 days.

**Clinical symptoms**: Between 3% and 28% of cases may be asymptomatic. Acute phase symptoms include a sudden onset of continuous or intermittent high fever (usually >102ºF) with severe joint pain. Tendons may also be involved. Joint and tendon pain commonly involves the hands and feet, is usually bilateral, and often is accompanied by swelling. Other joints may be involved and back pain is reported in up to 50% of cases. Maculopapular rash is reported in approximately half of all patients, usually 2–5 days after fever onset. Children and infants may demonstrate vesiculobullous skin lesions. These symptoms can last 3–10 days. Other symptoms may include headache, fatigue, depression, nausea, vomiting and muscle pain. Mild thrombocytopenia, leukopenia and elevated liver function tests may be reported. Relapse of joint and tendon pain can occur after initial improvement of clinical signs; relapse is most common within one to three months after symptom onset. Some patients have prolonged fatigue and depression lasting weeks or months. Chronic joint pain lasting years may also occur in some patients, with those over the age of 45 or with pre-existing joint conditions at increased risk. Persons at risk for more severe disease include: neonates exposed intrapartum, adults >65 years of age, and persons with underlying medical conditions (e.g., hypertension, diabetes, or

cardiovascular disease). Fatalities related to chikungunya infection are rare. Infection is believed to provide life-long immunity.

CHIKV, DENV, and Zika virus (ZIKV) infections are difficult to differentiate clinically. However, maculopapular rash is more frequent with chikungunya. Polyarthralgia or pain associated with chikungunya is often more localized in joints and tendons, particularly the hands and feet, and may be associated with visible swelling. Signs of shock or hemorrhage are more typical of severe dengue. It is also important to note that chikungunya and dengue can occur as co-infections and are vectored by the same mosquito species. Several of these co-infections were identified in 2014 when CHIKV was spreading in the Americas. Co-infection with Zika could occur for the same reason.

For guidance on the investigation of CHIK cases, please review the Guide for Surveillance and Investigation of Dengue/Chikungunya. A document with answers to frequently asked questions about chikungunya fever is included in the List of Appendices. A one-page document for medical providers, "Chikungunya Fever – Information for Clinicians," can be found in the List of Appendices and should be paired with the Dengue Fever – Information for Clinicians document.

### Other Viruses Similar to Chikungunya

Other arthrogenic alphaviruses characterized by fever and severe arthralgia include **Ross River virus** (Australia, Papua New Guinea, and Oceania with zoonotic/animal and human reservoirs); **Mayaro virus** (South and Central America, Caribbean with zoonotic/animal reservoirs and suspected human reservoirs); **O'nyong nyong virus** (Africa with suspected human and zoonotic/animal reservoirs); **Barmah Forest virus** (Australia with zoonotic/animal and human reservoirs); and **Sindbis virus** (Africa, Europe, Asia, Australia, Papua New Guinea with zoonotic/animal reservoirs).

Chikungunya, Ross River, Mayaro and O'nyong nyong all belong to the Semliki Forest virus complex. Barmah Forest virus belongs to the Barmah Forest virus complex, and Sindbis virus belongs to the Western equine encephalitis virus complex.

**Ross River virus** (RRV) is transmitted by several *Aedes* and *Culex* mosquito species. Marsupials are thought to be the main reservoir host; however, humans can transmit the virus to mosquitoes and are thought to significantly contribute to the transmission cycle during outbreaks. While most people exposed to the virus are asymptomatic, those who develop symptoms may experience joint pain, joint swelling, fatigue, muscle pain, and rash. Most people recover within a few weeks, but similar to chikungunya virus, individuals may experience chronic joint pain for months.

## Zika Fever

**Epidemiology**: Zika fever (ZIKF) is caused by an infection with ZIKV, a virus in the family *Flaviviridae*. The virus was originally isolated from a rhesus macaque in Uganda in 1952 and the first identified human case was in Nigeria in 1954. Until 2007, very few cases were reported, all of which occurred in Africa and Southeast Asia. In 2007, ZIKF was documented on several islands in the Pacific Ocean belonging to the Micronesia, Melanesia, and Polynesia regions. Yap Island in Micronesia had a large outbreak of the virus, with a subsequent serosurvey demonstrating 74% of the population exposed to the virus. Additional outbreaks of ZIKF have been reported in these areas in 2013–2014. Cases of ZIKV infection were identified in Brazil in

2015 and it subsequently spread throughout South and Central America, Mexico, and the Caribbean.

In December 2015, the first imported cases of ZIKV infection in Florida were identified in people who traveled to Zika virus-affected countries. There were 1,122 travel-associated cases in 2016. The number of imported cases has decreased dramatically since 2016, with 225 cases reported in 2017. Six travel-related cases (3 in 2016 and 3 in 2017) were the result of sexual transmission. The first locally acquired case was identified in Miami-Dade County in July 2016.[2] Ultimately, 287 locally acquired cases were reported in Miami-Dade, with many of the local cases exposed within four areas of active transmission (Wynwood, South Miami Beach, North Miami Beach, and Little River communities). Sporadic autochthonous cases were also reported in Broward (1), Palm Beach (5), and Pinellas (1) counties in 2016. Six additional cases had unknown county of exposure due to residence in a county reporting local transmission and travel to Miami-Dade County. Only two locally acquired cases were identified in 2017, in Manatee and Miami-Dade counties.

Response to ZIKV was complicated by two hurricanes in 2016 (Hermine and Matthew), and Tropical Storm Emily and major hurricanes Irma and Maria in 2017. Although direct weather impacts to Florida from Hurricane Maria were relatively limited, the storm passed directly over Puerto Rico, making landfall as a Category 4 hurricane. Thousands of families evacuated from Puerto Rico to the United States mainland, with many settling in Florida, including some families impacted by ZIKV.

Similar to DENV and CHIKV, ZIKV is transmitted by two main vectors: *Ae. aegypti* (primarily) and *Ae. albopictus*. Humans serve as the primary reservoir for ZIKV; however, other vertebrates such as non-human primates may also serve as potential hosts. Although mosquito transmission is most common, Zika has the potential to spread through intrapartum or sexual transmission, and rarely through blood transfusions. There are highly sensitive blood screening tests available and Zika blood donation screening is currently required nationally by FDA similar to WNV. Blood bank laboratories are required to report ZIKV-reactive blood donors to DOH as for WNV. There is no vaccine available for ZIKV, so travelers to endemic areas should use measures to avoid mosquitoes.

Zika virus infection during pregnancy can cause certain birth defects, including microcephaly.[3] Due to this risk, DOH participated in CDC's U.S. Zika Pregnancy Registry. More than 450 pregnant women/infants with possible ZIKV exposure during pregnancy are being followed for a two-year period. Nine infants (five born in 2016 and four born in 2017) in Florida have had laboratory evidence of congenital ZIKV infection after birth. Seven of these infants had symptoms consistent with congenital Zika syndrome. For pregnancies that resulted in fetal or infant death, attempts were made to collect samples for ZIKV testing. Samples from one fetal death in 2016 and two fetal deaths in 2017 tested positive for ZIKV. Fetuses and infants of women infected with ZIKV during pregnancy should be evaluated for possible congenital infection and neurologic abnormalities. Pregnant women in any trimester should consider postponing travel to areas where ZIKV transmission is ongoing. Pregnant women who must travel to these areas should talk to their doctors or other health care providers first and strictly follow steps to avoid mosquito bites during trips. In addition, pregnant women and their sexual partners should consistently and correctly use condoms or other barrier precautions or abstain

[2] Likos et al., 2016. Local Mosquito-Borne Transmission of Zika Virus – Miami-Dade and Broward Counties, Florida, June–August 2016. MMWR. 2016. 65(38);1032-1038.
[3] Rasmussen et al., 2016. Zika Virus and Birth Defects – Reviewing the Evidence for Causality. N Engl J Med. 2016 May. http://dx.doi.org/10.1056/NEJMsr1604338.

from sex for the duration of the pregnancies if the partners travel to an area with ZIKV activity. Women and men trying to become pregnant should consult with their health care providers before traveling to areas with ZIKV activity and strictly follow steps to prevent mosquito bites during trips. Couples should consider delaying attempts to become pregnant for two months following female partners' travel to ZIKV-active areas. Couples should consider delaying attempts to become pregnant for three months if male partners traveled to ZIKV-active areas.

**Incubation period:** The incubation period for Zika is approximately 2–14 days.

**Clinical symptoms**: The virus causes an acute febrile illness that is similar to dengue fever, but generally more mild. About one in five people infected with ZIKV become ill. Symptoms of infection include fever, headache, conjunctivitis, rash, arthralgia, and myalgia. Other symptoms associated with infection include abdominal pain, anorexia, constipation, diarrhea, edema, retro-orbital pain, and vomiting. Neurological complications such as Guillain-Barré syndrome are rare but have been observed. Two cases of Guillain-Barré syndrome associated with ZIKV infection were reported in Florida in 2016. Infection during pregnancy can result in fetal birth defects.

For guidance on the investigation of ZIKV infection cases, please review the Guide for Surveillance and Investigation of Zika Virus. A document with answers to frequently asked questions about Zika fever is included in the List of Appendices. A one-page document for medical providers, "Zika Fever – Information for Clinicians," can be found in the List of Appendices.

## Yellow Fever

**Epidemiology:** Yellow fever (YF) is caused by infection with yellow fever virus (YFV), a flavivirus in the same family as WNV, DENV, and ZIKV. Like dengue, it is transmitted to humans by infected *Ae. aegypti* mosquitoes and there is no animal reservoir in the U.S. YF was previously a major public health concern in the U.S. and was one of the major driving forces for the creation of many state health departments, including in Florida, which had large outbreaks in the 1700 and 1800s. The last epidemic in North America occurred in New Orleans in 1905.

Currently, YFV circulates occurs only in tropical regions of Africa, parts of South America, Panama, and on several Caribbean islands. In recent years, YF has resurged in many endemic areas, including in South America, due to re-emergence of *Ae. aegypti* mosquitoes and changes in vaccination practices. Changes in vaccination practices in urban areas in Brazil, coupled with limited availability of vaccine, have resulted in an increased risk for an urban outbreak in that country. In 2018, YFV activity in popular tourist destinations near urban areas in Brazil resulted in multiple infections in unvaccinated tourists, including four deaths, and highlighted the increased risk for introduction into non-endemic areas with competent vectors.[4] Planned manufacturing facility upgrades resulted in temporary limitations of yellow fever vaccine in the United States in 2017–2018. DOH worked with FDA and CDC to ensure that a European vaccine, Stamaril, was available for Florida travelers planning trips to endemic areas during that time.

YF is a rare cause of illness in U.S. travelers to endemic countries. Fortunately, it can be prevented by vaccination. Travelers should be vaccinated for yellow fever before visiting areas where it occurs. Rare vaccine-associated infection can occur. International regulations require proof of vaccination for travel to and from certain countries. Travelers should also take the

[4] Hamer DH, et. al. Fatal yellow fever in travelers to Brazil, 2018. MMWR. 2018;67:340-341.

precautions against mosquito bites found in this guide. Additional travel information can be found in CDC's Health Information for International Travel book: wwwnc.cdc.gov/travel/page/yellowbook-home or at www.cdc.gov/vaccines/vpd/yf/index.html.

**Incubation period**: The incubation period of YF is usually three to six days.

**Clinical symptoms**: Illness ranges in severity from a self-limited febrile illness to severe hepatitis and hemorrhagic fever. Symptoms of severe infection are high fever, chills, headache, muscle aches, vomiting, and backache. After a brief recovery period, the infection can lead to shock, bleeding, and kidney and liver failure. Liver failure causes jaundice, the yellowing of the skin and the whites of the eyes. Severe infections can be fatal. There is no specific treatment; only supportive care and treatment of symptoms. Aspirin should be avoided.

For guidance on the investigation of YF cases, please review the Guide for Surveillance and Investigation of Yellow Fever. A document with answers to frequently asked questions about yellow fever is included in the List of Appendices. A one-page document for medical providers, "Yellow Fever – Information for Clinicians," can be found in the List of Appendices.

## Rift Valley Fever

Rift Valley fever (RVF) is caused by infection with the RVF virus (RVFV), in the family *Bunyaviridae*. The virus primarily affects livestock, such as cattle, buffalo, sheep, goats, and camels, and can cause large epizootic outbreaks. Humans, primarily those in direct contact with diseased animals, can also be infected. Humans can be infected through the bite of an infected mosquito as well. If introduced to Florida, RVF would be a significant threat to the agriculture industry, with cattle and small ruminants especially affected. This could result in an export ban on beef to other countries, causing billions of dollars in economic loss. Suspect cases should be immediately reported to the State Arbovirus Coordinator.

**Epidemiology**: Humans can act as an occasional RVFV reservoir. RVFV is not present in the U.S. and is generally found in regions of eastern and southern Africa, but also exists in sub-Saharan Africa and Madagascar. RVFV was first documented outside Africa in Saudi Arabia and Yemen in 2000. RVFV is transmitted by a number of different species of mosquitoes. Infected female mosquitoes can pass the virus into their eggs, where the virus can remain viable for years. Mechanical transmission is possible with some other types of biting insects. Humans can also get the disease if they are exposed to the blood, body fluids, or tissues of infected animals. RVFV is one of the few zoonotic arboviruses that can result in infected humans developing viremia significant enough to infect biting mosquitoes.

**Incubation period:** Two to six days.

**Clinical symptoms**: Many infected individuals have no illness or mild symptoms. People who become ill usually experience fever, generalized weakness, back pain, dizziness, and extreme weight loss. However, some patients (8-10%) can experience ocular disease, hemorrhagic fever, or potentially fatal encephalitis. Case fatality rates are significantly higher in infected animals. Serological tests such as enzyme-linked immunosorbent assay (ELISA) may confirm the presence of specific IgM antibodies to the virus. The virus may be isolated from the blood during the first few days of infection.