WISCONSIN DEPARTMENT of HEALTH SERVICES

Division of Public Health
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2023 Arbovirus Management Protocol

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Important Information for 2023

A. The Division of Public Health (DPH) will continue to confirm all presumptive positive laboratory results reported by physicians and private laboratories at the Wisconsin State Laboratory of Hygiene (WSLH). Case-patients testing positive at the WSLH with confirmatory testing at the CDC (Centers for Disease Control and Prevention), and who meet other clinical and epidemiological surveillance criteria, will be reported to CDC as confirmed. Case-patients for whom specimens are unavailable for confirmatory testing at the CDC may be reported to CDC as probable. Prompt notification of all immunoglobulin M (IgM) antibody test results to DPH is essential for us to obtain specimens at commercial laboratories for confirmation.

B. As of January 2020, DPH no longer collects dead birds for West Nile virus (WNV) testing and has deactivated the Dead Bird Reporting Hotline (1-800-433-1610) indefinitely.

Local or Tribal health departments (LTHD) that receive calls from the public regarding dead bird reporting and testing should indicate that the Dead Birth Reporting Hotline is no longer operational, and should refer callers to the Wisconsin Department of Natural Resources (DNR) Wildlife Health Program for instructions on which species of birds should be reported to the DNR for wildlife health-related investigations. Most individual dead birds do not need to be reported or collected, and can be discarded. To safely dispose of a dead bird, use gloves or an inverted plastic bag to place the carcass in a garbage bag, which can then be placed in the regular trash. Dead birds should not be handled with bare hands.

C. During the 2023 mosquito and tick season, data updates will be posted on DPH websites weekly or as new arboviral activity is detected. Data updates will include numbers of confirmed and probable human cases of locally acquired arboviruses by county, as well as other county-level arboviral activity detected through mosquito or tick surveillance or veterinary testing.

D. Human Jamestown Canyon virus (JCV) surveillance data from 2017–2020 have identified a relatively low positive predictive value for confirmatory serologic testing (that is, positive IgM and positive PRNT in the same or later specimen). Many case-patients who have both IgM and PRNT evidence of a recent JCV infection do not meet clinical or epidemiological criteria to be reported as a confirmed or probable case. During the 2023 mosquito season, DPH plans to continue enhanced laboratory investigations for Jamestown canyon virus (JCV) by requesting convalescent serum for all patients with positive JCV IgM results at WSLH for repeat PRNT.

E. Wisconsin will continue to offer fee-exempt Zika virus (ZIKV) testing for Wisconsin residents with possible ZIKV exposure meeting specified criteria. Under current CDC guidelines, fee-exempt molecular testing is approved for pregnant women with a possible ZIKV exposure who have a fetus with ultrasound findings consistent with congenital ZIKV syndrome, symptomatic patients with a possible ZIKV exposure, and for asymptomatic pregnant women with repeated, unavoidable travel to areas with a risk of ZIKV. Fee-exempt serologic testing is approved only for pregnant women with a possible ZIKV exposure who have a fetus with ultrasound findings consistent with congenital ZIKV syndrome. All ZIKV testing at WSLH must be approved by a DPH epidemiologist (608-267-9003 or DHSDPHBCD@wi.gov) prior to submission. For more information relating to ZIKV surveillance in Wisconsin, please visit DHS' Zika Virus webpage.

Arbovirus Surveillance in Wisconsin

Arboviral infections may be asymptomatic or result in a febrile illness of variable severity, sometimes associated with neurologic symptoms ranging from headache to aseptic meningitis and encephalitis. Arboviral encephalitis cannot be distinguished clinically from infection with other neurotropic viruses. Symptoms may include fever, headache, nausea, vomiting, confusion, or other sensory alterations. Signs of severe illness may include evidence of elevated intracranial pressure, meningeal irritation, cranial nerve palsies, paresis or paralysis, altered reflexes, or convulsions. Less common neurological syndromes can include cranial and peripheral neuritis or neuropathies, including Guillain-Barré syndrome.

Arboviruses may also cause non-neuroinvasive syndromes, most commonly manifesting as febrile illnesses. These are non-localized, self-limited illnesses with headache, myalgias, and arthralgias, and sometimes accompanied by a skin rash or lymphadenopathy. Although rare, non-neuroinvasive syndromes caused by these viruses may also include myocarditis, pancreatitis, or hepatitis. Laboratory confirmation of arboviral illnesses lacking a documented fever does occur and overlap of the various clinical syndromes is common.

Arboviruses known to cause illness among Wisconsin residents include the following:

Mosquito-borne viruses

- West Nile virus
- St. Louis encephalitis virus
- Eastern equine encephalitis virus
- La Crosse virus
- Jamestown Canyon virus

Tick-borne virus

- Powassan virus

Some mosquito-borne viruses associated with travel

Dengue virus | Chikungunya virus | Zika virus

WISCONSIN SURVEILLANCE CASE DEFINITION: An illness is classified as a case if it meets one or more of the following clinical criteria, **and** one or more of the following laboratory criteria, **and** occurred when and where there is a high likelihood of vector activity.

A. REPORTING CRITERIA:
- Laboratories should report all positive test results.
- Health care providers should report demographic and clinical information and onset date of suspected or known cases.

B. CLINICAL CRITERIA: Clinical cases of domestic arboviral diseases are classified according to the following criteria:

Neuroinvasive disease requires **at least one** of the following signs and symptoms, as documented by a physician, and in the absence of a more likely clinical explanation:
- Acutely altered mental status (for example, disorientation, confusion, memory deficit, stupor, coma)
- Aseptic meningitis, encephalitis
- Acute flaccid paralysis (AFP), which may result from anterior "polio" myelitis, peripheral neuritis, or post-infection peripheral demyelinating neuropathy (that is, Guillain-Barre syndrome)
- Stiff neck, seizures, limb weakness, sensory deficits, abnormal reflexes, abnormal movements, cranial nerve palsies
- Pleocytosis (increased white blood cell count) in cerebrospinal fluid (CSF) or abnormal neuroimaging

Non-neuroinvasive disease requires the presence of documented fever (≥100.4°F or 38°C), as measured by the patient or clinician; the absence of neuroinvasive disease (above); and the absence of a more likely clinical explanation for the illness. Other signs and symptoms may include headache, stiff neck, myalgias, arthralgias, rash, lymphadenopathy, nausea, or vomiting.

C. LABORATORY CRITERIA FOR DIAGNOSIS: Cases of arboviral disease are classified according to the following laboratory criteria:

Confirmed result (at least one of the following):
- Isolation of virus from or demonstration of specific viral antigen or nucleic acid in tissue, blood, cerebrospinal fluid (CSF), or other body fluid
- Fourfold or greater change in virus-specific quantitative antibody titers between acute (within two weeks after onset date) and convalescent sample (two to four weeks after onset date)
- Virus-specific immunoglobulin M (IgM) antibodies in serum by antibody-capture enzyme immunoassay (MAC-ELISA) or microsphere immunoassay (MIA) AND confirmed by demonstration of virus specific neutralizing antibodies (PRNT) in the same or later specimen
- Virus-specific IgM antibodies in CSF and a negative result for other arbovirus IgM antibodies in CSF endemic to the region where exposure occurred

Probable result: Virus-specific IgM antibodies in CSF or serum, but with no other testing in the same or later specimen.

Arboviral transmission varies according to local climatic conditions, and in some patients, virus-specific IgM antibody can be detectable for more than a year following infection. IgG antibody can be detected throughout a person's lifetime after an infection. Thus, a positive IgG and a negative IgM may indicate previous infection at some point in time or a cross-reactive result.

Laboratory Testing to Detect Human Infections

Diagnosis of an arboviral disease is usually made by serology. Negative serologic results from a single acute phase specimen do not rule out infection as the specimen may have been obtained prior to the development of an antibody response. Repeat serologic testing 2–4 weeks after acute phase testing may be necessary to confirm a diagnosis. Positive results from a single serologic test can be misleading because serologic cross-reactivity often occurs between closely related arboviruses. Therefore, it is recommended that an arbovirus IgM panel, which includes testing for arboviruses occurring in Wisconsin (WNV, SLEV, LACV, EEEV, JCV, and POWV), be requested when there is clinical suspicion of arboviral disease, rather than requesting individual tests.

Available diagnostic tests for domestic arboviruses at WSLH include IgM antibody-capture enzyme immunoassays (MAC-ELISA) that can identify IgM antibodies in serum and CSF specific to LACV, JCV, and POWV. Microsphere immunoassay (MIA) is used to test serum and CSF for IgM antibody specific to WNV, SLEV, and EEEV. Clinicians should also consider enterovirus PCR (WSLH test code VR01703) testing of the CSF for patients with suspect aseptic meningitis.

Available diagnostic tests for ZIKV, DENV, and CHIKV at WSLH include a trioplex real-time RT-PCR in serum to detect viral RNA. Real-time RT-PCR in urine is also available for the detection of ZIKV RNA. Molecular testing is recommended in qualifying patients whose specimen is collected within seven days of illness onset. MAC-ELISA is used to identify IgM antibodies in serum specific to ZIKV, DENV, or CHIKV, and may be indicated in qualifying patients whose specimen is collected eight days to 12 weeks after illness onset. ZIKV and CHIKV MAC-ELISA is performed at CDC's Arboviral Diseases Branch.

ZIKV testing at WSLH is only offered fee-exempt, and submission of specimen requires prior authorization from a DPH epidemiologist (608-267-9003 or DHSDPHBCD@wi.gov). Concurrent testing for ZIKV, DENV, and CHIKV may be recommended, depending on the clinical presentation and travel history of the patient. DENV and CHIKV IgM testing is available both fee-for-service (no prior authorization required) and fee-exempt (prior authorization required).

Requests for testing for other arboviruses will be forwarded to the CDC.

Confirmatory testing: Confirmatory testing for arboviruses using plaque reduction neutralization test (PRNT) is performed by the CDC. The decision to perform confirmatory testing requires approval from DPH or WSLH.

Fee-exempt testing: Fee-exempt testing for domestic arbovirus infections may be offered to clinicians whose patients meet **at least one** of the following criteria:

- The patient is experiencing a financial barrier to accessing laboratory testing (for example, inadequate or lack of insurance), reported to DPH by the submitting provider or facility, **and** the patient meets certain clinical and epidemiological criteria
- Confirmatory testing of positive test results performed at laboratories other than WSLH
- The patient is over 65 years of age with signs and symptoms of meningitis (fever, headache, and stiff neck) or encephalitis (fever, headache, and altered mental status ranging from confusion to coma) with no other laboratory diagnosis
- The patient has a diagnosis of Guillain-Barré syndrome and no other laboratory diagnosis
- The local health department or DPH requests fee-exempt testing during an investigation

Fee-for-service: With the exception of ZIKV testing, WSLH provides fee-for-service testing for arbovirus infections. Obtaining authorization from an epidemiologist prior to submission or meeting clinical criteria

are **not** required to submit serum or CSF specimens to WSLH for fee-for-service, non-ZIKV, arboviral testing.

Collection and shipping of clinical specimens to WSLH

- Specimens submitted to WSLH for fee-exempt domestic arbovirus testing must include WSLH **Enhanced Wisconsin Arbovirus Surveillance Form** (Attachment A).
- Specimens submitted to WSLH for fee-exempt ZIKV testing must include a WSLH **Enhanced Wisconsin Travel-Related Arbovirus Surveillance Form** (faxed to the submitter directly after test authorization is granted).
- Specimens submitted for fee-for-service testing must use WSLH **CDD Requisition Form B**.
- Specimen requirements: A minimum of 2 ml of serum or 1 SST tube; 1 ml of CSF in a sterile screw-capped vial. CSF must be accompanied by a serum specimen. Store specimens at 2–8°C and ship on cold packs (WSLH Kit 22). Please contact the WSLH-Clinical Stock Orders at 1-800-862-1088 or 608-224-4275 to order kits and to obtain WSLH CDD Requisition Form B.
- To facilitate testing, it is **essential** that the lab requisition forms be completed to include **the patient's name, address, date of birth, specimen type, submitting agency, collection date, onset date, clinical signs and symptoms, and any travel**.

Positive Human Arbovirus Reporting and Follow-Up

- WSLH will report all human arboviral test results by electronic reporting (ELR) or by fax to DPH. All test results will also be reported to the submitter.
- For lab results reported via fax or mail to local and Tribal health departments (LTHDs), the health department should enter information into the Wisconsin Electronic Disease Surveillance System (WEDSS) within 24 hours so that specimens can be quickly obtained from the commercial laboratories for confirmation. LTHDs have the option of using the Arbovirus Infection Follow-Up form (available in WEDSS) to aid in the follow-up investigation. When follow-up has been completed and entered into WEDSS, please send to state with a Resolution Status of **Suspect** for review. Often, results from confirmatory testing are necessary before the appropriate Resolution Status can be assigned and the case finalized.
- If it is determined that the patient does not reside within the jurisdiction of the LTHD, that health department is expected to forward the case to the appropriate Wisconsin LTHD for follow-up. For patients residing outside of Wisconsin, the WEDSS jurisdiction for that case should be set to "non-Wisconsin."
- The LTHD should ensure the test results have been relayed to the health care provider, patient, or hospital infection preventionists (IPs) before any patient follow-up investigation.
- Except for the first human **confirmed case** of WNV disease identified in the state for the season, an unusual outbreak of cases, or introduction of a new arbovirus into the state, any of which may prompt a statewide press release, the decision about releasing information on subsequent positive cases will be up to the LTHD. DPH can provide the LTHD with a press release template if needed.
- The only information DPH will release regarding positive human cases includes acknowledgement of the positive case, the month of illness onset, and county of residence of the positive individual. No patient demographic information (address, phone, physician, where patient is hospitalized, or illness status) will be released. Protection of an individual's privacy is of paramount concern when releasing information on human infections. The same criteria will apply should any individuals succumb to the disease.

Significant Wild Avian Mortality and Wild Mammal Surveillance

Wisconsin Department of Natural Resources (DNR) Arboviral Surveillance

Refer to the DNR Wildlife Health Program for instructions on which species of sick or dead wild birds or mammals should be reported to the DNR for wildlife health-related investigations. The DNR will continue to report positive arboviral lab results in wild birds or mammals to the DPH Vectorborne Disease Program. These data will be included in routine arbovirus data updates and reported to CDC via the national arboviral surveillance system (ArboNET).

Equine WNV and EEEV Surveillance

- The Department of Agriculture, Trade and Consumer Protection (DATCP) will continue to notify DPH of positive WNV and EEEV results in equines. Equine WNV and EEEV cases are not required to be reported to DPH, so the number and distribution of cases is dependent upon optional reporting by veterinarians and labs. Vaccines to prevent WNV and EEEV disease in equines are available, so the number and distribution of cases is also dependent upon vaccination rates in equine populations.
- DPH will enter specific information on individual cases in WEDSS, and also forward either by phone or by fax, basic information on the animal and test results to the LTHD where the animal or animal owner resides. Please be aware that equine information related to arboviral surveillance held by LTHD staff **is not** protected by medical confidentiality. Past requests to LTHDs for equine information resulted in health departments being legally obligated to provide the information requested.
- Once the LTHD, veterinarian, and horse owner are informed of the test results, WNV and EEEV positive horse case counts will be added to routine arbovirus data updates and reported to the CDC via ArboNET. Information included in publicly available data will only identify a positive horse and the county-level location of the horse.

Attachment A

Enhanced Wisconsin Arbovirus Surveillance (Rev. 04/2019). This form should be used to order human arbovirus testing, enclosed with the samples, and sent to the WSLH.

ENHANCED WISCONSIN ARBOVIRUS SURVEILLANCE
WISCONSIN STATE LABORATORY OF HYGIENE (WSLH)

Patient Information		**SUBMITTING AGENCY**	
Name (Last, First, MI)		Agency Name and Address (Print or use stamp/label)	
Patient Street Address			
City			
Patient State (if not Wisconsin)		Physician's Name	
Patient Telephone No. ( )		Agency Telephone No. ( )	Agency Fax No. ( )
Date of Birth	Patient Sex ☐ Male ☐ Female	WSLH Agency No.	**Bill to: 609** **Study: Arbo Surv**

Specimen type: *(Note: Both CSF and serum are recommended in acute cases. **Transport with cold packs.**)* ☐ CSF ☐ Acute Serum ☐ Convalescent Serum	**Collection date**:	**Onset date:** **Illness/Symptoms:**

Hospitalized ☐ Yes ☐ No	Travel ☐ Yes ☐ No	If Yes, provide destination and date(s):

Reason for Testing: (Note: The request must meet one of the following criteria to qualify for fee-exempt testing.)

- ☐ Confirmatory testing of positive test results performed at laboratories other than the WSLH.
  Commercial lab arboviral positive test results:
- ☐ The patient is over 65 years old with signs and symptoms of meningitis (fever, headache, and stiff neck) or encephalitis (fever, headache, and altered mental status ranging from confusion to coma) with no other laboratory diagnosis.
- ☐ The patient is diagnosed with Guillain-Barre' syndrome with no other laboratory diagnosis.
- ☐ Approved by Wisconsin Division of Public Health _____

WSLH Test Names and Codes

☐ Arbovirus IgM Panel (SS02201)	☐ Powassan virus IgM CEIA Ab (SS02251)
☐ Eastern Equine encephalitis IgM CEIA Ab (SS02211)	☐ West Nile virus/ St. Louis encephalitis IgM (SS02241)
☐ Jamestown Canyon IgM CEIA Ab (SS02261)	**CDC request:**
☐ La Crosse encephalitis IgM CEIA Ab (SS02231)	

Specimen Shipping Instructions: CSF and serum **MUST** be shipped on ice. This form must be included with the specimen. **No Saturday delivery.**
Ship Specimen(s) To:
Wisconsin State Laboratory of Hygiene, 2601 Agriculture Drive, Mailbox 7904, Madison, WI 53718
(Note: Separate specimen(s) and form should be submitted if other testing is desired).

Attachment B

WISCONSIN DOMESTIC ARBOVIRUS ANTIBODY TESTING: Specimen Collection and Submission Instructions

For individuals who meet Centers for Disease Control and Prevention (CDC) testing criteria, both fee-for-service testing and fee-exempt testing (requires approval by a Division of Public Health epidemiologist) for the domestic arbovirus IgM antibody panel is available at the Wisconsin State Laboratory of Hygiene (WSLH).

Specimen Collection

Interpretation of tests are dependent on the time elapsed between clinical disease onset and specimen collection date. West Nile virus, St. Louis encephalitis virus, Powassan virus, La Crosse encephalitis virus, Eastern Equine encephalitis virus, and Jamestown Canyon virus have been documented as locally transmitted in the State of Wisconsin. Diagnostic testing for these viral infections can be complicated by cross-reactivity with other related viruses in IgM antibody tests, and requires ample quantity of the specimen(s) to perform confirmatory testing to accurately interpret test results.

Specimens for Arboviral antibody testing (IgM, PRNT)

- **Serum specimen**: Collect 5–10 ml of blood in a tube with NO anticoagulant or preservative. **Promptly separate (centrifuge) serum from cells**. Use of serum separator tubes (SST) is encouraged. Store the SST refrigerated up to five days. Submit 2–5 ml of serum in a sterile screw-capped vial and transport with a cool pack.
  - Collect blood between three days and 12 weeks after symptom onset for reliable antibody detection. Samples collected less than eight days after illness onset may not demonstrate IgM reactivity due to the time required for the development of an antibody response, and a convalescent sample may be indicated.
  - Plasma is NOT an acceptable specimen for arbovirus antibody testing at the WSLH.
- **CSF specimen:** During acute phase illness, collect a minimum of 1 ml of CSF in a tube with **no** anticoagulant or preservative. Submit CSF in sterile screw-capped vial and transport with a cool pack. It is recommended that a serum specimen be submitted with a CSF specimen.

Specimen Submission

Specimens submitted to the WSLH for endemic arbovirus testing that are preapproved by a Division of Public Health communicable disease epidemiologist must include the **WSLH Enhanced Wisconsin Endemic Arbovirus Surveillance** specimen submission form provided at time of approval. Ensure that all information on the form above the reason for testing is accurate. Physician's phone and fax numbers are critical for communicating testing approval, test results, and public health follow-up.

- Serum and CSF specimens should be submitted in sterile screw-capped vials on cold packs using a WSLH kit #22 or equivalent. Specimens should be triple packaged as a Category B Biological Substance (include UN3373 label).
- Transport—Specimens approved for testing by WDHS may be transported to the WSLH by calling Gold Cross Courier Service (763-233-0099) for pick-up.
- Ship specimen(s) and form to: **Wisconsin State Laboratory of Hygiene**
  2601 Agriculture Drive
  Mailbox 7904
  Madison, WI 53718
  Customer Service: 800-862-1013

***Note**: Use both street address and mailbox when mailing.*