LACROSSE VIRUS DISEASE

(LAC, LaCrosse encephalitis, California encephalitis)

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day after 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)
  - Via the Ohio Disease Reporting System (ODRS) or telephone
  - The Ohio Department of Health (ODH) 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 ODH, unless otherwise requested. If requested, the form can be faxed to 614-564-2456.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset and all the fields in the Epidemiology module.

AGENT

LaCrosse virus, California encephalitis serogroup viruses. Six California serogroup viruses have caused human infections in North America. Three have been isolated from mosquitoes in Ohio: LaCrosse virus (LAC), Jamestown Canyon and Trivittatus viruses. LaCrosse 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.

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. Guillan-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 for Diagnosis

A clinically compatible case is 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 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 or serum.

Case Classification

Probable:

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

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 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.

Comments

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

Imported arboviral diseases: Human 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. Healthcare providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual 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.

SIGNS AND SYMPTOMS

LaCrosse virus disease 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 LaCrosse virus disease occurs in <1% of clinical cases. [See also the Aseptic Meningitis chapter.]

DIAGNOSIS

Preliminary diagnosis is often based on the patient's clinical features, places and dates of travel (if patient is from a non-endemic country or area), activities and epidemiologic history of the location where infection likely occurred. In addition to other more common causes of encephalitis and aseptic meningitis (e.g. herpes simplex virus and enteroviruses), arboviruses such as LaCrosse, St. Louis encephalitis, Eastern equine encephalitis, Western equine encephalitis, Powassan and West Nile viruses should also be considered in the differential etiology.

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 LaCrosse virus in nature, since the virus is transovarially transmitted to the offspring. Vertebrates are amplifying hosts, particularly small mammals such as chipmunks and squirrels.

Occurrence

Most cases of LaCrosse are reported from the North Central states primarily between July and October. From 1963-2012, 1,114 serologically documented cases were reported in Ohio, more than in any other state. Seven fatalities, all children, have been documented in Ohio. LaCrosse is primarily a disease of children. The average age of the LaCrosse 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 LaCrosse in adults.

Mode of Transmission

Humans contract LaCrosse virus 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 LaCrosse 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 LaCrosse 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

Investigation

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 LaCrosse 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 LaCrosse 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 LaCrosse 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 LaCrosse virus is transmitted by the female mosquito to her offspring, these containers constitute the source of infected mosquitoes. 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 ODH Zoonotic Disease Proram (ZDP) at 614-752-1029, option 1.

Special Information

LaCrosse virus disease is under-diagnosed in Ohio and nationally. There is a need to improve awareness of this disease.

The transovarial passage of LaCrosse 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 LaCrosse 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 1981-1983, and represented the single most significant source of *Aedes triseriatus.* LaCrosse can be prevented through community awareness activities. The fact that LaCrosse 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 LaCrosse virus disease?
LaCrosse is a rare disease that is caused by a virus spread by infected mosquitoes. LaCrosse virus, also known as California encephalitis, is one of a group of mosquito-transmitted viruses that can cause inflammation of the brain (encephalitis). In the United States, about 80-100 LaCrosse virus disease cases are reported each year. Ohio averages 20 cases each year, more than in any other state. Seven fatalities, all children, have been documented in Ohio.

How do people get infected with LaCrosse virus?
LaCrosse virus is transmitted by the bite of an infected mosquito. Most people are infected 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. LaCrosse virus is not transmitted from person to person.

When and where have most cases of LaCrosse virus disease occurred?
Most cases of LaCrosse virus disease have been reported from upper Midwestern, mid-Atlantic and southeastern states. LaCrosse virus disease cases occur primarily from late spring through early fall, but in subtropical areas where the mosquito is found (e.g., the Gulf states), rare cases can occur in the winter.

Who is at risk for LaCrosse virus disease?
Anyone bitten by a mosquito in an area where the virus is circulating can get infected with LaCrosse virus. The risk is highest for people who live, work or recreate in woodland habitats because of the greater exposure to potentially infected mosquitoes.

How soon do people get sick after being bitten by an infected mosquito?
It takes 5 to 15 days after the bite of an infected mosquito to develop symptoms of LaCrosse virus disease.

What are the symptoms of LaCrosse virus disease?
Most persons infected with LaCrosse virus have no apparent illness. Initial symptoms in those who become ill include fever, headache, nausea, vomiting and tiredness. Severe disease (involving encephalitis, an inflammation of the brain) occurs most commonly in children under age 16, and is often accompanied by seizures. Coma and paralysis occur in some cases.

How is LaCrosse virus disease diagnosed?
Diagnosis is based on tests of blood or spinal fluid. These tests typically look for antibodies that the body makes against the viral infection.

What is the treatment for LaCrosse virus disease?
There is no specific treatment for LaCrosse virus disease. Antibiotics are not effective against viruses, and no effective anti-viral drugs have been discovered. Severe illnesses are treated by supportive therapy which may include hospitalization, respiratory support, IV fluids and prevention of other infections.

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

How can people reduce the chance of getting infected with LaCrosse virus?
Prevent mosquito bites. It only takes one bite from an infected mosquito to transmit disease.

- Use insect repellent containing DEET, picaridin, IR3535 or oil of lemon eucalyptus on exposed skin and/or clothing. The repellent/insecticide permethrin can be used on clothing to protect through several washes. Always follow directions on the package.
- Wear long sleeves and pants when weather permits.
- Have secure, intact screens on windows and doors to keep mosquitoes out.
- Eliminate mosquito breeding sites by emptying standing water from flower pots, buckets, barrels and other containers. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their side after use.
- LaCrosse virus can survive the winter in mosquito eggs that will hatch into infected mosquitoes in the spring. Cleaning potential breeding sites such as old tires or tin cans can reduce the number of infected eggs developing into infected mosquitoes. As the Aedes triseriatus mosquito prefers treeholes for breeding sites, you can reduce mosquitoes by filling treeholes in/around your yard with soil.

What should I do if I think a family member might have LaCrosse virus disease?
If you or anyone in your household has symptoms that are causing you concern, consult a healthcare provider for proper diagnosis.

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/westnile/faq/repellent.html