Human Mosquito-Borne Disease Surveillance

Please refer to the Guides to Surveillance and Investigation for more information on surveillance and response to arboviruses of public health importance in Florida.

West Nile virus (WNV) infections, St. Louis encephalitis (SLE), Eastern equine encephaltis (EEE) malaria, dengue fever, chikunguya fever, yellow fever, and Zika virus (ZIKV) infections are reportable are human disease in Florida per section 381.0031, Florida Statutes and rule 64D-3, Florida Administrative Code. County health departments (CHDs) provide case information to the Department of Health (DOH) Bureau of Epidemiology (BOE) for data analysis and dissemination. When dealing with cases of human arthropod-borne diseases, close communication and coordination among partner agencies is essential to prevent further human disease transmission.

DOH protects the confidentiality of all persons who may have arboviral or other notifiable diseases (section 381.0055). However, when there is a need to protect the public's health, DOH is allowed to share confidential information with people who need to know (section 381.0031, F.S.). Such instances include sharing mosquito exposure information from human arbovirus cases with recent disease onset with mosquito control districts to ensure appropriate mosquito surveillance and control. The information should be shared between one contact at the CHD (the case investigator) and one contact at the mosquito control district (mosquito control operations chief), and the information shared should be limited to **only** that necessary for effective mosquito control. Information should be shared over the phone; email correspondence with the DOH is public record and should not contain personal identifiers of persons with arboviral disease. The exact address of the human case may or may not be needed to ensure effective mosquito control. In urban areas, a city block or neighborhood may be sufficient while in rural areas it may be necessary to share the exact address of the patient's residence. It is expected that those in possession of confidential information treat it in such a way that the privacy of the individual is maintained. It is expected that mosquito control district personnel will shred notes with confidential information when they are no longer needed.

Example of a shared information agreement:
The parameters that xxxxxx County Health Department and Mosquito Control District have agreed upon are as follows:

- Block number (i.e., 900 Adam Street) and street address of the residence of the WNV human case (criteria may vary with arbovirus depending on virus ecology)
- ZIP Code of the person's residence
- Notification of both confirmed and suspect human arboviral cases
- Patient's date of onset
- CHD and mosquito control work as partners and as stewards of the privacy of affected citizens

See the List of Appendices for a written business agreement template: Agreed Protocol for Reporting Arbovirus Human Cases to Mosquito Control Jurisdictions by County Health Departments.

Surveillance for endemic arbovirus diseases includes human, domestic and wild animal disease surveillance and monitoring for arbovirus activity through sentinel chicken and mosquito testing. Chapter 10 provides details related to non-human arbovirus disease surveillance. Human surveillance is the primary surveillance tool for arboviruses such as dengue, chikungunya, and Zika for which humans are the primary reservoirs.

Transfusion- and Transplant-Associated Infections

Although uncommon, a number of arthropod-borne diseases can also be transmitted via blood transfusion or tissue transplant. Blood banks in the U.S. are required to screen blood donations for WNV and Zika virus (ZIKV) and viremic blood donors are reported to CDC. DOH performs confirmatory testing on WNV- and ZIKV-reactive blood donors and the local CHD determines the likely exposure location. If the donor is confirmed positive for WNV or ZIKV at the DOH Bureau of Public Health Laboratories (BPHL), and exposure occurred in Florida, blood donors can trigger mosquito-borne illness advisories or alerts. People found to be positive are not permitted to donate blood for 120 days. In addition, donors are typically questioned about travel to malaria-endemic countries and are not permitted to donate within a year of travel or within three years of their last malaria symptoms. Despite these precautions, infections through donation can still occur.

Currently, blood banks in the U.S. do not test donated blood for chikungunya virus (CHIKV), dengue virus (DENV), or yellow fever (YFV) viruses. While transmission of these viruses by blood transfusion is possible, these events are considered rare. During outbreaks, however, the risk increases due to the possibility of individuals donating blood while asymptomatic. During outbreaks of locally acquired disease, strategies that focus on excluding donors who may be at higher risk of infection will be implemented. Donor deferrals will occur when two or more locally acquired dengue or chikungunya cases are identified in multiple locations or households. The Arbovirus Surveillance Coordinator will provide blood banks with the residential ZIP Code(s) of locally acquired cases in these instances or for one case of locally acquired ZIKV or YFV infection in order to help identify populations at higher risk. This will continue until the outbreak has been resolved.

Laboratory Evaluation

BPHL provides confirmatory laboratory testing services for patients with clinical signs of arboviral disease. Due to the potential for false-positive test results, positive private laboratory test results, including blood bank-reactive donor test results, must be confirmed by BPHL (i.e., specimens testing positive at private laboratories must be forwarded to the state laboratory for confirmation). Health care providers should submit acute and convalescent serum and/or cerebrospinal fluid (CSF) samples to either the Tampa or Jacksonville BPHL for endemic arbovirus cases. Acute serum samples from imported and locally acquired dengue and chikungunya should also be forward to BPHL. Even though a very early acute serum may be negative, it is recommended that it be collected and submitted without waiting for the convalescent specimen. The convalescent specimen (drawn two weeks later) should be routinely sent to confirm negative and positive results.

It is important to confirm identification of a specific agent in instances of a suspected arbovirus infection. This results in appropriate patient therapy and effective vector control operations designed to limit transmission to additional susceptible human hosts. Confirmation is dependent upon viral isolation/detection or antibody detection by serologic assays such as the plaque

reduction neutralization test (PRNT) or enzyme-linked immunosorbent assay (ELISA) tests. Interpretation of each of the tests is dependent upon the time of specimen collection relative to the date of symptom onset, the patient's previous arbovirus infection history, and serum cross-reactivity within the antigenic complex. In Florida, previous flavivirus infection (i.e. WNV, SLEV, ZIKV, or DENV) or previous yellow fever vaccination are the most common factors that can complicate the interpretation of antibody tests. In addition, current infections with herpes simplex virus, Epstein-Barr virus, *Streptococcus* species, influenza, or other pathogens may also complicate the interpretation of antibody tests.

Laboratory Testing Available at BPHL

Routine tests

Capture Enzyme Immunoassay for IgM Antibody: IgM antibodies can be detected in either serum or CSF using a capture enzyme immunoassay. The presence of significant levels of IgM is generally a reliable indicator of recent infection. However, a subset of case patients may have serum IgM antibody to flaviviruses persisting for over a year, thus somewhat limiting the value of the assay as a measure of recent infection. Since IgM antibody does not cross the blood-brain barrier, its presence in CSF indicates local antibody synthesis in response to a central nervous system infection and is usually diagnostic. Cross-reactivity within a virus group (e.g., flaviviruses) is common.

Enzyme Immunoassay (EIA) for IgG Antibody: IgG antibodies can be detected in serum using EIA. A positive IgG result is indicative of infection or immunization with a group B flavivirus at an undetermined time. Dengue re-infection can also cause a significant elevation in IgG antibody titers (generally >6.0) and may indicate a recent dengue infection that might be detectable by PCR if symptom onset was within the past seven days.

Virus Detection (Reverse Transcriptase Polymerase Chain Reaction [RT-PCR] Assays and Other Nucleic Acid Tests [NAT]): DENV, CHIKV, and ZIKV frequently may be detected using RT-PCR from blood during the first few days after onset of illness. Virus may also be detected in blood donated prior to development of clinical symptoms using RT-PCR for WNV and ZIKV.

Additional supportive and confirmatory tests

Serum Neutralization (SN) or Plaque Reduction Neutralization Test (PRNT): Neutralizing antibody is primarily IgG. SN antibody rises late in the course of infection, and may persist for life after some viral infections. BOE, in conjunction with BPHL, will determine when this testing is warranted.

Virus Isolation (Culture): It is rare to isolate SLEV or WNV from blood or CSF taken during the acute phase of encephalitis due to a brief viremic stage prior to onset of illness. SLEV and WNV can be detected in brain tissue collected at autopsy or necropsy (veterinary testing). Eastern equine encephalitis virus (EEEV) and Western equine encephalitis virus (WEEV) are also usually only isolated from the brain. BOE, in conjunction with BPHL, will determine when this testing is warranted.

Interpretation of Laboratory Results for Arboviruses

BPHL EIA/ELISA results are reported as positive, negative, or inconclusive/equivocal; numeric values should not be interpreted as an antibody titer. Positive to negative control ratios (P/N) are available from BPHL for many antibody tests and may also be useful for interpretation. Antibody titer values are provided for SN or PRNT testing performed at BPHL. IgM should be present in serum within nine days of symptom onset. IgM is detectable in CSF before serum in patients exhibiting neurologic signs.

Note: All specimens tested for flaviviruses at BPHL are tested for antibodies to multiple viruses when appropriate (i.e. WNV, SLEV, DENV, and ZIKV) before considered confirmed. Antibodies cross-reactive to multiple viruses are often present in flavivirus-positive sera. Specific antibodies to the virus causing the infection generally have the highest titers (may not always be the case, as seen with DENV and ZIKV). There is less cross-reactivity seen among alphaviruses such as EEEV and CHIKV, as they belong to different antigenic complexes. In addition, all samples that are tested for DENV, ZIKV, or CHIKV at BPHL are tested for all three viruses when appropriate.

	Laboratory Test	**Interpretation**
1	**RT-PCR on serum, tissue, blood, CSF or other body fluids**	Confirmed case
2	**Virus isolation in serum, tissue, blood, CSF or other body fluids**	Confirmed case
3	**Demonstration of specific viral antigen (immunohistochemistry [IHC]) in serum, tissue, blood, CSF or other body fluids**	Confirmed case
4	**CSF (EIA or ELISA) IgM + for an arbovirus**	
4a	Negative for other endemic arboviral IgM antibodies in the same family in CSF	Confirmed case
4b	Not tested for other endemic arboviral IgM antibodies in the same family in CSF	Probable case
5	**Serum (EIA or ELISA) IgM + for an arbovirus**	
5a	Positive for virus-specific neutralizing antibodies in the same or a later specimen (SN or PRNT)	Confirmed case
5b	Negative or not tested for virus-specific neutralizing antibodies in the same or a later specimen (SN or PRNT)	Probable case
6	**Serum or CSF (EIA or ELISA) IgM – for an arbovirus**	
6a	IgG -	Not a case

6b	IgG +	If results are for EEEV or CHIKV: Not a case – indicative of past infection at an undetermined time. If results are for DENV, WNV and/or SLEV: Not a case – indicative of infection or immunization with a group B flavivirus at an undetermined time; PCR testing may be warranted for DENV and ZIKV if acute sample is available.