I. Statement of the Problem:
The “clinical criteria for diagnosis” defined in the current surveillance case definition to classify a neuroinvasive or non-neuroinvasive case of arboviral disease as a probable or confirmed case requires a measured fever of $\geq 100.4^\circ F$ or $38^\circ C$ as reported by the patient or a health-care provider. This required clinical criterion is leading states to adopt different approaches in the surveillance for arboviral diseases, particularly West Nile disease. A revision to the national surveillance case definition for Arboviral neuroinvasive and non-neuroinvasive diseases is needed to standardize surveillance and provide data that has conformity across state jurisdictions as well as consistency to evaluate trends across multiple years of West Nile virus activity and that of other arboviruses.

Additionally, the current surveillance case definition for non-neuroinvasive arboviral disease includes laboratory criteria which is indicative of neuroinvasive infection, including demonstration of virus, nucleic acid, or arbovirus–specific IgM antibodies in cerebrospinal fluid (CSF).

II. Background and Justification:
Arboviral diseases are a condition under public health surveillance. More than 130 arboviruses are known to cause human disease with West Nile virus (WNV), St. Louis encephalitis virus, Eastern Equine Encephalitis virus, Powassan virus, and California Serogroup viruses endemic in various regions of the United States (US). Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis.

In 2012, the US experienced the largest outbreak of WNV since 2003 with greater than 5,300 human cases reported by 48 states. As infectious disease surveillance personnel in state and local health departments applied the 2011 Case Definition for Arboviral neuroinvasive and non-neuroinvasive diseases, it was recognized that cases with laboratory, epidemiologic and clinical evidence of WNV disease were failing to meet the probable or confirmed case definition due to the lack of a measured fever $\geq 100.4^\circ F$ or $38^\circ C$. Among non-neuroinvasive (West Nile fever) cases, frequent explanations included subjective report of a fever or chills without a measurement obtained by the patient; resolved fever by the time of presentation to a health-care provider for persistent weakness, vertigo or headache; or lowered body temperature after taking over-the-counter anti-pyretic medications. Neuroinvasive cases of West Nile disease were also potentially excluded solely due to the absence of fever because persons with severe encephalitis may be hypothermic and unstable at the point of healthcare entry. Persons with underlying immunocompromising medical conditions are at greater risk of developing neuroinvasive disease and may not mount a febrile response to an arboviral infection. As epidemiologists attempted to appropriately characterize the WNV activity in their public health jurisdictions, different approaches were taken for the classification and reporting of cases. An informal e-mail survey of arbovirus surveillance coordinators in March 2013 indicated that 50% (12 of 24 states) did not strictly adhere to the surveillance case definition, but elected to accept subjective reports of fever for cases of non-neuroinvasive West Nile disease when the remaining criteria were satisfied, and classify neuroinvasive cases as probable or confirmed based on clinical features of a neurologic dysfunction with no other likely explanation and the requisite laboratory criteria met. Analysis of the impact of the measured fever criterion on WNV surveillance in two states (OK and CO) suggests that 43-45% of non-neuroinvasive cases and 3-9% of neuroinvasive cases were not captured by the current case definition.

CSTE requests that CDC revise the current case definition for Arboviral neuroinvasive and non-neuroinvasive diseases to:

1. Remove fever as a required clinical criterion for case classification of neuroinvasive disease;
2. Substitute subjective fever or chills as reported by the patient or health-care provider in place of measured fever (≥ 100.4°F or 38.0°C) as a required clinical criterion for non-neuroinvasive disease; and

3. Restrict the laboratory criteria of isolation of virus from CSF, demonstration of specific viral antigen or nucleic acid in CSF, and detection of virus-specific IgM antibodies in CSF to the neuroinvasive disease case classification.

III. Statement of the desired action(s) to be taken:

1. Utilize standard sources (e.g. reporting*) for case ascertainment for Arboviral Diseases. Surveillance for Arboviral Diseases should use the following recommended sources of data to the extent of coverage presented in Table III.

Table III. Recommended sources of data and extent of coverage for ascertainment of cases of Arboviral neuroinvasive and non-neuroinvasive diseases.

<table>
<thead>
<tr>
<th>Source of data for case ascertainment</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population-wide</td>
</tr>
<tr>
<td>Clinician reporting</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory reporting</td>
<td>X</td>
</tr>
<tr>
<td>Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)</td>
<td>X</td>
</tr>
<tr>
<td>Death certificates</td>
<td>X</td>
</tr>
<tr>
<td>Hospital discharge or outpatient records</td>
<td>X</td>
</tr>
<tr>
<td>Extracts from electronic medical records</td>
<td>X</td>
</tr>
<tr>
<td>Telephone survey</td>
<td></td>
</tr>
<tr>
<td>School-based survey</td>
<td></td>
</tr>
<tr>
<td>Other _______________________</td>
<td></td>
</tr>
</tbody>
</table>

2. Utilize standardized criteria for case identification and classification (Sections VI and VII) for Arboviral Diseases and add this condition to the Nationally Notifiable Condition List. [Select timeframe below. Specify subsets of cases if applicable (e.g. suspected intentional release, clusters or outbreaks).]

- [ ] 2a. Immediately notifiable, extremely urgent (within 4 hours)
- [ ] 2b. Immediately notifiable, urgent (within 24 hours)
- [X] 2c. Routinely notifiable

CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

3. CDC should publish data on Arboviral Diseases as appropriate in MMWR and other venues (see Section IX).

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outlined above.
Terminology:
* Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local or state public health
**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

IV. Goals of Surveillance:
To provide information on the temporal, geographic, and demographic occurrence of arboviral diseases to facilitate prevention and control for these vector-borne infections.

V. Methods for Surveillance:
Surveillance for Arboviral neuroinvasive and non-neuroinvasive diseases should use the recommended sources of data and the extent of coverage listed in Table III.

VI. Criteria for case identification:
A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.
Report any illness to public health authorities that meets any of the following criteria.

- Any person with laboratory evidence of recent arboviral infection as indicated by:
  - Isolation of arbovirus from, or demonstration of specific arbovirus antigen or nucleic acid in, tissue, blood, cerebrospinal fluid (CSF), or other body fluid
  - Four-fold or greater change in arbovirus-specific quantitative antibody titers in paired sera
  - Arbovirus-specific immunoglobulin M (IgM) antibodies in CSF or serum

- A person whose healthcare record contains a diagnosis of an arboviral infection

- A person whose death certificate lists an arboviral infection as a cause of death or a significant condition contributing to death

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Arboviral Neuroinvasive Disease</th>
<th>Arboviral Non-neuroinvasive Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthcare record contains a diagnosis of arboviral infection</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Death certificate lists arboviral disease as a cause of death or a significant condition contributing to death</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Laboratory Evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of arbovirus from, or demonstration of arbovirus-specific antigen or nucleic acid in, tissue, blood, CSF, or other body fluid</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Four-fold or greater change in arbovirus-specific quantitative antibody titers in paired sera</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Arbovirus-specific immunoglobulin M (IgM) antibodies in CSF or serum</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

Notes:
S = This criterion alone is Sufficient to report a case.
N = All “N” criteria in the same column are Necessary to report a case.
O = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to report a case.
* A requisition or order for any of the “S” laboratory tests is sufficient to meet the reporting criteria.

C. Disease-specific data elements

Clinical Information

Underlying chronic illness
Immune suppression
Blood transfusion in past 30 days
Blood donation in past 30 days
Organ transplant recipient in past 30 days
Organ donor
Pregnant
Prenatal exposure
Breast fed
Laboratory exposure
Hospitalized
Fatality

Epidemiologic Risk Factors

Occupation
Travel in 5-15 days prior to onset of illness
County and State where infection was presumably contracted
Mosquito exposure

VII. Case Definition for Case Classification:

A. Narrative: Description of criteria to determine how a case should be classified.

Subtypes of Arboviruses

- California Serogroup Viruses (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, 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 purpose 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 CSF pleocytosis. AFP may result from anterior (“polio”) myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barre’ 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. Other physical complaints may include vertigo, stiff neck, or muscle weakness without progression to more clinically apparent neurological involvement.

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.

Non-neuroinvasive disease

- Fever or chills 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

- 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.

Case classification

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.

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.

Comments

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.

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.

### B. Classification Tables

**Table VII-B. Criteria for defining a case of Arboviral Disease.**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Neuroinvasive</th>
<th>Non-neuroinvasive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confirmed</td>
<td>Probable</td>
</tr>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Headache</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Myalgia</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Rash</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Vertigo</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Vomiting</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Paresis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Nuchal rigidity</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Myelitis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Disorientation</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Obtundation</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Peripheral demyelinating neuropathy</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Acute Flaccid Paralysis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Nerve palsies</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Peripheral neuritis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Sensory deficit</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Abnormal reflexes</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Seizures</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Absence of a more likely clinical explanation for the illness</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Laboratory evidence**

<table>
<thead>
<tr>
<th></th>
<th>Neuroinvasive</th>
<th>Non-neuroinvasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF pleocytosis</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Isolation of arbovirus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, or other body fluid, excluding CSF</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Isolation of arbovirus or demonstration of specific viral antigen or nucleic acid in CSF</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Four-fold or greater change in virus-specific quantitative antibody titers in paired sera</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td><strong>Arbovirus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in same or later specimen</strong></td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Arbovirus-specific IgM antibodies in CSF and a negative result for IgM antibodies in CSF for other arboviruses endemic to the region where exposure occurred</strong></td>
<td>O</td>
<td></td>
</tr>
<tr>
<td><strong>Arbovirus-specific IgM antibodies in CSF but with no other testing</strong></td>
<td>O</td>
<td></td>
</tr>
<tr>
<td><strong>Arbovirus-specific IgM antibodies in serum but with no other testing</strong></td>
<td>O</td>
<td>N</td>
</tr>
<tr>
<td><strong>Criteria to distinguish a new case:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Not counted as a new case if previously classified as a case, e.g., previously documented to have virus-specific IgM antibodies in CSF or serum</strong></td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Notes:**

S = This criterion alone is Sufficient to classify a case.
N = All "N" criteria in the same column are Necessary to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below).
A = This criterion must be absent (i.e., NOT present) for the case to meet the classification criteria.
O = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case. (These optional criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an "O" indicates that this criterion is only required for a specific disease/condition subtype.
VIII. Period of Surveillance:

Surveillance should be ongoing.

IX. Data sharing/release and print criteria:

- Notification to CDC of confirmed and probable cases of arboviral diseases is recommended.
- CDC Division of Vector-Borne Diseases (DVBD) staff review, analyze, and summarize the national data weekly. Provisional state-specific arboviral disease case counts are provided weekly in the MMWR nationally notifiable diseases tables. Tables and maps are also provided on the CDC DVBD and U.S. Geologic Survey (USGS) websites. These provisional data are used to: 1) Monitor the epidemiology and geographic spread of arboviral diseases; 2) Provide timely information regarding regional and national trends in arboviral diseases to public health officials and others; and 3) Identify geographic areas where additional prevention and control efforts may be needed. In circumstances where there is a potential for an international health impact, data from these notifications may be shared with international partners (e.g., PHAC, ECDC, WHO, PAHO).
- Final data are published annually in the MMWR Summary of Notifiable Diseases, posted on the CDC DVBD website, and presented or published at scientific meetings and in peer-reviewed literature. Additional tables and limited use datasets are available to researchers, pharmaceutical companies, media, and the general public upon request to the CDC DVBD. These final data are used to: 1) Monitor the epidemiology, incidence, and geographic spread of arboviral diseases; 2) Identify geographic areas in which it may be appropriate to conduct analytic studies of control methods, risk factors, disease severity, or other public health aspects; and 3) Evaluate arboviral disease funding needs and allocate resources.
- All cases are verified with the state health departments before publication. Individual case notifications are made to state and local health departments depending on circumstances. For example, viremic blood donors or transplant or transfusion-associated cases require rapid notification and investigation.
- To facilitate access to ArboNET data while maintaining patient confidentiality, and to ensure that users understand the limitations of the data, the CDC Arboviral Diseases Branch has developed data sharing and release guidelines, a data request form, and a data use agreement. These policies and procedures are consistent with those developed by CDC and the CSTE for the release and sharing of data reported to the Nationally Notifiable Diseases Surveillance System (NNDSS).

X. References

XI. Coordination

Agencies for Response

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