

LA CROSSE VIRUS DISEASE

(La Crosse encephalitis, California encephalitis, LACV)

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:
 - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the [Ohio Confidential Reportable Disease form](#) (HEA 3334).
 - The ODH [Mosquito-borne Illness Case Investigation Form](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and not sent to ODH, unless otherwise requested. If requested, the form can be faxed to ODH, Bureau of Infectious Diseases at (614) 564-2456 or uploaded to the ODRS record.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset, symptoms, all fields in the Epidemiology module and travel details in the Travel History module (with accurate departure and return dates along with city, province/county, state and country).

AGENT

La Crosse virus is an RNA virus, a California encephalitis serogroup virus that belongs to the genus *Bunyavirus* in the family *Bunyaviridae*. Six California serogroup viruses have caused human infections in North America. Three have been isolated from mosquitoes in Ohio: La Crosse virus (LACV), 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 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 cerebrospinal fluid (CSF) pleocytosis. 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, myalgia, arthralgia, rash or gastrointestinal symptoms. Some viruses can also cause more characteristic clinical manifestations,

such as severe polyarthralgia or arthritis due to chikungunya virus or other alphaviruses (e.g., Mayaro, Ross River, O'nyong-nyong).

Clinical Criteria

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. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/or nuchal rigidity.

Non-neuroinvasive disease:

- Fever (chills) as reported by the patient or a healthcare provider **and**
- Absence of neuroinvasive disease **and**
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/or nuchal rigidity.

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:
 - 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, with or without a reported pleocytosis, 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:

- 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., 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

La Crosse 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 years and is characterized by seizures, coma, paralysis and a variety of neurological sequelae after recovery. Death from La Crosse 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) and febrile illnesses, arboviruses such as chikungunya, dengue, Eastern equine encephalitis, Jamestown Canyon, Powassan, St. Louis encephalitis, West Nile, Western equine encephalitis and Zika 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.

For clinical samples being sent to CDC's Arbovirus Diagnostic Laboratory for testing, the [CDC Specimen Submission Form](#) must accompany the samples. Be sure the date of illness onset and travel history fields are completed. Use test order code CDC-10282 for arbovirus serology. Please contact ODH at (614) 995-5599 to arrange for testing at CDC.

EPIDEMIOLOGY

Source

The treehole mosquito, *Aedes triseriatus*, is both the vector and reservoir of La Crosse virus in nature, since the virus is transovarially transmitted to the offspring. Vertebrates are amplifying hosts, particularly small mammals such as chipmunks and squirrels.

Susceptibility

All individuals not previously infected with La Crosse virus (naïve individuals) are at risk for infection and developing disease. People who engage in outdoor work and recreational activities in endemic areas near woodland habitats are at increased risk of infection. La Crosse is primarily a disease of children. The average age of the La Crosse patient is about eight years; the disease is rarely seen in adults, but does occur. Focus on pediatric cases has probably resulted in under-diagnosis of La Crosse in adults.

Occurrence

Most cases of La Crosse are reported from the north central United States primarily between July and October. Recently, more cases have been reported from mid-Atlantic

and southeastern United States. From 1963-2016, 1,194 serologically documented cases were reported in Ohio, more than in any other state. Seven fatalities, all children, have been documented in Ohio. La Crosse virus disease is underdiagnosed in Ohio and nationally. There is a need to improve awareness of this disease.

The typical La Crosse 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 La Crosse patients during 1981-1983, and represented the single most significant source of *Ae. triseriatus*. La Crosse can be prevented through community awareness activities. The fact that La Crosse 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.

Mode of Transmission

Humans contract La Crosse virus from the bite of an infected mosquito, primarily *Aedes triseriatus*, the eastern treehole mosquito. The virus is maintained and amplified in *Ae. 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. *Ae. canadensis*, *Ae. sollicitans* and *Ae. vexans* have also been found infected with La Crosse virus in Ohio and probably contribute in a secondary way to the amplification of the virus in nature. *Ae. canadensis* has been shown capable of virus transmission to mice and chipmunks in the laboratory.

The transovarial passage of La Crosse virus enables this agent to persist in *Ae. 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. *Ae. 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 *Ae. triseriatus* include cavities in trees ("tree holes"), 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 tree holes.

Period of Communicability

Humans are dead-end hosts for the virus (i.e., they do not circulate sufficient numbers of the La Crosse 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

With serologic identification of La Crosse virus infection, a complete travel history for the two weeks prior to onset should be obtained. The patient should also be questioned about donating or receiving blood, blood products and organs in the 4 weeks prior to onset of symptoms. Female patients should be asked whether they were pregnant at the time of infection, and infants should be checked whether they were breastfed before illness onset. An accurate travel history is important to identify likely locations of exposure to implement vector control strategies. Sites of outdoor exposure and

activities can be evaluated for the presence of *Aedes* mosquitoes by standard collection techniques (BG sentinel traps, light traps, larval samples).

Treatment

There is no specific therapy for La Crosse virus disease. Some patients require hospitalization, where supportive care is indicated.

Isolation and Follow-Up Specimens

Since the diagnosis of La Crosse 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

High. Identification of a single case of La Crosse virus disease 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 or preventive drug currently available.

Vector Investigation

When La Crosse cases are identified, a vector assessment should be made in the vicinity of home and travel sites to identify potential breeding sites for tree hole mosquitoes, especially tree holes, containers such as tires, cans, buckets, etc. which hold water. For advice on vector assessment, contact the ODH Zoonotic Disease Program (ZDP) at (614) 752-1029. Those jurisdictions with capacity should consider:

- Adult mosquito control:
 - *Ae. triseriatus* are daytime biting mosquitoes that may not be as effectively controlled by standard ultra-low volume (ULV) applications. Early morning or late evening applications are recommended.
 - Focus ULV or barrier applications to the habitats where human cases were likely exposed to reduce local transmission.
- Larval mosquito control:
 - Remove larval habitats. 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).
 - Encourage the public to participate in efforts by discarding materials or closing containers (e.g., flower pots, buckets, tires, garbage cans).

Mosquito Bite Avoidance

The best way to prevent La Crosse virus infection is to avoid mosquito bites. Prevention tips are similar to those for other viral diseases transmitted by mosquitoes, such as dengue or West Nile virus:

- Use insect repellent [registered with the U.S. Environmental Protection Agency \(EPA\)](#) on exposed skin. Always follow the directions on the package. When using both sunscreen and insect repellent, apply the sunscreen first then the repellent.
- Wear long sleeves, pants and socks if feasible.
- Wear permethrin-treated clothing to repel and kill mosquitoes.
- Use screens on windows and doors to exclude mosquitoes. And, when available, A/C

- can make households less hospitable to mosquitoes.
- Participation in community and homeowner based vector-control strategies:
 - Ensure that water does not collect in containers around the home and community by emptying water from containers such as flowerpots, buckets, barrels and tires. Change the water in pet dishes, and replace the water in bird baths weekly. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their sides after use.
 - Use chemical or biological control of larvae and adult mosquitoes when necessary.

What is La Crosse virus disease?

La Crosse is a rare disease that is caused by a virus spread by infected mosquitoes. La Crosse 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 La Crosse 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 from 1963 to 2016.

How do people get infected with La Crosse virus?

La Crosse 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. La Crosse virus is not transmitted directly from person to person.

When and where have most cases of La Crosse virus disease occurred?

Most cases of La Crosse virus disease have been reported from upper Midwestern, mid-Atlantic and southeastern states. La Crosse 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 La Crosse virus disease?

Anyone bitten by a mosquito in an area where the virus is circulating can get infected with La Crosse 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 La Crosse virus disease.

What are the symptoms of La Crosse virus disease?

Most persons infected with La Crosse 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 La Crosse 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 La Crosse virus disease?

There is no specific treatment for La Crosse 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 La Crosse virus?

There is no human vaccine for La Crosse virus, and none are currently being developed.

How can people reduce the chance of getting infected with La Crosse 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.
- La Crosse 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 La Crosse 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:

- ODH La Crosse Information: <http://www.odh.ohio.gov/lacv>
- CDC La Crosse Information: <http://www.cdc.gov/lac/>
- CDC Insect Repellent Use and Safety: <http://www.cdc.gov/westnile/faq/repellent.html>
- U.S. Geologic Survey La Crosse Human Case Maps: <http://diseasemaps.usgs.gov/mapviewer/>