LA CROSSE ENCEPHALITIS VIRUS DISEASE

(LAC, La Crosse encephalitis, California encephalitis)

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 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

La Crosse virus; California encephalitis serogroup viruses. Six California serogroup viruses have caused human infections in North America. Three have been isolated from mosquitoes in Ohio: La Crosse virus (LAC), Jamestown Canyon and Trivittatus viruses. La Crosse virus is the principal virus in this group causing human encephalitis in Ohio.

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. [See also the Aseptic Meningitis chapter.]

Clinical Criteria for Diagnosis

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

- Fever (≥100.4°F or 38°C) as reported by the patient or a healthcare 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 (≥100.4°F or 38°C) as reported by the patient or a healthcare 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.

Comment
The seasonality of La Crosse encephalitis is predictable. In Ohio, cases can occur from May to October, when the specific vector mosquito is active.

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

LAC encephalitis initially presents as a nonspecific summertime illness with fever, headache, nausea, vomiting and lethargy. Severe disease occurs most commonly in children under the age of 16 and is characterized by seizures, coma, paralysis and a variety of neurological sequelae after recovery. Death from LAC encephalitis occurs in <1% of clinical cases.

DIAGNOSIS

Laboratory diagnosis of arboviral infections is generally accomplished by testing of serum or 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

The treehole mosquito, *Aedes triseriatus*, is both the vector and reservoir of LAC in nature, since the virus is transovarially transmitted to the offspring.

Occurrence

Most cases of LAC are reported from the North Central States primarily between July and October. From 1963-2010, 1,050 serologically documented cases were reported in Ohio, more than in any other state. Seven fatalities, all children, have been documented in Ohio. LAC is primarily a disease of children. The average age of the LAC patient is about eight years; the disease is rarely seen in adults, but does occur. Focus on pediatric cases has probably resulted in underdiagnosis of LAC in adults.

Mode of Transmission

Humans contract LAC from the bite of an infected mosquito, primarily *Aedes triseriatus*, the eastern treehole mosquito. The virus is maintained and amplified in *Aedes triseriatus* populations through transovarial and venereal transmission. The virus overwinters in the mosquito egg. Amplification also occurs in chipmunks and squirrels, upon which the mosquitoes feed. *Aedes canadensis*, *Aedes sollicitans* and *Aedes vexans* have also been found infected with LAC virus in Ohio and probably contribute in a secondary way to the amplification of the virus in nature. *Aedes canadensis* has been shown capable of virus transmission to mice and chipmunks in the laboratory.

Period of Communicability

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

Incubation Period

5-15 days.

PUBLIC HEALTH MANAGEMENT

Case

<u>Investigation</u>

If the case is suspect based upon test results of an acute serum sample, obtain a second (convalescent) serum sample to confirm the case diagnosis and sent it to the same laboratory which tested the acute sample. The ODH Laboratory will send samples to CDC for confirmation. Because private labs often discard a single serum sample shortly after completing the test, they are unable to perform

confirming serologic tests, as defined under **Laboratory Criteria for Diagnosis**, above. With serologic evidence of LAC infection, a history of travel and locations of potential mosquito exposure is obtained for the three weeks prior to onset.

Treatment
Some patients require hospitalization, where supportive care is indicated. There is no specific therapy.

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

Public Health Significance
Significant. Identification of a single case of LAC indicates risk of infection to others in the neighborhood, especially children.

Contacts
No treatment or prophylaxis of contacts is indicated.

Prevention and Control
Vaccination
There is no vaccine.

Vector Investigation
Home and travel sites are evaluated for treehole mosquito breeding potential, especially treeholes, containers such as tires, cans, buckets, etc. which hold water. Since the LAC virus is transmitted by the female mosquito to her offspring, these containers constitute the source of infected mosquitoes. Samples of water with mosquito larvae and small containers may be collected and sent to the Zoonotic Disease Program (ZDP), for vector evaluation. Containers should be disposed of, placed under cover so they will not collect rainwater or properly maintained (e.g. flushing bird baths weekly, cleaning out gutters). For advice on vector assessment, contact the ZDP at 614-752-1029, option 1.

Special Information
La Crosse encephalitis is under-diagnosed in Ohio and nationally. There is a need to improve awareness of this disease.

The transovarial passage of LAC virus enables this agent to persist in *Aedes triseriatus* populations, creating endemic foci of the disease. Cases among siblings and neighborhood children have occurred over a period of years, identifying foci of virus activity. *Aedes triseriatus*, the principal vector, breeds exclusively in containers of water. It does not breed in stagnant pools of water on the ground. Some types of containers commonly found breeding *Aedes triseriatus* include cavities in trees (“treeholes”), especially old tire casings, tin cans, bottles and other man-made items which retain water more than seven days. Silver maple, oak and beech trees are often found with treeholes.

The typical LAC patient has played near discarded man-made containers in or at the edge of large woods or woodlots. Tires were found associated with 36 of 81

Ohio LAC patients during 1981-83, and represented the single most significant source of *Aedes triseriatus.* LAC can be prevented through community awareness activities. The fact that LAC virus is carried primarily by one type of mosquito that breeds exclusively in containers of water should be stressed. Backyard container clean-up and treehole filling by the homeowner can significantly reduce the populations of this vector species in proximity to humans.

What is LAC?
It is a rare illness caused by a virus transmitted by mosquitoes. It typically affects children, but all ages are susceptible. LAC, also known as California Encephalitis, is one of a group of similar illnesses, including eastern equine encephalitis (EEE) and St. Louis Encephalitis (SLE), which can affect the central nervous system in people and cause severe complications or even death.

In the United States, most cases of LAC are reported from the upper Midwest, mid-Atlantic and southeastern states, primarily between July and October. Approximately 80-100 cases are diagnosed each year. Ohio averages 20 cases each year, more than in any other state. Seven fatalities, all children, have been documented in Ohio.

How is LAC transmitted?
It is transmitted through the bite of an infected mosquito. Most cases are transmitted by the treehole mosquito (*Aedes triseriatus*), which is commonly found in wooded areas of Ohio. Mosquitoes can pass the virus on to their offspring, or contract the virus from infected squirrels or chipmunks. Disease transmission does not occur directly from person-to-person.

How long after infection before symptoms appear?
Symptoms usually occur 5 to 15 days after an infected mosquito bites.

What are the symptoms of LAC?
LAC is usually a mild illness with fever, headache, nausea, vomiting and tiredness. People with severe disease, usually children, can have seizures, coma, paralysis and lasting brain damage. Less than 1% of cases are fatal.

How is LAC treated?
There is no specific treatment for LAC. Antibiotics are not effective against viruses, and no effective anti-viral drugs have been discovered. Patient care centers on treatment of symptoms and complications.

Is there a vaccine for LAC?
There is no human vaccine for LAC, and none are currently being developed.

How can I prevent LAC?
Prevent mosquito bites. It only takes one bite from an infected mosquito to transmit disease.

Avoid mosquito bites.

- Avoid areas where mosquitoes are active.
- Avoid outdoor activities during the peak mosquito biting times of dawn, dusk and early evening.
- When outdoors, apply mosquito repellant as directed to clothing and exposed skin.
- Reapply mosquito repellant as needed, especially if swimming or sweating.
- Clothing will help protect you from mosquito bites. If weather permits, wear long pants, long sleeves and/or socks.
- Install or repair window and door screens to keep mosquitoes outside.

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 LAC information http://www.cdc.gov/lac/

CDC insect repellant use and safety
http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm