

ST. LOUIS ENCEPHALITIS VIRUS DISEASE (St. Louis Encephalitis, SLE)

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 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 ODH, unless otherwise requested. If requested, the form can be faxed to ODH 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 the 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

St. Louis encephalitis (SLE) virus is an RNA virus in the genus *Flavivirus* of the Flaviviridae family. There is substantial serologic cross-reaction with other flaviviruses (e.g., dengue, Japanese encephalitis, Powassan, West Nile, yellow fever, Zika viruses).

Infectious dose: A single bite from 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 of arboviral disease 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

Imported Arboviral Diseases

Human disease cases due to dengue or yellow fever 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 arboviral 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

Less than 1% of St. Louis encephalitis virus infections are clinically apparent, and the vast majority of infections remain undiagnosed. Onset of illness is usually abrupt with fever, headache, dizziness, nausea and malaise. Signs and symptoms intensify over a period of several days to a week. Some patients spontaneously recover after this period; others develop signs of central nervous system infections, including stiff neck, confusion, disorientation, dizziness, tremors and unsteadiness. Coma can develop in severe cases. The disease is generally milder in children than in older adults. About 40% of children and young adults with St. Louis encephalitis virus disease develop only fever and headache or aseptic meningitis; almost 90% of elderly persons with St. Louis encephalitis virus disease develop encephalitis. The overall case-fatality ratio is 5%-15%. The risk of fatal disease also increases with age. [See also the [Aseptic Meningitis](#) chapter.]

DIAGNOSIS

Preliminary diagnosis is often based on a 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 the 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, LaCrosse, Powassan, St. Louis encephalitis, West Nile, Western equine encephalitis and Zika viruses should also be considered in the differential etiology.

Serologic testing is the primary method for diagnosing St. Louis encephalitis virus infection because of the absence of a sensitive and non-invasive virus detection method. Combined with a consistent clinico-epidemiologic presentation, a rapid and accurate diagnosis of acute neuroinvasive St. Louis encephalitis virus disease can be made by the detection of St. Louis encephalitis virus-specific IgM antibody in serum or CSF. St. Louis encephalitis virus IgM tests are available commercially, in some state health department laboratories and at CDC. Because of the potential for cross-reactivity with other flaviviruses (such as dengue, Powassan, West Nile, yellow fever and Zika viruses), positive St. Louis encephalitis virus IgM test result should be confirmed by neutralizing antibody testing of acute- and convalescent-phase serum specimens at a state public health laboratory or CDC.

In acute St. Louis encephalitis virus neuroinvasive disease cases, cerebrospinal fluid (CSF) examination shows a moderate (typically lymphocytic) pleocytosis. CSF protein is elevated in about a half to two-thirds of cases. Computed tomography (CT) brain scans are usually normal; electroencephalographic (EEG) results often show generalized slowing without focal activity.

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 vector in Ohio is the northern house mosquito, *Culex pipiens*. Birds are the amplification host. Humans are dead-end hosts.

Susceptibility

All individuals not previously infected with St. Louis encephalitis virus (naïve individuals) are at risk for infection and developing disease. St. Louis encephalitis virus infection is thought to confer life-long immunity. The risk is highest for persons who engage in outdoor work and recreational activities and those living in low-income areas. Elderly persons are at increased risk of severe disease if they are infected.

Occurrence

St. Louis encephalitis virus disease is only known in the Western hemisphere. Virus isolation and a small number of human cases have been documented from Central and South America, but outbreaks are not known from this region. In North America, widespread epidemics of St. Louis encephalitis virus disease have occurred. The elderly experience more morbidity and mortality from St. Louis encephalitis virus than children, giving St. Louis encephalitis virus epidemics a distinctive age distribution. However, all age groups are affected. The most recent and largest epidemic of St. Louis encephalitis virus disease occurred in 1975 in the Midwestern states, resulting in 1,815 cases with 416 cases and 29 fatalities, from Ohio. In the post-epidemic years, 1976-2016, Ohio has documented 23 cases. The risk of exposure to St. Louis encephalitis virus in Ohio is statewide because the northern house mosquito is abundant and has been found in every county. In temperate areas of the United States, St. Louis encephalitis virus disease cases occur primarily in the late summer or early fall. In the southern states where the climate is milder, cases can occur year-round.

Mode of Transmission

St. Louis encephalitis virus is transmitted to humans through the bite of infected *Culex* species mosquitoes. Summer amplification of virus occurs in birds. The over-wintering mechanism is not understood.

Period of Communicability

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

Incubation Period

5 to 15 days.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

With serologic identification of St. Louis encephalitis 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. Sites of outdoor exposure and after-dark activities can be evaluated for the presence of *Culex* mosquitoes by standard collection techniques (shelter collections, light traps, biting and larval samples, bait traps and oviposition [gravid] traps).

Treatment

There is no specific therapy for St. Louis encephalitis virus disease. Supportive care is indicated.

Isolation and Follow-up Specimens

Since the diagnosis of St. Louis encephalitis virus disease is often not known until after patient discharge, enteroviral precautions (i.e., fecal, respiratory) are usually indicated for encephalitis. A convalescent serum sample 2-4 weeks after the acute may be required to confirm a case. A plaque reduction neutralization (PRNT) test is required for confirmatory testing.

Public Health Significance

Significant. Identification of a single case of St. Louis encephalitis virus disease during summer months might signify that an outbreak is developing. A statewide epidemic of St. Louis encephalitis virus disease last occurred in 1975.

Contacts

No treatment or prophylaxis of contacts is indicated.

Prevention and Control

Vaccination

There is no vaccine.

Vector Investigation

Likelihood of St. Louis encephalitis virus transmission is reduced if populations of the vector species, *Culex pipiens*, are kept under control by larviciding and control of breeding sites, including catch basins and backyard containers (tires, cans, bottles) in urban areas. Sewage-polluted ditches and stagnant water are more important in the rural setting. Education of the public about backyard breeding sites, screening of windows and personal protection are also recommended as a means of preventing cases. Surveillance of urban avians for seropositivity rates greater than 5% for St. Louis encephalitis virus is useful in detecting an impending outbreak. For advice on vector assessment, contact the ODH Zoonotic Disease Program (ZDP) at (614) 752-1029, option 1.

Because of the potential for epidemic St. Louis encephalitis virus, the diagnosis of a single human case should be followed by prompt mosquito control.

- Adult mosquito control:
 - *Culex* mosquitoes are most active at dusk and dawn.
 - Aerosol application (ultra-low volume cold fog or thermal fog) of an approved pesticide is recommended. This is required to break the transmission cycle.
- Larval mosquito control:
 - Remove larval habitats.
 - 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 St. Louis encephalitis 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 \(EPA\)](#) 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 St. Louis encephalitis?

St. Louis encephalitis is a rare disease caused by a virus spread by infected mosquitoes. St. Louis encephalitis virus is one of a group of mosquito-transmitted viruses that can cause inflammation of the brain (encephalitis). Nationally, widespread epidemics of St. Louis encephalitis have occurred. The largest and most recent one occurred in 1975 in the Midwestern states, resulting in 1,815 cases; 416 of those, including 29 fatalities, were from Ohio. Between 1976 and 2016, Ohio has documented only 23 cases.

How do people get infected with St. Louis encephalitis virus?

St. Louis encephalitis virus is transmitted by the bite of an infected *Culex* mosquito. Mosquitoes become infected when they feed on birds carrying the St. Louis encephalitis virus. Infected mosquitoes then transmit the virus to other birds and to humans when they bite them. St. Louis encephalitis virus cannot be transmitted directly from person to person.

Where and when have most cases of St. Louis encephalitis virus disease occurred?

Cases have been reported throughout the country, but periodic outbreaks and epidemics have primarily occurred in the Mississippi Valley and along the Gulf Coast. In temperate areas of the United States, St. Louis encephalitis virus disease cases occur primarily in the late summer or early fall. In southern states, cases can occur year round.

Who is at risk for infection St. Louis encephalitis virus?

Anyone bitten by a mosquito in an area where the virus is circulating can get infected with St. Louis encephalitis virus. The risk is highest for persons who engage in outdoor work and recreational activities and those living in low-income areas. Elderly persons are at risk for severe disease if they are infected.

How soon do people get sick after getting bitten by an infected mosquito?

It takes 5 to 15 days after the bite of an infected mosquito to develop symptoms of St. Louis encephalitis virus disease.

What are the symptoms of St. Louis encephalitis virus disease?

Most people who are infected with St. Louis encephalitis virus have no symptoms or only mild non-specific flu-like illness. However, in some individuals, especially the elderly, St. Louis encephalitis virus can cause serious illness that affects the central nervous system. Symptoms often include fever, headache, stiff neck, disorientation and altered level of consciousness. Coma, convulsions and paralysis may also occur.

How is St. Louis encephalitis virus disease diagnosed?

Diagnosis is based on test of blood or spinal fluid. These tests typically look for antibodies that the body makes against the viral infection.

What is the treatment for St. Louis encephalitis virus disease?

There is no specific treatment for St. Louis encephalitis virus disease. Antibiotics are not effective against viruses. Severe illnesses are treated by supportive therapy which may include hospitalization, respiratory support, IV fluids and prevention of other infections.

Is there a vaccine against SLE?

There is no human vaccine, and none are currently being researched.

How can people reduce the chance of getting infected with St. Louis encephalitis 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 the 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.

For more information please visit these websites:

- CDC St. Louis Encephalitis Virus Disease Information: <http://www.cdc.gov/sle>
- CDC Insect Repellent Use and Safety: <http://www.cdc.gov/westnile/faq/repellent.html>
- U.S. Geologic Survey St. Louis Encephalitis Human Case Maps: <http://diseasemaps.usgs.gov/mapviewer/>