Overview of Selected Zoonotic Mosquito-Borne Viruses in Florida

Background

Arthropod-borne viruses, i.e. “arboviruses,” are viruses that are maintained in nature through transmission between susceptible animal hosts by blood-feeding arthropods (e.g., mosquitoes, ticks, and biting flies). This document will focus on viruses transmitted by mosquitoes. Most arboviruses that cause human encephalitis are members of three of the major virus families: the Togaviridae (genus Alphavirus), Flaviviridae, and Bunyaviridae.

Zoonotic arboviruses are maintained in complex life cycles involving a non-human primary vertebrate host and a primary mosquito vector. These viruses usually cycle undetected until humans encroach on a natural focus, or the virus escapes this focus via a secondary vector or vertebrate host as the result of some ecologic change. For some arboviruses (West Nile virus and Eastern equine encephalitis virus), humans and domestic animals can develop clinical illness but usually are dead-end hosts because they do not produce significant enough viremia to infect biting mosquitoes. Many arboviruses that cause encephalitis have a variety of different vertebrate hosts and some are transmitted by more than one vector. Maintenance of the viruses in nature may be facilitated by vertical transmission in the vector (e.g., the virus is transmitted from the female to the offspring) or overwintering of the virus in mosquito or reservoir hosts.

Arboviral diseases have a global distribution. Zoonotic arboviruses transmitted by mosquitoes in the United States include: St. Louis encephalitis virus (SLEV), West Nile virus (WNV), Eastern equine encephalitis virus (EEEV), Western equine encephalitis virus (WEEV), Everglades virus (EVEV), and the California serogroup viruses, including La Crosse encephalitis virus. Most cases of arboviral encephalitis occur from June through September, when arthropods are most active. In Florida, where arthropods may be active year-round, cases can occur into the winter months. Most human infections are asymptomatic or may result in a nonspecific flu-like syndrome. Onset may be insidious or sudden with fever, headache, myalgias, malaise and occasionally prostration. Infection may lead to encephalitis, with a fatal outcome or permanent neurologic sequelae. Fortunately, only a small proportion of infected people progress to developing encephalitis.

Laboratory criteria for arboviral disease diagnosis include: virus-specific seroconversion of IgM or IgG between acute and convalescent testing; isolation of virus from or demonstration of specific viral antigen or nucleic acid in tissue, blood, CSF, or other body fluid; virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for related arboviruses endemic to the region where exposure occurred; or virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen.

Because the zoonotic arboviruses are viral diseases, antibiotics are not helpful for treatment and the effectiveness of antiviral agents has not been shown. Treatment is supportive, attempting to deal with problems such as swelling of the brain, respiratory paralysis and other treatable complications like bacterial pneumonia. There are currently no commercially available human vaccines for zoonotic arboviruses in the U.S., although some work was done to develop
a WNV vaccine in the past and there is a vaccine available for an exotic arbovirus (Japanese encephalitis). See the specific disease sections for more information on vaccines for animals.

Arboviral disease can be prevented through personal and community protective measures. Personal protective measures include:

- Reducing time outdoors when mosquitoes are most active.
- Wearing long pants and long-sleeved shirts.
- Maintaining intact screens on windows and doors.
- Applying Environmental Protection Agency (EPA)-approved mosquito repellent to exposed skin areas as recommended by product label.
  - Repellents containing DEET (N,N-diethyl-m-toluamide), picaridin or permethrin (on clothing) are excellent tools for personal protection. Additional options on the market, specifically IR3535, para-menthane-diol, and oil of lemon eucalyptus are registered with the EPA and have performed well in evidence-based, peer-reviewed publications.\(^1\) Some references indicate that picaridin is reportedly less irritating to the skin than DEET.\(^2\)
  - See the repellent frequently asked questions document in the List of Appendices for more information.
- Residual insecticide applications, on and around screen doors, may give added protection.
- Community preventive measures include reducing mosquito breeding sites around residences, businesses, and other areas where people spend time outside. Standing water should be drained at least once a week.
  - Some common sources of standing water include garbage cans, house gutters, buckets, pool and boat covers, coolers, toys, pet water bowls, bird baths, non-native bromeliad plants, flower pots, or any other containers.
  - It is important to remove/destroy discarded tires, bottles, cans, pots and pans, and broken appliances.
  - The use of insecticides (larvicides and adulticides) to kill mosquitoes may be required.

For CDC's latest repellent guidelines, see [www.cdc.gov/westnile/faq/repellent.html](http://www.cdc.gov/westnile/faq/repellent.html).

For more information on choosing repellent, use the EPA search tool at: [www.epa.gov/insect-repellents/find-repellent-right-you#searchform](http://www.epa.gov/insect-repellents/find-repellent-right-you#searchform).

For more information on the use of insecticides, please visit: [https://fmel.ifas.ufl.edu/fmel---gen---info---v3/fmc-white-paper/](https://fmel.ifas.ufl.edu/fmel---gen---info---v3/fmc-white-paper/).


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**Occupational Precautions**

Although arboviruses are most often transmitted by the bite of infected mosquitoes, many of these viruses can also be transmitted through needle sticks, cuts, or mucous membrane contact with infected animal body fluids or tissues (particularly brain and cerebral spinal fluid). Workers involved in necropsies or other procedures involving potentially infectious materials should use every precaution to minimize their risk for exposure to fluids or tissues during handling, including standard droplet and contact precautions; using and disposing of needles, scalpels, and other sharp instruments safely; and minimizing the generation of aerosols.

Several local, state, and federal agencies are involved with the surveillance and control of arboviral diseases. Mosquito-borne encephalitis surveillance activities include monitoring mosquito vector population numbers; screening sentinel chickens, wild birds, and veterinary cases to detect increased arbovirus activity before infections occur in people; and instituting interventions to significantly reduce risk of transmission to humans. An important component of any surveillance system is the establishment of baseline data against which current disease activity can be measured. All stakeholders involved in arbovirus surveillance should collect and maintain baseline data for each surveillance activity, and utilize this information to assess the level of risk to the human population. In addition, the rapid diagnostic techniques used in threat recognition can shorten public health response time and reduce the geographic spread of infected vectors, and thereby the cost of containing them.

The surveillance required to determine risk is being increasingly refined by the utilization of technologies which allow for rapid identification of zoonotic viruses in bird and mosquito populations. Virus isolation and molecular diagnostic tools are useful to identify viral agents in mosquito vectors. While virus isolation still depends upon growth of virus in cell culture or neonatal mice, virus detection has been greatly facilitated by the availability of virus-specific genomic sequence information for use in polymerase chain reaction (PCR) assays, and monoclonal antibodies (MAbs) for use in immunofluorescence assay (IFA) and enzyme-linked immunosorbent assay (ELISA) tests. MAbs with avidities sufficiently high to allow for specific binding to virus antigens in a complex protein mixture (e.g., mosquito pool suspensions) have also enhanced the ability to rapidly identify virus agents in situ.

**Zoonotic Arboviruses Endemic to Florida**

**St. Louis Encephalitis (SLE)**

**Epidemiology:** St. Louis encephalitis virus (SLEV), a flavivirus, was the most common mosquito-transmitted human pathogen in the U.S. prior to the introduction of WNV in 1999. During the summer season, SLEV is maintained in a mosquito-bird cycle, with periodic amplification by birds and *Culex pipiens*, *Cx. quinquefasciatus*, and *Cx. tarsalis* mosquitoes. In Florida, the principal vector is *Culex nigripalpus*, a ubiquitous species found throughout Florida. Infection with SLEV results in inapparent infections in a variety of birds and mammals with a resultant period of viremia that lasts a matter of days. Humans represent an incidental, dead-end host.

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While the geographical range of the virus extends from Canada to Argentina, human cases have almost exclusively occurred in the United States. Most cases in the United States have been reported in the eastern and central states; however, several western states have also reported activity. The first recognized SLE outbreak occurred in St. Louis, Missouri in 1933. Since then, many SLE epidemics have been documented in North America with the vector species varying by region. These outbreaks stimulated the establishment of research into mosquito-borne diseases and mosquito control activities including two arbovirus research facilities in Tampa and Vero Beach. In Florida, SLE outbreaks were documented in 1959 (n=68), 1961 (n=25), 1962 (n=222), 1977 (n=110), 1980 (n=10), 1990 (n=223), 1993 (n=8) and 1997 (n=9). The epicenter of the historical outbreaks was the Tampa Bay area for all years but 1977 and 1990.

In 1980, six sporadic cases of SLE were reported from counties around Tampa Bay (Pinellas, Hillsborough, Pasco, Manatee and Sarasota). In addition, four cases were reported from residents of Fort Walton Beach in Okaloosa County. This incident was particularly interesting in that human cases of SLE had never been previously documented in the Panhandle of Florida. These cases also occurred between July 10 and August 2, much earlier than the normal transmission peak seen in September and October. In October 2012, SLEV was identified in an Anopheles crucians mosquito pool collected in Bay County during a WNV outbreak. Two human cases of SLE were identified in Duval County in August 2014, representing the first human cases identified since 2003. Activity was similar to the previous human cases in the Panhandle, occurring earlier than the historical transmission peak. Human cases of WNV illness were also reported in Duval County at the same time (August, September 2014).

The most widely used surveillance technique in Florida has been sentinel flocks, and these are maintained in about half of Florida’s 67 counties. SLEV activity in Florida has decreased dramatically since WNV was first detected in the state in 2001. Research suggests that antibodies for WNV may protect against SLEV infection in house finches. However, in 2011 (>60), 2012 (>80), 2013 (>80), and 2014 (>100) sentinel chickens tested positive for antibodies to SLEV in Pinellas, Hillsborough and several other counties in central and south Florida, suggesting potential for possible resurgence. This activity would go undetected without sentinel flock surveillance.

Testing capacity for SLEV antibody at commercial laboratories was limited from approximately 2014–2016. However, SLEV testing remained available at the DOH BPHL during that time.

**Incubation period:** The estimated incubation range is 5 to 15 days following the bite of an infected mosquito.

**Clinical symptoms:** The clinical spectrum of human SLEV infection includes inapparent infection, mild illness (fever with headache), aseptic meningitis, and encephalitis that can progress to coma and death. Less than 1% of SLEV infections in people are clinically apparent and the vast majority of infections remain undiagnosed. Encephalitis, especially that progressing to coma and death, is more common with older age. The case fatality rate in Florida SLEV epidemics has ranged from 4 to 30 percent. Deaths were almost exclusively among people aged 50 and older.

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For guidance on the investigation of human SLE cases, please review the Guide for Surveillance and Investigation of Zoonotic Mosquito-Borne Viruses. A document with answers to frequently asked questions about SLEV is included in the List of Appendices.

West Nile Fever and Neuroinvasive Disease

**Epidemiology:** West Nile virus (WNV), a flavivirus, was first identified in Uganda in 1937 and remained in the Eastern Hemisphere until introduced to the northeastern U.S. in the summer and fall of 1999. Since then the virus has spread and by the end of 2004, it had been detected in 48 states (not in Hawaii or Alaska). The virus is closely related to SLEV and cross reacts with SLEV in serological testing. WNV was first detected in Florida in July 2001 in a crow in Jefferson County. Since its initial detection, WNV activity has been reported in all 67 Florida counties.

Following multiple transfusion-acquired infections, screening of blood donations for WNV has been required in the U.S. since 2003. Rare virus transmission from mother to fetus or newborn has also occurred. Transmission from mother to infant via breastmilk may be possible. The benefits of breastfeeding outweigh the unknown risk of WNV transmission. Pregnant and breastfeeding women should routinely use mosquito bite precautions. Repellants with active ingredients that are registered with the EPA are safe for pregnant women when used according to the label instructions.

Risk factors for arbovirus exposure include spending time outside, not using repellent or other prevention methods routinely, outdoor smoking without using repellent, torn or no screens at the residence, and not using air conditioning. Persons at risk due to spending time outside include those with outside occupations or hobbies and the homeless.\(^7\)

The peak period of transmission in Florida is July through September. Like SLEV, the natural cycle of WNV appears to involve *Culex* mosquitoes and wild birds. However, unlike SLEV, WNV can cause high rates of mortality in certain families of birds, especially corvids (crows and jays), raptors (e.g. hawks and owls) and ratites (e.g., emus and ostriches). It is also pathogenic for horses and some camelids (camels, alpacas, and llamas). In Florida, WNV has been identified most frequently in *Cx. nigripalpus* mosquitoes. *Culex quinquefasciatus* has also been found to be an important vector in the southern U.S., particularly in urban areas. Over 300 human WNV illness cases were reported in Florida between 2001–2017, with the highest number of cases reported in 2003 (93). In 2012, a nationwide outbreak of WNV infections occurred, with high-intensity transmission in eastern Texas. The 2012 outbreak also involved north Florida, with all but 1 of 68 Florida-acquired cases reporting exposure in the northern part of the state. West Nile virus was isolated from two pools of *Cx. nigripalpus* mosquitoes collected in Duval County, where 28 of the human cases were reported in 2012. More than 1,000 cases of equine WNV infection were confirmed in Florida between 2001–2017; however, the number of equine cases of WNV infection have decreased dramatically over time, which in part is due to development of a licensed vaccine. A WNV disease outbreak also occurred in alligators at an alligator farm in Glades County in 2011. Infected alligators amplify virus and may transmit virus to other alligators and people through fecal shedding and contact with tissues while viremic.\(^8\) While widespread mosquito pool testing for WNV is not performed in Florida, Bay County has regularly

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identified positive *Cx. quinquefasciatus* mosquito pools from 2014 (5), 2015 (7), 2016 (5) and 2017 (2).

**Incubation period:** Symptoms appear between 2 to 14 days after the bite of an infected mosquito.

**Clinical symptoms:** The clinical spectrum for human WNV infection includes asymptomatic infection, mild illness (fever and headache), aseptic meningitis, and encephalitis that can progress to coma and death. Approximately 80% of those infected show no clinical symptoms. Twenty percent have mild symptoms, and less than 1% suffer from the neuroinvasive form of illness. Individuals over 60 years of age and those with pre-existing medical conditions seem to be at increased risk of severe disease. Immunosuppressed persons, including transplant recipients, are also at increased risk of developing severe disease. A growing body of scientific literature also indicates that in rare instances, animal and human WNV infections may be chronic. Economic impacts of WNV neuroinvasive disease have been calculated at $225,000 for each fatal infection and $136,839 for non-fatal cases. When taking into account the cost of hospitalization, medical care, and missed work, the resulting average annual burden due to WNV infection is estimated to be $56 million in the United States.

West Nile virus infections in **asymptomatic blood donors** do not meet reportable disease criteria; however, they do provide useful surveillance information for CHDs, as blood bank testing targets detection of the active viremic stage using nucleic acid-amplification testing (NAT). Donors who remain asymptomatic but whose blood samples test positive for WNV at BPHL are assumed to have been exposed in the two weeks prior to donation and can be used to meet the mosquito-borne illness advisory or alert criteria for the county in which exposure most likely occurred. Donors who develop symptoms are handled in the same way as other WNV illness cases.

**Vaccination:** Equine vaccines protecting against WNV have been on the market since 2001. Camels are susceptible to WNV infection and may develop the same clinical paralytic syndrome as humans and horses. In 2013, there was a fatal case of WNV disease reported in an alpaca in north Florida. Veterinarians and owners should immunize camels, alpacas, and llamas against WNV. There are no approved vaccines for these animals, and use of the horse vaccine is considered off-label; however, there are research studies that demonstrate development of an adequate immune response when they are given the horse vaccines.

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For guidance on the investigation of human cases of WNV infection, please review the Guide for Surveillance and Investigation of Zoonotic Mosquito-Borne Viruses. A document with answers to frequently asked questions about WNV is included in the List of Appendices. A one-page document for medical providers, “West Nile Fever and Neuroinvasive Disease – Information for Clinicians,” can be found in the List of Appendices.

Eastern Equine Encephalitis (EEE)

Epidemiology: Eastern equine encephalitis virus (EEEV) is an alphavirus that was first identified in the 1930s and currently occurs in focal locations of the eastern United States. EEEV transmission has been identified throughout the Americas, but few human cases have been identified outside of North America. The Central and South American lineages of the virus which have been reclassified as the Madariaga virus, are less pathogenic to humans and follow a different transmission cycle than the North American lineage of the virus.20

EEEV occurs in natural cycles involving birds and Culiseta melanura mosquitoes in freshwater swampy areas with a peak of activity between May and August. In this usual cycle of transmission, virus does not escape from the swampy areas because the mosquitoes involved prefer to feed upon birds and will only occasionally bite humans or other mammals. While the role of non-avian vertebrates in the transmission cycle of EEEV is unclear, a study in 2012 indicated that snakes in the wild may harbor the virus through winter brumation (the reptilian form of hibernation), acting as a bridge to the next season.21 For reasons not fully understood, the virus may escape from endemic foci in swamp areas in birds or bridge vectors such as Coquillettidia perturbans, Aedes atlanticus, Cx. nigripalpus, Cx. quinquefasciatus, Aedes sollicitans and Aedes vexans mosquitoes. These species feed on both birds and mammals and can transmit the virus and cause disease in people, horses, dogs, deer, camels, cattle, sheep, seals, some rodents, possibly some reptiles and amphibians, and some non-passerine birds such as turkeys, pheasants, quail, ostriches and emus. Native passerine bird species are rarely clinically affected by the virus. Emus and other raites in particular are highly vulnerable to infection and may develop a fatal hemorrhagic enteritis. Exposure to body fluids (particularly feces, saliva, and blood) from infected emus and other raites can lead to additional birds being infected and potential exposure of humans and other animals. Outbreaks of EEE in multiple emu flocks (Levy, Marion, Volusia, Okeechobee, and Nassau counties) were reported in 2018, with suspected bird-to-bird transmission, and in one case suspected transmission to an ostrich in an adjoining pen.

While small focal outbreaks of human disease have occurred in the United States, equine epizootics can be a common occurrence in unvaccinated populations since horses typically live outdoors and can attract hordes of biting mosquitoes. Human cases may be preceded by those in horses; therefore, horse cases may be used as a potential surveillance tool. Migratory birds may introduce EEEV to northern states in the spring each year. Human and equine cases typically occur within five miles of Cs. melanura-producing swamps. All evidence indicates that human EEE does not have epidemic potential in Florida. Continuous surveillance in Florida since 1957 has documented less than 100 sporadic cases in people (average 1.5 cases per

In none of the years was the total number of human cases greater than five. Although sentinel chicken serosurveillance may not be as predictive of human infections for EEEV as for WNV or SLEV, if the level of activity is high, mosquito control and personal protection is recommended to reduce human risk.

Whereas *Cs. melanura* is distributed statewide, human (and equine) cases of disease have predominantly been in areas north of Lake Okeechobee. Historically, there have been clusters of cases in seven areas: Escambia County; Walton-Holmes-Jackson counties; Duval County; Alachua-Marion counties; Leon-Wakulla-Jefferson-Madison counties; the lower St. Johns area of Volusia, Flagler, Putnam and Clay counties; and the Green Swamp region of Lake, Orange, Pasco, Polk, Osceola, Pinellas, Hillsborough and Manatee counties.

**Incubation period:** It takes from 3 to 10 days after the bite of an infected mosquito for an individual to develop symptoms of EEE.

**Clinical symptoms:** Compared with some other arboviral diseases, fewer EEEV infections are likely to be asymptomatic. In New Jersey it is estimated that for every 23 people bitten by an infected mosquito, one will develop clinical disease. The symptoms begin with a sudden onset of fever, myalgia, malaise, and a headache of increasing severity. Many individuals will progress to more severe symptoms such as seizures and coma. Approximately 30–45% of all patients with clinical encephalitis caused by EEEV will die from the disease, with some deaths occurring following extended illness more than a year after infection (Michelle George, DOH unpublished data). Of those who recover, many will suffer permanent brain damage requiring long-term medical care. Individuals under 15 years of age seem to be at increased risk of severe disease and account for 53% of reported cases in Florida. Persons over 50 years of age may also be at increased risk.

**Vaccination:** A vaccine is licensed for horses, and equine EEEV products are sometimes used off-label for ratites (ostriches and emus), which are susceptible to EEEV.22

For guidance on the investigation of human EEE cases, please review the Guide for Surveillance and Investigation of Zoonotic Mosquito-Borne Viruses. A document with answers to frequently asked questions about EEEV is included in the List of Appendices.

**Other Zoonotic Arboviruses**

Other zoonotic arboviruses of interest in Florida include the following:

**Additional Alphaviruses**

**Venezuelan equine encephalitis viruses** (VEEV) are a complex of viruses that have been identified throughout the Americas and are characterized into two groups, enzootic and epizootic. Enzootic subtypes of VEEV circulate in sylvatic or swamp habitats and only occasionally cause overt disease in humans or domestic animals. These virus subtypes are most often associated with a rodent-mosquito transmission cycle. Enzootic subtypes have been found in the United States, including *Everglades virus* (EVEV) in Florida and Tonate virus in Colorado and South Dakota. EVEV circulates among rodents and vector mosquitoes in south

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Florida. While serologic evidence of EVEV infection has been documented in south Florida, only three clinical cases have ever been identified, two near Homestead and Florida City in Miami-Dade County (1968 and 1971) and one near Vero Beach (1968). Epizootic subtypes of VEEV are highly pathogenic to equines and can also be transmitted to humans. For these viruses, equines are capable of transmitting the virus to mosquitoes and are considered the main virus amplifiers. Epidemics caused by epizootic subtypes tend to occur in South and Central America, but some outbreaks have spread into North America.

**Western equine encephalitis virus** (WEEV) activity is primarily in the western and central United States. The transmission cycle of WEEV is similar to EEEV with the exception that it is transmitted by the *Culex tarsalis* mosquito. Unlike EEE, the fatality rate for WEE is low, with infants most at risk for severe disease. To date, no reported human cases of WEE have been acquired in Florida.

**Highlands J virus** (HJV) is a mosquito-transmitted alphavirus that is similar to EEEV in its natural cycle. HJV is transmitted from *Cs. melanura* mosquitoes to songbirds in freshwater swamps. It has a low pathogenicity in mammals and rarely causes disease in humans or horses. However, HJV is an indicator of fruitful conditions for mosquitoes. During the 1990–91 SLE outbreak in Florida, four patients were reported to be infected with SLEV and HJV; however, exposure to HJV has not been associated with human illness. There have been outbreaks reported in caged birds but the symptoms were mild.

### Additional Flaviviruses

**Japanese encephalitis** (JE) is caused by infection with the JE virus (JEV), in the family *Flaviviridae* and is closely related to WNV and SLEV. It is the leading cause of vaccine-preventable encephalitis in people residing in Asia and the western Pacific. JEV infection can also cause fetal losses in pigs resulting in significant economic impacts, and encephalitis in horses.

JEV is not present in the United States or the Western Hemisphere, but is present throughout much of Asia and the western Pacific. The virus is maintained in a mosquito-vertebrate host cycle, primarily involving *Culex* mosquitoes, especially *Culex tritaeniorhynchus*, and pigs and wading birds. Dogs, sheep, mules, and horses can also amplify the virus. Humans, cattle, domestic poultry, and reptiles are considered dead-end hosts. Activity occurs most frequently in agricultural areas with rice fields and flooding irrigation, which sometimes can be located close to urban areas.

The incubation period is 5–15 days. Less than 1% of infected people experience symptoms. Symptoms can include fever, headache and vomiting followed by neurologic symptoms, weakness, and movement disorders. Seizures may occur, particularly in pediatric infections. Mortality rate is 20–30% in those with neurologic symptoms, and 40–50% of survivors have long-term neurologic, cognitive, or psychiatric sequelae.

Inactivated Vero cell culture-derived JEV vaccine, manufactured as IXIARO, is the only JEV vaccine licensed and available in the United States. This product is licensed for use in those 2 months of age and older. The primary series is two vaccinations 28 days apart. A booster

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vaccination may be recommended if it has been longer than one year from the last vaccination. Other products are available outside the United States. For more information see: www.cdc.gov/japaneseencephalitis/vaccine/index.html.

Murray Valley encephalitis virus (MVEV) is a mosquito-borne flavivirus endemic to Australia and Papua New Guinea. MVEV is transmitted by several *Culex* mosquito species and water birds serve as the main reservoir host. While most people exposed to the virus are asymptomatic, those who develop symptoms report a febrile illness, with some cases developing neuroinvasive disease.

**Bunyaviruses**

**California Serogroup**

La Crosse encephalitis virus (LACV) is found in the Appalachian and Midwestern regions of the United States. It is not believed to be present in Florida, however imported cases are identified regularly. It is part of the California serogroup viruses. LACV is maintained in a transmission cycle between the *Aedes triseriatus* mosquito and small mammals such as chipmunks and squirrels. The incubation period is 5–15 days. Symptoms can range from fever, headache, nausea, vomiting, and fatigue to neuroinvasive disease with seizures. Neuroinvasive disease occurs most frequently in children under the age of 16. Fatal cases are rare, but neurological sequelae have been reported in some cases.

Keystone virus (KEYV) is an arbovirus involved in a transmission cycle with small mammals in the southeastern mid-Atlantic regions of the United States. The only recorded human case of Keystone virus illness in Florida occurred in a young child from Sarasota in 1964. Additional serosurveys involving healthy individuals estimated that 1–6% of the Tampa Bay area population possessed antibodies to the California serogroup viruses.

The majority of studies on KEYV were conducted in the 1960s to 1970s. Studies have indicated that the virus is present in the southeastern U.S. and along the eastern seaboard. It was first identified in Florida in 1964.24 KEYV was initially identified in mosquito pools from the Tampa Bay area. The virus was first isolated from *Aedes atlanticus* mosquitoes, but isolations have also occurred in *Aedes infirmatus* and rare isolations were identified in other *Aedes* and *Culex* species. Transovarial transmission (virus transmission from the infected female mosquito directly to her offspring via infection of the eggs) has been identified in some field studies with *Ae. atlanticus* mosquitoes and is also noted with at least one other California serogroup virus (LACV). The first full genome sequence for KEYV was published in 2015, from virus present in two *Ae. atlanticus* mosquito pools collected from Sarasota County in 2005.

Past Florida wildlife serosurveys found evidence of KEYV antibodies in several species including white-tailed deer (Collier, Monroe/Miami-Dade), rabbits (Hillsborough), opossums (Hillsborough), raccoons (Hillsborough), squirrels (Hillsborough, Alachua), cotton rats (Hillsborough) and a blue jay (Alachua).

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**Jamestown Canyon virus** (JCV) is an uncommon California serogroup arbovirus involved in a transmission cycle with deer and is found throughout North America. Illness is most frequently identified in adults. One human case of JCV encephalitis was confirmed in Lee County in 1993.

Other California serogroup viruses of interest in the United States include **California encephalitis virus**, **Snowshoe hare virus**, and **Trivittatus virus**, all of which are uncommon and thought to have zoonotic/animal reservoirs. Trivittatus virus has been isolated from mosquitoes in Florida and identified in several wildlife serosurveys.

**Other Bunyaviruses**

**Cache Valley virus** (CVV) is an uncommon arbovirus suspected to be involved in a transmission cycle with deer or other ungulates such as sheep, horses, and cattle. Very few human cases have been identified in the United States and no cases have been reported in Florida.

**Tensaw virus** (TENV) is an arbovirus initially identified in Alabama. TENV has been isolated from mosquitoes in Florida and identified in several wildlife serosurveys. Serologic evidence of infection with TENV has been documented in humans in south Florida.\(^\text{25}\)

Information on Rift Valley fever, another important Zoonotic arbovirus, is included with the chapter on **exotic mosquito-borne viruses with primary or occasional human reservoirs**.