

Committee: Infectious Disease

Title: Public Health Reporting and National Notification for Eastern Equine Encephalitis Virus Disease

I. Statement of the Problem:

CSTE position statement 07-EC-02 recognized the need to develop an official list of nationally notifiable conditions and a standardized reporting definition for each condition on the official list. The position statement also specified that each definition had to comply with American Health Information Community recommended standards to support “automated case reporting from electronic health records or other clinical care information systems.” In July 2008, CSTE identified sixty-eight conditions warranting inclusion on the official list, each of which now requires a standardized reporting definition.

II. Background and Justification:

Background¹

Eastern equine encephalitis (EEE) is a mosquito-borne viral disease that occurs in the eastern half of the United States. An average of 5 to 10 human cases are reported in the U.S. each year. Many persons infected with the virus have no apparent illness. In those persons who do develop illness, symptoms range from mild flu-like illness to encephalitis (inflammation of the brain), coma, and death. The mortality rate from EEE is approximately 30 to 40%, making it one of the most deadly mosquito-borne diseases in the United States. Approximately half of those persons who survive EEE will have neurologic sequelae. Ongoing surveillance is necessary to detect outbreaks and monitor the effectiveness of control strategies.

Justification

Arboviral disease (*e.g.*, Eastern equine encephalitis virus [EEEV]) disease meets the following criteria for a nationally and **standard** notifiable condition, as specified in CSTE position statement 08-EC-02:

- A majority of state and territorial jurisdictions—or jurisdictions comprising a majority of the US population—have laws or regulations requiring **standard** reporting of EEEV disease infections to public health authorities
- CDC requests **standard** notification of EEEV disease infections to federal authorities
- CDC has condition-specific policies and practices concerning the agency’s response to, and use of, notifications

¹ Much of the material in the background is directly quoted from the CDC’s Eastern equine encephalitis Website, <http://www.cdc.gov/EasternEquineEncephalitis/index.html>. See the references for further information on this source.

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

CSTE requests that CDC adopt this standardized reporting definition for EEEV disease to facilitate more timely, complete, and standardized local and national reporting of this condition.

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of EEEV disease to facilitate its prevention and control.

V. Methods for Surveillance:

Surveillance for EEEV disease should use the sources of data and the extent of coverage listed in Table V.

Table V. Recommended sources of data for case identification and extent of coverage for ascertaining cases of EEEV disease.

Source of data for case identification	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies)	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Extracts from electronic medical records	X	
Telephone survey		
School-based survey		
Other		

VI. Criteria for case identification

A. Narrative description of 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 EEEV disease as evidenced by:
 - Isolation of EEEV from, or demonstration of specific EEEV antigen or nucleic acid in, tissue, blood, cerebrospinal fluid (CSF), or other body fluid
 - Four-fold or greater change in EEEV-specific quantitative antibody titers in paired sera
 - EEEV-specific immunoglobulin M (IgM) antibodies in CSF or serum

- A person whose healthcare record contains a diagnosis of EEEV infection.
- A person whose death certificate lists EEEV infection as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases of EEEV disease should be reported.
- Reporting should be on-going and routine.
- Frequency of reporting should follow the state health department's routine schedule.

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. Requirements for reporting are established under State and Territorial laws and/or regulations and may differ from jurisdiction to jurisdiction. These criteria are suggested as a standard approach to identifying cases of this condition for purposes of reporting, but reporting should follow State and Territorial law/regulation if any conflicts occur between these criteria and those laws/regulations.

Criterion	Reporting
Healthcare record contains a diagnosis of Eastern EEEV infection	S
Death certificate lists EEEV infection as a cause of death or a significant condition contributing to death	S
<i>Laboratory findings</i>	
Isolation of EEEV from, or demonstration of specific EEEV antigen or nucleic acid in, tissue, blood, CSF, or other body fluid	S
Four-fold or greater change in EEEV-specific quantitative antibody titers in paired sera	S
EEEV-specific immunoglobulin M (IgM) antibodies in CSF or serum	S

Notes:

S = This criterion alone is Sufficient to identify a case for reporting.

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 to EEEV
Hospitalized
Fatality

Epidemiological 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.

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 EEEV 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 case:

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.

Comments

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.
- **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.

B. Classification Tables:

Table VII-B. Criteria for case classification for a case of EEEV disease.

Criterion	Confirmed		Probable	
	Non-neuroinvasive	Neuroinvasive	Non-neuroinvasive	Neuroinvasive
<i>Clinical Evidence</i>				
Fever	N	N	N	N
Aseptic meningitis	A	O	A	O
Encephalitis	A	O	A	O
Myelitis	A	O	A	O
Disorientation	A	O	A	O
Obtundation	A	O	A	O
Stupor	A	O	A	O
Coma	A	O	A	O
Paresis	A	O	A	O
Paralysis	A	O	A	O
Nerve palsies	A	O	A	O
Sensory deficit	A	O	A	O
Abnormal reflexes	A	O	A	O
Abnormal movements	A	O	A	O
Convulsions	A	O	A	O
Absence of a more likely clinical explanation for the illness	N	N	N	N
<i>Laboratory evidence</i>				
Isolation of EEEV from, or demonstration of specific EEEV antigen or nucleic acid in,	O	O	A	A

tissue, blood, CSF, or other body fluid				
Four-fold or greater change in EEEV-specific quantitative antibody titer in paired sera	O	O	A	A
EEEV-specific immunoglobulin M (IgM) antibodies in serum with confirmatory virus-specific neutralizing antibodies in same or later specimen	O	O	A	A
EEEV-specific IgM antibodies in CSF and a negative result for IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred	O	O	A	A
EEEV-specific IgM antibodies in CSF or serum with no other testing	A	A	N	N

Notes:

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.)

VIII. Period of Surveillance:

Surveillance should be on-going.

IX. Data sharing/release and Print criteria:

- Notification to CDC of confirmed and probable cases of EEEV disease is recommended.
- CDC Division of Vector Borne Infectious Diseases (DVBID) 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 and posted on EpiX. Tables and maps are also provided on the CDC DVBID 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 DVBID 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 from CDC DVBID. 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 important public health issues; 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, possible 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 Council of State and Territorial Epidemiologists (CSTE) for the release and sharing of data reported to the Nationally Notifiable Diseases Surveillance System (NNDSS).
- Additional tables are available that include a) Total counts of a particular nationally notifiable arboviral disease reported to ArboNET by state, month, and year, or b) Total counts of a particular nationally notifiable arboviral disease reported to ArboNET by county and year (but not month). Upon request, CDC DVBID will provide a limited use data set that contains a linelisting of case-specific data for any of the particular nationally notifiable arboviral diseases reported to ArboNET. The variables in the data file may include clinical syndrome (neuroinvasive or non-neuroinvasive), state, year, month, age group (<1 yr, 1-4 yrs, and by 5 year intervals thereafter), sex, race, and ethnicity. If the total number of cases in a state in a year for a given arboviral disease is <3, then race and ethnicity will be suppressed for all cases in that state in that year. To receive a case-specific data set, the investigator must complete a data request form and data use agreement confirming that they have read and understand the data release policies.

X. References:

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