

**Maryland Department of Health and Mental Hygiene
Infectious Disease & Environmental Health Administration
June 2013**

**Revised Guidelines for Encephalitis and Aseptic Meningitis, including
Infection with West Nile virus (WNV) and other Arboviruses: Enhanced Case
Investigation by Local Health Departments (LHDs)**

Introduction

This document provides guidance for 1) conducting enhanced investigations of human cases of encephalitis and aseptic meningitis in order to confirm or rule out enteroviruses or arboviruses [including West Nile virus (WNV)] as causes and 2) conducting investigations of arboviral disease, including non-encephalitis/non-meningitis infections. To conduct these investigations, LHD staff must seek additional clinical information and other pertinent information using the “Arboviral/Encephalitis/Aseptic Meningitis Surveillance Form”, and attempt to have appropriate (enteroviral and/or arboviral) testing conducted for each encephalitis, meningitis and arboviral case.

This surveillance for human cases of encephalitis and aseptic meningitis is one component of the overall plan for arboviral disease control that also encompasses animal and mosquito surveillance and extends from July through October.

Report of Encephalitis, Aseptic Meningitis or Arboviral Disease to LHD

Case Investigation:

- 1) Contact the health care provider or reporting source. Verify diagnosis and determine if an agent has been identified. Request a copy of laboratory results, if none was received.
- 2) Enter suspect encephalitis/aseptic meningitis/arboviral investigation information into the NEDSS database on the same working day as receipt of report or after verifying diagnosis.

Note: In general, add lab results to the Investigation’s General Comments field – even negative bacterial cultures or the fact that no lab evidence could be obtained. If an Electronic Lab Report (ELR) is received, however, it is not necessary to re-enter that information into the Comments field.

- If encephalitis is reported with a negative bacterial culture of the CSF and no identified etiology then “Encephalitis, Viral (non-arboviral)” is probably the correct condition code. If no laboratory evidence accompanies an encephalitis report then code as “Encephalitis, Unspecified.”
- If meningoencephalitis is reported, enter as an encephalitis case (see above).

- If meningitis is reported with a negative (if performed) bacterial culture of the CSF and no identified etiology then “Aseptic Meningitis” is probably the correct condition code (as long as Gram stain and antigen detection tests, if done, are negative).
- If a non-arboviral viral agent (e.g. herpes simplex, enteroviral, echo, coxsackie, etc) is reported, enter under appropriate clinical condition (e.g. “Aseptic Meningitis” or “Encephalitis, Viral (non-arboviral)”).
- If a positive arboviral test (**usually a WNV MIA (Microsphere Immunoassay) or WNV Immunoglobulin M (IgM) antibody**) result is reported, enter the NEDSS Condition code appropriate for the agent and clinical condition (e.g. “Arboviral, West Nile (neuroinvasive)”, “Arboviral, St. Louis (neuroinvasive)”, etc. West Nile “fever” cases should be entered as “Arboviral, West Nile (non-neuroinvasive)”.
- Asymptomatic WNV infections (those identified by blood donor screening) should be reported to Amy Bergmann by phone or fax. They should not be entered into NEDSS at this time.

Note: A patient with a positive WNV **IgG** result (without evidence of a positive IgM result) should **NOT** be considered as a WNV case; such a result only means that the patient was previously exposed to a flavivirus. In the event of only a positive IgG result, please follow-up with the provider to verify that the IgM result was negative and that the patient was not diagnosed with encephalitis/meningitis. If IgM is negative and no encephalitis/meningitis diagnosis was made, **no further action is required.**

Table: Commonly Reported Conditions/Lab Reports and Corresponding NEDSS Entry.

Reported condition/lab result	Proper NEDSS Entry
Encephalitis, unknown etiology	Encephalitis (unspecified)
Encephalitis, neg. bacterial culture	Encephalitis, Viral (non-arboviral)
Meningoencephalitis	Encephalitis (unspecified) or Encephalitis, Viral (non-arboviral)
Meningitis w/ neg. bacterial culture	Aseptic Meningitis
Meningitis w/ non-arboviral viral agent	Aseptic Meningitis
WNV MIA or IgM pos. test with encephalitis/meningitis illness	Arboviral, West Nile (neuroinvasive)
WNV MIA or IgM pos. test with fever/non-neuroinvasive illness	Arboviral, West Nile (non-neuroinvasive)
WNV IgG pos. test and IgM neg./unknown test	NONE
Asymptomatic blood donor pos. test	NONE

3) Complete page 1 of the “Arboviral/Encephalitis/Aseptic Meningitis Surveillance Form” (note: if no additional information is available, a faxed copy of the morb card is acceptable).

Work with reporting source/health care provider to obtain information on:

- clinical information, including date of onset (necessary in order to determine the appropriateness of serologic testing and whether specimens will be classified as acute or convalescent), and
- existing pertinent lab information (directed toward the identification or ruling out of the etiologic agent; it is not necessary to report every lab test performed)

Note: It is not necessary to fax the surveillance form unless there is evidence of arboviral findings (see #4 below).

4) In the event of a **positive arboviral result**:

- a) Contact the patient or significant spokesperson to complete page 2 of surveillance form (additional clinical information, risk factor information, vaccination history, etc.) and obtain any missing information on page 1.
- b) Educate. Use appropriate fact sheet(s): “Arboviral Encephalitis”, “West Nile Virus”, “Eastern Equine Encephalitis” and “Viral Meningitis” available on the website at <http://ideha.dhmmh.maryland.gov/SitePages/fact-sheets.aspx> .
- c) Arrange additional testing, if necessary (see Arboviral Testing information below).
- d) Fax surveillance form to Amy Bergmann (410-225-7615).

Note: Please be aware that commercial lab results have in previous years had a high false positive rate – additional testing at DHMH Laboratories (especially early in the arboviral season) may be necessary. Confirmation at DHMH Laboratories of the first case of the season will be required.

5) Update NEDSS record on an ongoing basis. Refer to the case definitions (located at the end of this document) to determine the case STATUS. In some cases the Investigation will need to be re-entered into NEDSS (see information below) as additional laboratory evidence becomes available.

- If a viral (non-arboviral) agent (e.g. herpes simplex, enteroviral, echo, coxsackie, etc) is identified, add information to the existing Investigation’s General Comments field.
- If a positive arboviral test is reported after an “unspecified” Investigation (e.g. “Aseptic meningitis”, “Encephalitis, Unspecified”, etc.) has been created, the original “unspecified” Investigation will have to be ruled out, and the case information re-entered as a new arboviral Investigation. Re-enter using the condition code for the appropriate agent and clinical condition (e.g. “Arboviral, West Nile (neuroinvasive)”, “Arboviral, St. Louis (neuroinvasive)”, etc. Use the General Comments field on the original Investigation to explain why that Investigation was ruled out, and how the case was re-entered (including the new case ID).
- Complete the “Condition Specific Custom Fields” for all NEDSS arboviral Investigations – such fields include test results, travel, and exposure information also requested on the “Arboviral/Encephalitis/Aseptic Meningitis Surveillance Form”.

Laboratory Investigation:

Our goal is to collect appropriate clinical specimens to identify viral agents responsible for aseptic meningitis and encephalitis cases.

Enteroviral testing

On-site enteroviral testing is strongly encouraged for all hospitalized cases of encephalitis and aseptic meningitis with unknown etiology. Testing (cultures and/or PCR) is also available at DHMH Laboratories. Recommended specimens for enteroviral/herpes testing are:

CSF: collect at least 2 ml of specimen (if possible) with usual aseptic precautions, transport in sterile plastic screw-capped tube using dry ice to keep specimen frozen. If dry ice is not available, transport using cold packs.

Stool: collect 4-8 grams of specimen in plastic screw cap container and ship using cold packs.

Throat: swab tonsillar area and back of pharynx, place swab in viral transport media, ship with cold packs.

Arboviral Testing

Serological antibody tests are recommended for suspect arboviral cases. PCR tests are only useful for acutely ill patients (<10 days post-onset) who have not yet developed a complete antibody response to WNV, or immunocompromised patients who may not develop an adequate antibody response to WNV.

WNV testing at DHMH Laboratories should be prioritized for patients with:

- a) **encephalitis (all ages)** without laboratory evidence confirming a specific agent
- b) **aseptic meningitis (≥17years, hospitalized)**, that does not have laboratory evidence confirming a specific agent
- c) **previous positive arboviral test result** (at DHMH or commercial lab)

Arboviral testing is not recommended for mildly symptomatic, non-hospitalized patients, although commercial testing is available. Testing is discouraged for asymptomatic mosquito bite victims.

Note: Specimens sent to DHMH laboratories for arboviral testing might be screened first for enteroviruses if not previously performed at the hospital. If the specimen is positive for enteroviruses, arboviral testing will probably not be performed.

- 1) Obtain **serum** specimen (≥2ml) from patient. Place on cold packs for delivery to the DHMH Laboratories Administration for IgM testing. If initial serum sample is collected <10 days post-onset, a second serum specimen collected at least 2 weeks following first specimen should be submitted to address the possibility of false negative results. Both acute and convalescent serum samples are desired, if possible.
- 2) Determine if a **CSF** specimen (≥1cc) is available. CSF intended for antibody detection (IgM only) should be placed on cold packs and delivered to the Laboratories Administration. Virus detection by PCR or isolation is best performed if CSF is collected during the first seven days of illness, frozen at -70°C within two hours of collection, and maintained frozen on dry ice during transport. Antibody testing can be performed on both frozen and refrigerated CSF.
- 3) Complete on a Serological Testing laboratory test requisition (DHMH Form No. 4677) for each specimen collected (**see lab form instructions on pg. 6**):
 - Submitter's name and phone number
 - Patient's name, date of birth, and address
 - Date of illness onset
 - Date of specimen collection
 - Specimen source (S=serum, CSF=cerebrospinal fluid)

- Clinical diagnosis, symptoms, whether patient is immunocompromised
 - Patient's travel history / other risk factors
- 4) Label the shipping container **“Specimen(s) for West Nile Virus Testing.”**
 - 5) Facilitate transport of specimen(s) to DHMH Laboratory using storage and packaging guidelines outlined above. Direct any collection, packaging or shipping questions to Heather Peters (410 / 767-6153).
 - 6) Send specimen(s) to:
Maryland Department of Health and Mental Hygiene
Laboratories Administration
Virus Isolation Laboratory Room 4-C-3
201 W. Preston Street
Baltimore, Maryland 21201

Arbovirus Test Requisition

Laboratories Administration MD DHMH
 200 North Street, Suite 2120
 P.O. Box 2355 • Baltimore, MD 21203-2355
 410-767-6100 www.dhmh.state.md.us/labs
 John M. DeBooy, Dr. P. H., Director

SEROLOGICAL TESTING

Lab. Ref. #	DMTYP/PA/IN/DNOZ/DSTD/DTB/DGD/DOOR	Patient SSF (last 4 digits)	CSR CLR	Other
Submitter		Last Name	M.I.	Maiden
Address		Date of Birth (mm/dd/yyyy)		
City	County	State	Zip Code	County
Contact Name	Phone #	Fax #	State	Zip Code
Ethnicity	ChHispanic/Latino	ChNot Hispanic/Latino	DUknown	Sex
Race	ChWhite	ChAfrican American	ChAsian/Pacific	ChHispanic/Latino
Case #	DOCF	DOB	DOB	DOB
Collect Date	Collect Time	Cham	Chpm	Cham
Previous Test Done?	ChNo	ChYes	ChNo	ChYes
Name of Test	Onset Date	Onset Date	Onset Date	Onset Date

Must complete submitter information and include the name of the authorized person requesting the test.

Fill in the date specimen was collected.

Indicate CSF or serum to order Arbovirus IgM Panel testing. Complete patient's travel history, symptoms, and vaccination history.

Onset date field must be completed. Onset date of patient's symptoms is required for Arbovirus results interpretation.

Indicate patient's race, ethnicity and sex.

Patient's first and last names must be on the specimen container and match exactly to the lab slip.

Use only these codes to provide the source of the specimen.

<input type="checkbox"/> Arbovirus (West Nile Virus Panel) Serum or CSF Provide dates of onset & collection (see above) Required information, check all that apply: DIAGNOSIS: ChEpidemic meningitis Chencephalitis Chleth Chother SYMPTOMS: ChHeadache Chfever Chstiff neck Chaltered mental status Chmuscle weakness Chrash Chother ILLNESS FATAL? ChYes ChNo TRAVEL HISTORY (dates and places) IMMUNIZATIONS: Yellow fever? ChYes ChNo ChPolio? ChYes ChNo ChMM? ChYes ChNo ChMM2? ChYes ChNo ChMM3? ChYes ChNo ChMM4? ChYes ChNo ChMM5? ChYes ChNo ChMM6? ChYes ChNo ChMM7? ChYes ChNo ChMM8? ChYes ChNo ChMM9? ChYes ChNo ChMM10? ChYes ChNo ChMM11? ChYes ChNo ChMM12? ChYes ChNo ChMM13? ChYes ChNo ChMM14? ChYes ChNo ChMM15? ChYes ChNo ChMM16? ChYes ChNo ChMM17? ChYes ChNo ChMM18? ChYes ChNo ChMM19? ChYes ChNo ChMM20? ChYes ChNo ChMM21? ChYes ChNo ChMM22? ChYes ChNo ChMM23? ChYes ChNo ChMM24? ChYes ChNo ChMM25? ChYes ChNo ChMM26? ChYes ChNo ChMM27? ChYes ChNo ChMM28? ChYes ChNo ChMM29? ChYes ChNo ChMM30? ChYes ChNo ChMM31? ChYes ChNo ChMM32? ChYes ChNo ChMM33? ChYes ChNo ChMM34? ChYes ChNo ChMM35? ChYes ChNo ChMM36? ChYes ChNo ChMM37? ChYes ChNo ChMM38? ChYes ChNo ChMM39? ChYes ChNo ChMM40? ChYes ChNo ChMM41? ChYes ChNo ChMM42? ChYes ChNo ChMM43? ChYes ChNo ChMM44? ChYes ChNo ChMM45? ChYes ChNo ChMM46? ChYes ChNo ChMM47? ChYes ChNo ChMM48? ChYes ChNo ChMM49? ChYes ChNo ChMM50? ChYes ChNo ChMM51? ChYes ChNo ChMM52? ChYes ChNo ChMM53? ChYes ChNo ChMM54? ChYes ChNo ChMM55? ChYes ChNo ChMM56? ChYes ChNo ChMM57? ChYes ChNo ChMM58? ChYes ChNo ChMM59? ChYes ChNo ChMM60? ChYes ChNo ChMM61? ChYes ChNo ChMM62? ChYes ChNo ChMM63? ChYes ChNo ChMM64? ChYes ChNo ChMM65? ChYes ChNo ChMM66? ChYes ChNo ChMM67? ChYes ChNo ChMM68? ChYes ChNo ChMM69? ChYes ChNo ChMM70? ChYes ChNo ChMM71? ChYes ChNo ChMM72? ChYes ChNo ChMM73? ChYes ChNo ChMM74? ChYes ChNo ChMM75? ChYes ChNo ChMM76? ChYes ChNo ChMM77? ChYes ChNo ChMM78? ChYes ChNo ChMM79? ChYes ChNo ChMM80? ChYes ChNo ChMM81? ChYes ChNo ChMM82? ChYes ChNo ChMM83? ChYes ChNo ChMM84? ChYes ChNo ChMM85? ChYes ChNo ChMM86? ChYes ChNo ChMM87? ChYes ChNo ChMM88? ChYes ChNo ChMM89? ChYes ChNo ChMM90? ChYes ChNo ChMM91? ChYes ChNo ChMM92? ChYes ChNo ChMM93? ChYes ChNo ChMM94? ChYes ChNo ChMM95? ChYes ChNo ChMM96? ChYes ChNo ChMM97? ChYes ChNo ChMM98? ChYes ChNo ChMM99? ChYes ChNo ChMM100? ChYes ChNo	LAVERGNE TOP TUBE REQUIRED Hepatitis Serology (last 4 months) Blood transfusion? (last 4 months) ChYes ChNo Prevalent screen? ChYes ChNo Father of baby screen? ChYes ChNo Guardian's name if patient is a minor: Name of mother of "at risk" baby: Last Blood Patient hospitalized? ChYes ChNo Chetion therapy? ChYes ChNo Guardian's name if patient is a minor: Patient's phone number: SPECIMEN CODE: PLACE CODE IN BOX NEXT TO TEST B Blood CSF Cerebrospinal Fluid P Plasma S Serum UR Urine Barcode: 770322612
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Go to the DHMH Laboratory website for further information:
www.dhmh.maryland.gov/laboratories

Case definitions

The following encephalitis case definition is a Maryland case definition, as encephalitis is not nationally reportable. The remaining definitions (aseptic meningitis and arboviral disease) are CDC case definitions. Note that aseptic meningitis is no longer nationally reportable, but the CDC 1990 case definition is still used for Maryland cases.

Encephalitis

Clinical description

A syndrome usually characterized by fever, headache and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction.

Case classification

Confirmed: a clinically compatible illness diagnosed by a physician as encephalitis

Comments

Encephalitis may be caused by multiple etiologies. If no laboratory evidence conclusively identifies a particular agent, the Condition code “Encephalitis, Unspecified” should be used.

Aseptic Meningitis

Reference: CDC. Case definitions for public health surveillance. MMWR 1990;39(no. RR-13):6.

<http://ftp.cdc.gov/pub/Publications/mmwr/rr/rr3913.pdf> [accessed June 27, 2013]

1990 Case Definition

Clinical description

A syndrome characterized by acute onset of meningeal symptoms, fever, and cerebrospinal fluid pleocytosis, with bacteriologically sterile cultures.

Laboratory criteria for diagnosis

- No evidence of bacterial or fungal meningitis

Case classification

Confirmed: a clinically compatible illness diagnosed by a physician as aseptic meningitis, with no laboratory evidence of bacterial or fungal meningitis

Comment

Aseptic meningitis is a syndrome of multiple etiologies, but many cases are caused by a viral agent.

Arboviral Diseases, Neuroinvasive and Non-Neuroinvasive:

Reference: CDC. National Notifiable Disease Surveillance System (NNDSS)

<http://wwwn.cdc.gov/NNDSS/script/conditionsummary.aspx?CondID=17> [accessed June 27, 2013]

2011 Case Definition

CSTE Position Statement Numbers: 10-ID-18, 10-ID-20, 10-ID-21, 10-ID-22, 10-ID-23, 10-ID-24

California Serogroup Viruses, (i.e., California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, and Trivittatus viruses)

Eastern Equine Encephalitis Virus

Powassan Virus

St. Louis 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, consumption of unpasteurized dairy products, 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 *Bunyavirus*.

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 stiff neck, altered mental status, seizures, limb weakness, cerebrospinal fluid (CSF) pleocytosis, or abnormal neuroimaging. 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, arthralgias, rash, or gastrointestinal symptoms. Rarely, myocarditis, pancreatitis, hepatitis, or ocular manifestations such as chorioretinitis and iridocyclitis can occur.

Clinical criteria for diagnosis

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

Neuroinvasive disease

- Fever ($\geq 100.4^{\circ}\text{F}$ or 38°C) as reported by the patient or a health-care provider, **AND**
- 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.

Non-neuroinvasive disease

- Fever ($\geq 100.4^{\circ}\text{F}$ or 38°C) as reported by the patient or a health-care provider, **AND**
- Absence of neuroinvasive disease, **AND**
- Absence of a more likely clinical explanation.

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 and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred, **OR**
- Virus-specific IgM antibodies in CSF or serum.

Case classification

Confirmed:

Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and one or more 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, 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.

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 CSF or serum but with no other testing.

Comment

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).

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.

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., Chikungunya, Japanese encephalitis, Tick-borne 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 of imported arboviral pathogens. Health-care 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.