

## La Crosse Virus

### Disease Agent:

- La Crosse virus

### Disease Agent Characteristics:

- Family: *Bunyaviridae*; Genus: *Bunyavirus* of the California encephalitis serogroup
- Virion morphology and size: Enveloped, helical nucleocapsid symmetry, spherical to pleomorphic particles, 90-110 nm in diameter
- Nucleic acid: Three segments of circular, negative-sense, single-stranded RNA, 12.5 kb in length
- Physicochemical properties: Bunyaviruses are sensitive to inactivation by heat, detergents, formaldehyde, and low pH.

### Disease Name:

- La Crosse encephalitis

### Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Very low but low in endemic areas

### Background:

- Early in the 1960s, physicians in southwestern Wisconsin and southeastern Minnesota investigated children with a summer “rural encephalitis.” La Crosse virus was isolated at autopsy from the brain of a fatal case. It is an arbovirus of the California encephalitis serogroup.
- La Crosse virus infections are identified predominantly in Mississippi and Ohio River basins and the mid-Atlantic states, but sporadic cases have been found in more than 20 states, generally from the Mississippi River and to the east.
- From 1964-2006, 3439 cases have been reported (mean 80/year).
- La Crosse virus and WNV account for the overwhelming majority of pediatric arboviral encephalitis cases in the US.

### Common Human Exposure Routes:

- It is transmitted by the bite of vector mosquitoes.

### Likelihood of Secondary Transmission:

- Viruses in the California encephalitis group are not known to be transmitted from person-to-person or through blood transfusion.

### At-Risk Populations:

- La Crosse encephalitis is predominantly a childhood disease; 75% of cases occur in children under 10 years of age and only 3% in persons 20 years or older.
- Seroprevalence surveys in endemic areas have tended to show higher prevalence rates in rural than in urban sites (30% vs. 15% in one study), many cases occur in suburban residential locations.

### Vector and Reservoir Involved:

- Transmitted by female *Aedes triseriatus*, a “tree-hole mosquito,” the reservoir and vector for La Crosse virus.
- Although their main breeding site is in holes in hardwood trees, the mosquitoes can also breed in artificial containers that hold rainwater, including discarded tires.
- Persistence in endemic areas is a result of vertical transmission of La Crosse virus from *Aedes triseriatus* females to their offspring, venereal transmission among adult mosquitoes, and horizontal transmission to small mammals (e.g., chipmunks, squirrels, woodchucks, and foxes) that serve as amplifying hosts.
- Humans do not maintain prolonged viremias and therefore are “dead-end” hosts unable to amplify the virus and reinfect the vector.
- The introduction and spread in the US of another potentially efficient vector, *Aedes albopictus*, have raised concern about further geographic spread of La Crosse virus infections.

### Blood Phase:

- No data available for blood phase in asymptomatic persons.
- Virus is introduced by the feeding mosquito, and viral replication is presumed to cause viremia; amplification of the viremia occurs in the reticuloendothelial system followed by invasion of the central nervous system (CNS).
- Entrance to the CNS is probably first gained by infection of vascular endothelial cells followed by infection of neurons and glial cells.
- Neither La Crosse nor other members of the California serogroup have been isolated from human blood. The length of the incubation period (about 1 week for La Crosse virus) provides time for antibody production and “quenching” of the relatively brief putative viremia (estimated duration, 1-3 days).

### Survival/Persistence in Blood Products:

- Unknown

**Transmission by Blood Transfusion:**

- La Crosse virus has not been associated with transmission by blood transfusion.

**Cases/Frequency in Population:**

- Incidence rates of La Crosse virus infection (symptomatic and asymptomatic) as high as 30 per 10,000 population have been published but are generally much lower.

**Incubation Period:**

- Approximately 1 week after exposure

**Likelihood of Clinical Disease:**

- Low, but highest in children and adolescents

**Primary Disease Symptoms:**

- Of children infected with La Crosse virus, only a tiny fraction (~0.3%-4%) have symptoms.
- Fever, headache, nausea, and vomiting are common. Symptomatic infection ranges from a mild febrile illness to aseptic meningitis and fatal encephalitis.

**Severity of Clinical Disease:**

- Most infections are asymptomatic, but children presenting to a physician generally have signs of encephalitis, which can be severe.
- Nearly one-half of hospitalized cases have seizures.

**Mortality:**

- The case fatality rate is much less than 1% overall but approaches 1% of hospitalized cases.

**Chronic Carriage:**

- None recognized

**Treatment Available/Efficacious:**

- No established treatment except supportive care. Isolated ribavirin use has been reported.

**Agent-Specific Screening Question(s):**

- No specific question is in use.
- Not indicated because transfusion transmission has not been demonstrated
- A question about mosquito contact in endemic areas would have low positive predictive value.

**Laboratory(s) Test Available:**

- No FDA-licensed blood donor screening test exists.
- Virus isolation from tissue is difficult.
- Serological tests (EIA, IFA, HAI, CF, neutralization) detect IgM and IgG antibodies.
- Nucleic acid amplification (primarily nucleic acid sequence-based amplification [NASBA] and RT-PCR)

has been used to detect RNA in CSF and CNS tissue, and appears very specific and more sensitive than virus isolation.

**Currently Recommended Donor Deferral:**

- No FDA Guidance or AABB Standard exists.
- The appropriate deferral period for clinical infection is not known but would likely be on the order of several weeks after the resolution of symptoms.

**Impact on Blood Availability:**

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Impact on Blood Safety:**

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Leukoreduction Efficacy:**

- Unknown

**Pathogen Reduction Efficacy for Plasma Derivatives:**

- No specific data available but presumed to be robust, as the agent is an enveloped virus that should be sensitive to many measures used in the fractionation process.

**Other Preventive Measures:**

- Unknown

**Suggested Reading:**

1. Calisher CH. Medically important arboviruses of the United States and Canada. *Clin Microbiol Rev*, 1994; 7:89-116.
2. Confirmed and Probable California Serogroup Viral (mainly La Crosse) Encephalitis Cases, Human, United States, 1964-2006. [cited 2009 May]. Available from: [http://www.cdc.gov/ncidod/dvbid/arbor/pdf/CAL\\_LAC.pdf](http://www.cdc.gov/ncidod/dvbid/arbor/pdf/CAL_LAC.pdf)
3. Gerhardt RR, Gottfried KL, Apperson CS, Davis BS, Erwin PC, Smith AB, Panella NA, Powell EE, Nasci RS. First isolation of La Crosse virus from naturally infected *Aedes albopictus*. *Emerg Infect Dis* 2001;7: 807-11.
4. Lambert AJ, Nasci RS, Cropp BC, Martin DA, Rose BC, Russell BJ, Lanciotti RS. Nucleic acid amplification assays for detection of La Crosse Virus RNA. *J Clin Micro* 2005;43:1885-9.
5. McJunkin JE, Khan RR, de los Reyes EC, Parsons DL, Minnich LL, Ashley RG, Tsai TF. Treatment of severe La Crosse encephalitis with intravenous ribavirin following diagnosis by brain biopsy. *Pediatrics* 1997;99: 261-7.
6. McJunkin JE, Khan RR, Tsai TF. California-LaCrosse encephalitis. *Infect Dis Clin North Am* 1998;12:83-93.

## APPENDIX 2

---

7. Peters CJ. California encephalitis, hantavirus pulmonary syndrome, and bunyavirid hemorrhagic fevers. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. Philadelphia: Elsevier, Churchill, Livingstone; 2005. p. 2086-90.
8. Slater B, Huang C, Bloch K, Jones T, Woodlief G, McPherson T. Detection of La Crosse virus in cerebrospinal fluid and tissues by reverse transcription polymerase chain reaction. International Conference on Emerging Infectious Diseases. Atlanta, GA. March 24-27, 2002. [cited 2009 May]. Available from: [http://www.cdc.gov/iceid/webcast/molecular\\_d2.htm](http://www.cdc.gov/iceid/webcast/molecular_d2.htm)