

EASTERN EQUINE ENCEPHALITIS VIRUS DISEASE

(Eastern equine encephalitis, EEE)

REPORTING INFORMATION

- **Class B1:** Report by the end of the next business day in which the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
 - [Ohio Confidential Reportable Disease form](#) (HEA 3334, rev. 1/09), [Positive Laboratory Findings for Reportable Disease form](#) (HEA 3333, rev. 8/05), the local public health department via the Ohio Disease Reporting System (ODRS) or telephone.
 - The Centers for Disease Control and Prevention (CDC) [Mosquito borne Illness Case Investigation worksheet](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into the Ohio Disease Reporting System (ODRS) and not sent to the Ohio Department of Health (ODH), unless otherwise requested. If requested, the mailing address for this form is: Ohio Department of Health, Outbreak Response and Bioterrorism Investigation Team, 246 North High Street, Columbus, Ohio 43215.
- Additional reporting information, with specifics regarding the key fields for ODRS reporting, can be located in [Section 7](#).

AGENT

Eastern Equine Encephalitis (EEE) virus is an RNA virus belonging to the genus *Alphavirus* (formerly group A of the arboviruses) of the family Togaviridae.

Infectious dose: A single bite of an infectious mosquito.

CASE DEFINITION

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.

Clinical Criteria for Diagnosis

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

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

- 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, cerebrospinal fluid (CSF) or other body fluid or
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera or
- Virus-specific immunoglobulin M (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

Probable:

- Neuroinvasive case: A case that meets the above clinical criteria for neuroinvasive disease and with virus-specific IgM antibodies in CSF or serum but with no other testing.
- Non-neuroinvasive case: A case that meets the above clinical criteria for non-neuroinvasive disease and with virus-specific IgM antibodies in CSF or serum but with no other testing.

Confirmed:

- Neuroinvasive case: 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 case: 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.

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. 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.

SIGNS AND SYMPTOMS

Eastern Equine Encephalitis can produce a febrile illness of variable severity associated with neurologic symptoms ranging from headache to aseptic meningitis or encephalitis. Arboviral encephalitis cannot be distinguished clinically from other central nervous system (CNS) infections. Symptoms can include headache, confusion or other alteration in sensorium, nausea and vomiting. Signs may include fever, meningismus, cranial nerve palsies, paresis or paralysis, sensory deficits, altered reflexes, convulsions, abnormal movements and coma of varying degree. [See also the Aseptic Meningitis chapter.]

DIAGNOSIS

Laboratory diagnosis of arboviral infections is generally accomplished by testing of serum or cerebrospinal fluid (CSF) to detect virus-specific IgM and neutralizing antibodies. During an acute infection, certain viruses can be isolated through culture or detected by nucleic acid amplification.

In fatal cases, nucleic acid amplification, histopathology with immunohistochemistry and virus culture of autopsy tissues can also be useful. Only a few state laboratories or other specialized laboratories, including those at CDC, are capable of doing this specialized testing.

EPIDEMIOLOGY

Source

EEE is a virus circulated between birds and certain mosquito species, especially in marshy areas and swamps. Horses, humans, pheasants, emus and other animals are accidental, dead-end hosts and are not usually a source of infection to humans.

Occurrence

EEE is the rarest of the mosquito-borne arboviral infections. A median of five sporadically occurring infections in humans are reported annually in the United States; however, the illness is fatal in at least 30% of cases and even higher case fatality rates are observed at the extremes of age. There are no records of human cases acquired in Ohio. Ohio's first recorded zoonotic outbreak of EEE occurred in 1991 in Wayne and Holmes counties where 19 confirmed cases in horses were documented.

Mode of Transmission

The reservoir of EEE is wild birds, and the virus is transmitted by certain mosquito species. In the upper Midwest, EEE is transmitted by two swamp and marsh-breeding mosquitoes, *Culiseta (Cs.) melanura* and *Coquillettidia (Cq.) perturbans*. *Cs. melanura* is the primary enzootic vector and is a rare mosquito in Ohio. *Cq. perturbans* is a "bridge" vector and can be abundant in marshy areas. *Cq. perturbans* is believed to be the epidemic vector in Ohio, responsible for transmitting the virus to humans and equines.

Period of Communicability

Humans are dead-end hosts for the virus; they do not circulate sufficient EEE virus in the blood stream to infect a mosquito, and the disease cannot be spread from person to person.

Incubation Period

The incubation period is 4 to 10 days.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

With serologic identification of EEE infection, a complete travel history for the three weeks prior to onset is obtained. Exposure sites can be evaluated for mosquito vectors by standard mosquito collection techniques (light traps, larval samples). Mosquitoes collected should be immediately placed on dry ice in sealed air-tight tubes and sent to the Zoonotic Disease Program (ZDP) for

arboviral assay. The geographic extent of EEE activity can be estimated by an avian serosurvey.

Treatment

There is no specific therapy for EEE. Supportive care is indicated.

Isolation and Follow-up Specimens

Since the diagnosis of EEE is often not known until after patient discharge, enteroviral precautions (i.e., fecal, respiratory) are usually indicated for encephalitis. A convalescent sample 2-4 weeks after the acute is required to confirm a case.

Public Health Significance

High. Because of the virulence of EEE virus, the prognosis is poor, with the high chance for fatality or severe neurologic sequelae. Report of a single case may signify an outbreak is developing. An outbreak in horses occurred in Wayne and Holmes counties for the first time in 1991.

Special Information

Specific diagnosis is critical to prevention.

Contacts

No treatment or prophylaxis of contacts is indicated.

Prevention and Control

Vaccination

There is no vaccine for the general public. An experimental vaccine is available for researchers who are working with the virus in a laboratory. There is a vaccine for horses only, but vaccination of horses will not prevent the spread of EEE to people.

Vector Investigation

With the report of a human or equine case of EEE, a vector assessment should be done to determine if an outbreak is developing. Mosquito and bird blood samples can be tested for EEE by the ZDP. For advice on vector assessment, contact the ZDP at (614) 752-1029 or via the e-mail at zoonoses@odh.ohio.gov.

Special Information

The risk of exposure to EEE virus is primarily in areas where a combination of acid bogs and cattail marshes exist. These are the breeding sites for the enzootic and epizootic vectors. Outbreaks are more likely in rural and suburban areas.

What is EEE?

EEE is a rare but serious mosquito-borne viral disease that affects humans, horses, and some birds. It is one of a group of similar illnesses, including St. Louis encephalitis and LaCrosse encephalitis, which can affect the central nervous system in people and cause severe complications or even death.

In the United States, EEE occurs in focal locations along the eastern seaboard, the Gulf Coast and some inland Midwestern locations. While small outbreaks of human disease have occurred in the United States, equine outbreaks can be a common occurrence during the summer and fall.

Generally less than 10 human cases are reported each year in the United States, mostly in those over 50 or under 15 years of age. No cases have been acquired in Ohio.

How is EEE transmitted?

Wild birds that live in freshwater swamps serve as the source for this virus. The mosquito most often responsible for transmitting the EEE virus from bird to bird prefers not to feed on humans or other mammals. Other mosquitoes sometimes bite the infected birds and then transmit the virus to humans and horses. Infected humans and horses can not spread the disease.

How long after infection before symptoms appear?

Symptoms generally develop within 7 to 10 days.

What are the symptoms of EEE?

Many people infected with EEE virus have no signs of illness. Those who do get sick generally have mild flu-like symptoms including high fever, stiff neck, muscle pain, headache and a lack of energy. In some cases inflammation of the brain, called encephalitis, can develop. About half of those with encephalitis who survive will have permanent nerve damage. Approximately 30% of EEE cases are fatal.

How is EEE diagnosed?

Specific antibodies can be found in the blood or spinal fluid. Other tests are available to confirm the diagnosis, but results may take weeks.

How is EEE treated?

There is no specific treatment for EEE. Antibiotics are not effective against viruses, and no effective antiviral drugs have been discovered. Patient care centers on treatment of symptoms and complications.

Are those previously infected with EEE immune?

Yes, infection will provide life-long immunity to the EEE virus. It does not however provide any protection for other mosquito-borne viruses.

Is there a vaccine for EEE?

There are no human vaccines available, and none are currently in development. A vaccine for horses is available through veterinarians.

How can I prevent EEE?

Prevent mosquito bites. It only takes one bite from an infected mosquito to transmit disease.

Avoid mosquito bites.

- Avoid wet, swampy areas where mosquitoes live and breed.
- Avoid activities during the peak mosquito biting activity of dawn, dusk and early evening.
- Install or repair window and door screens to keep mosquitoes outside.
- Use mosquito netting over infant carriers.

Repel mosquitoes when outdoors.

- If the weather permits wear long pants, long sleeves and/or socks.
- Apply mosquito repellent as directed to clothing and exposed skin.
- Reapply mosquito repellent as needed especially if swimming or sweating.

Eliminate mosquito breeding sites.

- At least once or twice a week, empty water from flower pots, pet food and water dishes, birdbaths, swimming pool covers, buckets, barrels and cans.
- Check for clogged rain gutters and clean them out.
- Remove discarded tires, and other items that could collect water.
- Be sure to check for containers or trash in places that may be hard to see, such as under bushes or under your home.

For more information, please visit these websites:

CDC EEE fact sheet <http://www.cdc.gov/ncidod/dvbid/arbor/eeefact.htm>

CDC insect repellent use and safety

http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm