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## Arboviral Diseases – Neuroinvasive and Non-Neuroinvasive

### SUBTYPES

California Serogroup Viruses including La Crosse Virus	Powassan Virus
Chikungunya Virus	St. Louis Encephalitis Virus
Eastern Equine Encephalitis Virus	Venezuelan Equine Encephalitis Virus
Heartland Virus	West Nile Virus
	Western Equine Encephalitis Virus

### Overview<sup>1, 2, 3, 5</sup>

**Arbovirus** is short for **arthropod-borne virus**. In nature, arboviruses are maintained in a biological cycle between vertebrates (mainly animals, sometimes humans) and blood-sucking arthropods that can include ticks, mosquitoes, sand flies, and black flies.

Arboviruses are responsible for causing a wide spectrum of clinical syndromes, ranging from mild to severe febrile illness to hemorrhagic fever to neuroinvasive disease. Until the introduction of West Nile virus (WNV) to the Western Hemisphere, most arboviral disease activity in the world was focused in tropical and sub-tropical climates. Global scale changes in travel, worldwide commercial trade, and landscape use have provided opportunities for these pathogens and their vectors to expand their geographical range.

Most arbovirus infections are asymptomatic or subclinical, but this generalization should be taken with caution as very high illness rates (between 75 – 97%) have been associated with epidemics of chikungunya virus (CHIKV). Arboviral illnesses can be classified into three clinical syndromes:

- Systemic acute febrile illness typically accompanied by headache, arthralgia, and myalgia, with or without rash and/or polyarthritides;
- Hemorrhagic fever that might be extensive, and associated with capillary leakage, shock, jaundice, liver damage, and death; and
- Acute central nervous system illness ranging from mild aseptic meningitis to encephalitis with coma, paralysis, and death.

Incubation periods for most arboviruses range between 2 days and 2 weeks. While vector transmission is the most common exposure pathway for arboviruses, blood transfusion, organ transplantation, and *in utero* and breast milk transmission have been documented. Laboratory technicians have been infected with WNV and CHIKV via accidental skin puncture with contaminated necropsy tools. With the exception of [yellow fever](#) and Japanese encephalitis, human vaccinations are not yet available for preventing arbovirus infections. Antiviral treatments have not yet proved effective for arbovirus infection, so the primary treatment is supportive care.

Humans infected with an arbovirus are usually classified as incidental or dead-end hosts. In WNV, St. Louis encephalitis virus (SLEV), eastern and western equine

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encephalitis virus, and California encephalitis virus infections, humans do not produce a level of viremia sufficient to contribute to the host-vector-host transmission cycle.

Two currently emerging arboviruses, however, [dengue virus](#) and CHIKV, are exceptions to this general rule because these pathogens produce significant viremia in infected persons. Until the infection resolves, a viremic person can serve as a reservoir of the virus, and uninfected mosquitoes can pick up and later transmit the infection to another person. Public health interventions in arboviral outbreaks involving a human reservoir host require not only traditional mosquito control efforts but measures to shelter viremic individuals from mosquito bites.

The seasonality of most North American arbovirus infections varies with the host-seeking behavior of the arthropod vector. Outbreaks of WNV and SLEV tend to occur in late summer after mosquitoes shift their host-seeking preferences from birds (the reservoir host) to mammals and humans. Epidemiologic investigations into the Heartland virus in Missouri have coincided with the host-seeking behavior of the Lone Star tick, the imputed vector of that virus.

Host behavior also influences the timing of disease reports, with imported cases of both [dengue virus](#) and CHIKV infections peaking during the winter months when vacationers from the United States are visiting tropical climates.

The nationally reportable arboviral diseases endemic to North America include the numerous viruses in the California serogroup (including La Crosse virus), chikungunya, eastern equine encephalitis, Powassan, St. Louis encephalitis, West Nile, and western equine encephalitis. Because it can be easily weaponized, human Venezuelan equine encephalitis virus disease is designated as reportable in Missouri. In addition, public health reporting of other emerging arboviral disease is encouraged, including Colorado tick fever, Rift Valley disease, tickborne encephalitis, and the newly recognized Heartland virus disease.

**Objectives of Domestic Arboviral Surveillance<sup>3</sup>**

The unpredictable nature of arbovirus disease outbreaks necessitates public health surveillance systems capable of detecting increases in arboviral activity. Human disease surveillance provides a nationwide assessment of the impact of arboviral diseases and over the past decade has demonstrated where arboviral incidence and total disease burden are greatest.

The annually robust WNV outbreaks of the upper Great Plains states illustrate that niche adaptations can develop even in newly-arrived viruses. A pattern like this is important to monitor from year to year to determine whether climatic variables and land use changes are affecting the ecological boundaries that influence the distribution of WNV. In addition, at the local level, public health surveillance is important to policy makers' evaluation of the effectiveness of insect bite prevention messaging and mosquito control strategies.

Surveillance systems and public health intervention measures developed for one arbovirus do not necessarily transfer to other arboviruses. Surveillance systems for WNV, for example,



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rely on detection of viral activity in mosquitoes and sentinel animals to provide early warning of increased human disease risk. In contrast, public health officials responding to the massive Caribbean outbreaks of CHIKV that began in 2013 determined that human syndromic surveillance was more effective in determining where mosquito spraying should occur.

In the absence of effective human arboviral vaccines, preventing disease in humans depends on large-scale outbreak prevention and public awareness activities to keep infected vectors from biting people.

For a more complete description of arboviral diseases, refer to the following texts:

- *Control of Communicable Diseases Manual*. (CCDM), American Public Health Association. 20<sup>th</sup> ed. 2015.
- American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29<sup>th</sup> ed. 2012.
- Centers for Disease Control and Prevention (CDC), *Epidemic/Epizootic West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control*, 4<sup>th</sup> ed. 2013.

**2015 Case Definition – Arboviral diseases, Neuroinvasive and Non-neuroinvasive<sup>4</sup>**

**Subtypes**

- |   |                                      |
|---|--------------------------------------|
| California Serogroup Viruses<br>including La Crosse Virus | Powassan Virus                       |
| Chikungunya Virus   | St. Louis Encephalitis Virus         |
| Eastern Equine Encephalitis Virus                         | Venezuelan Equine Encephalitis Virus |
|   | West Nile Virus                      |
|   | Western Equine Encephalitis Virus    |

***Background***

Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. Other modes of transmission for some arboviruses include blood transfusion, organ transplantation, perinatal transmission, breast feeding, and laboratory exposures.

More than 130 arboviruses are known to cause human disease. Most arboviruses of public health importance belong to one of three virus genera: *Flavivirus*, *Alphavirus*, and *Orthobunyavirus*.

California serogroup viruses include: California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, and Trivittatus viruses.

***Clinical Description***

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purposes of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and non-neuroinvasive disease.





**Neuroinvasive disease**

Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with headache, myalgia, stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid (CSF) pleocytosis. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barré syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

**Non-neuroinvasive disease**

Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, rash, or gastrointestinal symptoms. Some viruses also can cause more characteristic clinical manifestations, such as severe polyarthralgia or arthritis due to chikungunya virus or other alphaviruses (e.g., Mayaro, Ross River, and O'nyong-nyong).

***Clinical Criteria***

A clinically compatible case of arboviral disease is as defined as follows:

**Neuroinvasive disease**

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, **AND**
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis, and/ or nuchal rigidity.

**Non-Neuroinvasive disease**

- Fever (chills) as reported by the patient or a health-care provider, **AND**
- Absence of neuroinvasive disease, **AND**
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis, and/ or nuchal rigidity.

***Laboratory Criteria for Diagnosis***

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, **OR**
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, **OR**
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, **OR**
- Virus-specific IgM antibodies in CSF or serum.

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***Case Classification***

***Probable***

**Neuroinvasive disease**

A case that meets the above clinical criteria for neuroinvasive disease and the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

**Non-Neuroinvasive disease**

A case that meets the above clinical criteria for non-neuroinvasive disease and the laboratory criteria for a probable case:

- Virus-specific IgM antibodies in serum but with no other testing.

***Confirmed***

**Neuroinvasive disease**

A case that meets the above clinical criteria for neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, **OR**
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, **OR**
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, **OR**
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

**Non-Neuroinvasive disease**

A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, or other body fluid, excluding CSF, **OR**
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, **OR**
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen.

***Comment(s)***

*Imported arboviral diseases*

Human disease cases due to dengue or yellow fever viruses are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g., Japanese encephalitis, tickborne encephalitis, Venezuelan equine encephalitis, and Rift Valley fever viruses) are important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment

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of imported arboviral pathogens. Healthcare providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in international travelers. If a suspected case occurs, it should be reported to the appropriate local/state health agencies and CDC.

*Interpreting arboviral laboratory results:*

- **Serologic cross-reactivity:** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections within genera (e.g., *flaviviruses* such as West Nile, St. Louis encephalitis, Powassan, dengue, or Japanese encephalitis viruses).
- **Rise and fall of IgM antibodies:** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g., up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome.
- **Persistence of IgM antibodies:** Arboviral IgM antibodies may be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.
- **Persistence of IgG and neutralizing antibodies:** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.
- **Arboviral serologic assays:** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of arboviral-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).

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- **Other information to consider.** Vaccination history, detailed travel history, date of onset of symptoms, and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.

### **Information Needed for Investigation**

**Verify the diagnosis.** Obtain demographic, clinical, laboratory information, and other epidemiological information necessary to complete the [Arbovirus Infections Case Report Form](#) from the attending physician, hospital, and/or laboratory and patient or a knowledgeable family member. Epidemiologically significant attributes of an infection include:

- Demographics (age, sex, race/ethnicity, place of residence, occupation, or other characteristics that can reveal seasonal, geographic, and demographic patterns).
- Clinical symptoms and syndrome (e.g., asymptomatic blood donor, uncomplicated fever, meningitis, encephalitis, acute flaccid paralysis, other).
- Date of illness onset.
- Hospitalization and outcome.

**Investigate laboratory reports of presumptive viremic blood donors.** Presumptive viremic blood donors (PVDs) are people who had no symptoms at the time of donating blood, but whose blood, tissue, or hematopoietic progenitor cells tested positive when screened for the presence of WNV. The public health impact of PVD reporting and case investigation includes the following:

- PVDs that develop symptoms after donation should be included in morbidity counts.
- Identification of WNV infected persons – even those without illness – is a tool that municipal and county public works and public health mosquito control programs can use to prioritize areas for mosquito monitoring and pesticide treatment.
- An epidemiologic dataset of the demographic attributes, preexisting risk factors, and geographic incidence of both symptomatic and asymptomatic WNV infections can be used to evaluate the effectiveness of insect bite prevention messaging and mosquito control strategies.

**Establish the source of the infection.** Look back approximately two weeks:

- Travel history in the 2 weeks prior to illness onset (obtain from the patient or the patient’s family, neighbors, co-workers, social worker, or health care provider)
- Are there household or workplace contacts with a similar illness?
- Was the patient’s arthropod exposure (e.g., mosquito/tick bites) in-state, out-of-state, or out-of-country?
- Rule out non-arthropodborne transmission pathways (which may fall outside the two week timeframe):
  - ◆ Was case a transfusion or transplant recipient in the last two months?
  - ◆ Does case work in laboratory or clinical setting?
  - ◆ Is case a neonate, pregnant, or breast feeding?

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- If the patient is a recent organ, tissue (e.g., corneas, skin), or blood donor or recipient:
  - ◆ Assure relevant partners have been notified (blood collection agencies, hospitals, CDC, other health departments).
  - ◆ Assure quarantine of remaining co-component blood or tissues.
  - ◆ If necessary, investigate recipients of transfused co-components from implicated donation and other potentially contaminated donations from implicated donor(s).
  - ◆ Notify Bureau of Communicable Disease Control and Prevention (BCDCP).

**Provide information on Arboviral disease to persons at risk for infection and the general public as needed.** Efforts should be made to promote arboviral disease awareness among international travelers and persons visiting family and friends where these diseases are known to occur. To the extent possible, travelers should avoid known foci of epidemic disease transmission. Although mosquitoes may bite at any time, peak biting activity for vectors of chikungunya is during daylight hours. Residents of and travelers to areas with endemic arboviral disease can reduce their risk of infection by using mosquito repellent, wearing long-sleeved shirts and pants, and sleeping in locations with air conditioning or screens on doors and windows. Additional information on “Protection against Mosquitoes, Ticks, & Other Insects & Arthropods” can be found at: <http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-2-the-pre-travel-consultation/protection-against-mosquitoes-ticks-and-other-insects-and-arthropods>.

**Arboviral Disease Surveillance.** Medical providers should report arboviral cases promptly. Local public health agencies (LPHAs) should review WebSurv to determine whether there have been other cases reported. When cases are related by person, place, or time, efforts should be made to identify a common source.

Data collected from arboviral disease surveillance is used to monitor trends; identify areas of risk and risk factors in the United States. Further public health surveillance can enhance healthcare provider awareness of arboviral disease so that cases can be rapidly identified, thereby reducing the possibility of local transmission or establishment of endemicity in this country of certain arboviral diseases.

**Notification**

- The local public health agency (LPHA) should immediately contact the [District Communicable Disease Coordinator](#), or the [Senior Epidemiology Specialist](#) for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/Emergency Response Center (ERC) at (800) 392-0272 (24/7) immediately if an outbreak\* of an arbovirus is suspected.
- If a case(s) is associated with a childcare center, BCDCP or the LPHA will contact the Bureau of Environmental Health Services, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.



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- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.

\*Outbreak is defined as the occurrence in a community or region, illness(es) similar in nature, clearly in excess of normal expectancy and derived from a common or a propagated source.

**Prevention and Control**<sup>3, 5, 6, 7</sup>

Without a human vaccine for WNV and the other mosquito-transmitted viruses, the only way to prevent human infection and disease is to prevent infected mosquitoes from biting people. This is accomplished by:

- Community-based integrated mosquito management programs (described below under Integrate Vector Management)
- By effective personal protection behaviors and practices, particularly
  - Mosquito-avoidance
  - Use of personal repellents
  - Removal of residential mosquito breeding habitat (e.g., manmade and natural pools of stagnant water)

Every year, more and more personal repellent products are introduced onto the market. DHSS and CDC recommend products containing active ingredients that have been registered by the Environmental Protection Agency (EPA) for use as repellents that are applied to skin and clothing. Products that do not have an EPA registration number have not been scientifically evaluated and approved for effectiveness or human safety.

In addition, because repellents are used to prevent disease, over and above the annoyance of preventing insect bites, CDC also has reviewed scientific literature and data available from EPA. The result of this additional review is a list of several EPA-registered products that are recommended by CDC because they can be used to help people avoid the bites of disease-carrying mosquitoes. Products containing these active ingredients typically provide reasonably long-lasting protection:

- DEET (Chemical Name: N,N-diethyl-m-toluamide or N,N-diethyl-3-methylbenzamide)
- Picaridin (KBR 3023, Chemical Name: 2-(2-hydroxyethyl)-1-piperidinecarboxylic acid 1-methylpropyl ester )
- Oil of Lemon Eucalyptus or PMD (Chemical Name: para-Menthane-3, 8-diol) the synthesized version of oil of lemon eucalyptus (NOTE: This recommendation refers to EPA-registered repellent products containing the active ingredient oil of lemon eucalyptus (or PMD). “Pure” oil of lemon eucalyptus (e.g. essential oil) has not received similar, validated testing for safety and efficacy, and is not covered by this CDC recommendation.)
- IR3535 (Chemical Name: 3-[N-Butyl-N-acetyl]-aminopropionic acid, ethyl ester)



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*Reduce Mosquito Production at the Home*

Encourage residents to regularly remove standing water around the home, such as clogged rain gutters, flowerpots, old tires, empty containers, buckets, and wading pools. Water in birdbaths should be changed at least once per week. CDC provides resources that list these and other steps for reducing mosquito breeding habitat. (<http://www.cdc.gov/ncidod/dybid/westnile/ga/habitats.htm>).

*Integrated Vector Management*

Mosquito abatement programs can employ integrated pest management principles to reduce mosquito abundance, providing important community services to protect quality of life and public health. Prevention and control of WNV and other arboviral diseases is accomplished most effectively through a locally-based integrated vector management (IVM) program that conducts surveillance, assesses infectivity rates in mosquito populations, and monitors the effectiveness of control operations.

IVM is based on an understanding of the underlying biology of the arbovirus transmission system, and utilizes regular monitoring of vector mosquito populations and arboviral pathogen activity levels to determine if, when, and where interventions are needed to keep mosquito numbers below levels that produce risk of human disease, and to respond appropriately to reduce risk when it exceeds acceptable levels.

Operationally, IVM is anchored by a monitoring program providing data that describe:

- Conditions and habitats that produce vector mosquitoes.
- Abundance of those mosquitoes over the course of a season.
- Arbovirus transmission activity levels expressed as pathogen infection rate in mosquito vectors.
- Parameters that influence local mosquito populations and arboviral transmission.

Mosquito monitoring data inform decisions about implementing mosquito control activities appropriate to the situation, such as:

- Source reduction through habitat modification.
- Larval mosquito control using the appropriate methods for the habitat.
- Adult mosquito control using pesticides applied from trucks or aircraft when established thresholds have been exceeded.
- Community education efforts related to mosquitoborne disease risk levels and intervention activities.

IVM also provides quality control for the program, allowing evaluation of:

- Effectiveness of larval control efforts.
- Effectiveness of adult control efforts.
- Causes of control failures (e.g., undetected larval sources, pesticide resistance, and equipment failure).



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### *Vector Management*

- No models have been developed to provide long-term predictions of how and where a variety of biotic and abiotic factors will combine to produce WNV outbreaks.
- The use of public health human case surveillance by itself is insufficient for predicting or preventing outbreaks of WNV disease.
- Intensive early season adult mosquito control efforts can decrease WNV transmission activity and result in reduced human risk.
- As evidence of sustained or intensified virus transmission in a region increases, emergency vector control efforts to reduce the abundance of infected, biting adult mosquitoes must be implemented.
- Delaying adulticide applications until numerous human cases occur negates the value and purpose of the surveillance system. Timely application of an effective adulticide interrupts WNV transmission and prevents human cases.

### *Emergency Mosquito Abatement Protective Measures Following a Declared Emergency or Major Disaster*

- Federal Emergency Management Agency (FEMA) Recovery Policy RP9523.10 describes FEMA criteria to determine eligibility for mosquito abatement measures following a declared emergency or major disaster.
- Where possible, a determination of the need for mosquito abatement measures is based on surveillance data provided by local agencies, or on surveillance conducted as a component of the emergency response.
- Insecticide formulations must be among those registered by the U.S. Environmental Protection Agency for use in urban areas for mosquito abatement and must be applied according to label directions and precautions by appropriately trained and certified applicators.

### **Laboratory Procedures**<sup>8,9</sup>

The front-line screening assays for laboratory diagnosis of human WNV infection is the IgM enzyme-linked immunosorbent assay (ELISA) and the enzyme immunoassay (EIA). The Missouri State Public Health Laboratory (MSPHL) also uses a microsphere-based immunoassay for the detection of IgM antibodies that can differentiate WNV from SLE.

Because the IgM and IgG ELISA tests can cross-react among the various species in the flavivirus genus (e.g., WNV SLE, dengue, yellow fever, Japanese encephalitis), they should be viewed as screening tests only. For a case to be considered confirmed, serum samples that are antibody-positive on initial screening should be evaluated by a more specific test. Currently the plaque reduction neutralization test (PRNT) is the recommended test for differentiating between flavivirus infections.

Although WNV is the most common cause of arboviral encephalitis in the United States, there are several other arboviral encephalitides present in the country and in other regions of the world. Specimens submitted for WNV testing should also be

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tested by ELISA and PRNT against other arboviruses known to be active or be present in the area or in the region where the patient traveled.

Instructions for submitting diagnostic specimens for serological testing for WNV and SLEV are available on the MSPHL website at <http://www.health.mo.gov/lab/westnile.php>. In addition, testing for CHIKV infection is available through CDC following approval from a MDHSS epidemiologist to assure symptoms and likely exposure. Providers and disease investigators should contact the Vectorborne Disease Program at 573 526 4780 or afterhours contact the MDHSS/ERC at 800 392 0272 (24/7).

MSPHL testing for eastern equine encephalitis (EEE), western equine encephalitis (WEE), and La Crosse/California encephalitis group is available and also requires consultation with the Vector-Borne Disease Program 573 751 6113 or 800 392 0272 (24/7).

A completed MSPHL Virology Test Request form (LAB-158) must accompany all specimens and can be accessed at:

[https://webapp01.dhss.mo.gov/LIMSForm\\_APP/SelectLab.aspx](https://webapp01.dhss.mo.gov/LIMSForm_APP/SelectLab.aspx).

### **Reporting Requirements**

Arboviral diseases (neuroinvasive and non-neuroinvasive) are Category 3 reportable diseases and shall be reported to the [local public health agency](#) or to the Missouri Department of Health and Senior Services (MDHSS) within three days of first knowledge or suspicion by telephone, facsimile, or rapid communication. The MDHSS is requesting the following arboviral infections to be reported:

- |                                   |                                   |
|-----------------------------------|-----------------------------------|
| California Serogroup Viruses      | Powassan Virus                    |
| La Crosse Virus                   | St. Louis Encephalitis Virus      |
| Chikungunya Virus                 | West Nile Virus                   |
| Eastern Equine Encephalitis Virus | Western Equine Encephalitis Virus |

As Nationally Notifiable Conditions, all cases prior to classification are a **STANDARD** report to the CDC. **STANDARD** reporting requires the MDHSS to report to CDC by electronic transmission via WebSurv within the next normal reporting cycle.

**NOTE:** *The exception to this is Venezuelan equine virus neuroinvasive and non-neuroinvasive disease. Because of its possible use as a weapon of bioterrorism, it is classified as a Category IB condition and suspected or confirmed cases must be reported to the local health authority or to the Missouri Department of Health and Senior Services **within 24 hours**. MDHSS may be contacted 24 hours a day, 7 days a week at (800) 392-0272 (24/7).*

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1. For all reported cases, complete a “[Disease Case Report](#)” (CD-1) and a “[Arbovirus Infection Case Report](#)” (MO 580-2601) and send the completed forms to the [DHSS District Health Office](#).
2. Entry of the completed CD-1 into WebSurv negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. MDHSS will report to CDC following the above reporting criteria (see box).
4. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the [District Communicable Disease Coordinator](#) or the [District Senior Epidemiology Specialist](#). This can be accomplished by completing the [Missouri Outbreak Surveillance Report](#) (CD-51).
5. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

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