

## Lymphocytic Choriomeningitis Virus

### Disease Agent:

- Lymphocytic choriomeningitis virus (LCMV)

### Disease Agent Characteristics:

- Family: *Arenaviridae*; Genus: *Arenavirus*.
- Virion morphology and size: Enveloped, pleomorphic virions with filamentous helical nucleocapsids, diameter 50-300 nm (mean: 110-130 nm)
- Nucleic acid: Ambisense genomic organization (two viral genes separated by an intergenic region), bisegmented, negative-sense, single-stranded RNA genome, S (small, ~3.5 kb) and L (large, ~7.2 kb) segments
- Physicochemical properties: Inactivated by low-level disinfectants, such as quaternary ammonium-based products, phenolics, chlorine-based products, and iodophor formulations; susceptible to 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol, formaldehyde, and quaternary ammonium compounds; sensitive to heat inactivation; LCMV survives in rodent droppings.

### Disease Name:

- Lymphocytic choriomeningitis virus infection

### Priority Level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical because of documented transmission via transplants (but not transfusion)
- Public perception regarding blood safety: Absent
- Public concern regarding disease agent: Absent

### Background:

- This virus is widespread in rodents.
- Transmission to humans is generally the result of contact with rodent secretions and excretions in the environment.
- Transmission to four recipients of organ transplants from a single donor in 2005 and to another three recipients from one donor in 2003 has caused recent speculation about a theoretical risk of parenteral transmission by blood or blood components. An additional two renal allograft recipients from a single donor with aseptic meningitis had fatal LCMV infection in 2008. Donor infection was confirmed by reactive IgM and IgG anti-LCMV, and the recipients' LCMV nucleic acid sequences were identical.
- Three additional organ transplant recipients were fatally infected from a single donor with a novel arenavirus in 2008. The novel virus shared 80-90% homology with LCMV at the amino acid level. As in the other two reported clusters of transplant-

associated transmission, there was no evidence of other infection by culture or nucleic acid testing in the recipients, and no history of acute infectious disease was reported in the donor. However, a pet hamster that was present in the household of the donor was infected with the same virus detected in the recipients.

### Common Human Exposure Routes:

- Contact (broken skin, nares, eyes, mouth) with urine, saliva, feces, blood, or nesting materials of infected natural host, *Mus musculus* complex (the habitat of *Mus m. musculus* spans from Central Europe, east to China and Japan, while the habitat of *Mus m. domesticus* encompasses Western Europe and the Mediterranean basin, Near-East, Americas, and Australia)
- Exposure to urine or saliva of other wild, pet, or laboratory rodents (rats, guinea pigs, and hamsters)

### Likelihood of Secondary Transmission:

- Uncommon
- Maternal-fetal and solid organ transmission well documented

### At-Risk Populations:

- Children and adults

### Vector and Reservoir Involved:

- Domestic mice are the primary reservoir.
- Focality is common (uneven distribution of virus).

### Blood Phase:

- Viremia present during the acute febrile phase and during the meningitic phase; however, it is unknown to what extent viremia precedes the onset of symptoms.

### Survival/Persistence in Blood Products:

- Unknown

### Transmission by Blood Transfusion:

- Viremia in mild or asymptomatic infection possible but not documented
- No reported cases of transmission by blood transfusion
- Several reports of transmission by infected organ donors

### Cases/Frequency in Population:

- Studies in endemic areas show seroprevalence range of 1-10% (4%-5% in US inner cities)
- Incidence of acute LCMV infection in the US is very low with previous outbreaks witnessed in organ-transplant recipients or linked to exposure to pet

hamsters or virus-contaminated laboratory rodents and cell lines derived from them.

#### **Incubation Period:**

- 8-13 days after exposure

#### **Likelihood of Clinical Disease:**

- Recognized disease is rare but thought to be underdiagnosed.

#### **Primary Disease Symptoms**

- Illness is biphasic; usually recognized as aseptic meningitis
  - Phase 1: (common symptoms) fever, malaise, anorexia, muscle ache, nausea, vomiting; (less common) sore throat, cough, joint pain, testicular pain, parotid pain
  - Phase 2: (common) meningitis, encephalitis (diagnosed in 5%-34% of hospitalized patients); (less common) hydrocephalus, myelitis
  - May cause hydrocephalus transiently or congenital hydrocephalus and chorioretinitis after fetal infection

#### **Severity of Clinical Disease:**

- Full recovery is usual; patients developing meningitis or encephalitis usually recover without residua.
- Fetal infection can lead to permanent developmental deficits.

#### **Mortality:**

- Greater than 1% overall, but significant higher mortality has been observed in immunosuppressed organ-transplant patients receiving infected donor organs, resulting in multiorgan failure with hepatitis as a prominent feature in the infected organ recipient

#### **Chronic Carriage:**

- None described in humans

#### **Treatment Available/Efficacious:**

- None

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

- No specific question is in use.
- Not indicated because transfusion transmission has not been definitively demonstrated.
- No sensitive or specific question is feasible. Questions about contact with wild rodents, pet hamsters, or guinea pigs are unlikely to be sensitive or specific.

#### **Laboratory Test(s) Available:**

- No FDA-licensed blood donor screening test exists
- Clinical specimens may be tested by NAT, virus culture or immunohistochemical staining.

- Plasma and serum may be tested for IgM and IgG antibodies.

#### **Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.
- Because viremia can persist through the meningitic phase and neutralizing antibodies appear late, prudent practice would be to defer donor until full recovery.

#### **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 but not likely to be effective

#### **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 Prevention Measures:**

- LCMV testing of hamster colonies
- Rodent control
- Consider LCMV infection in patients presenting with aseptic meningitis or encephalitis, especially in alcoholics, who may be potential organ donors

#### **Suggested Reading**

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4. Centers for Disease Control and Prevention. Lymphocytic choriomeningitis virus transmitted through solid organ transplantation—Massachusetts, 2008. *Morb Mortal Wkly Rep MMWR* 2008;57:799-801.
5. Fischer SA, Graham MB, Kuehnert MJ, Kotton CN, Srinivasan A, Marty FM, Comer JA, Guarner J,

- Paddock CD, DeMeo DL, Shieh WJ, Erickson BR, Bandy U, DeMaria A Jr, Davis JP, Delmonico FL, Pavlin B, Likos A, Vincent MJ, Sealy TK, Goldsmith CS, Jernigan DB, Rollin PE, Packard MM, et al. LCMV in Transplant Recipients Investigation Team. Transmission of lymphocytic choriomeningitis virus by organ transplantation. *N. Engl J Med* 2006;354:2235-49
6. Paddock C, Ksiazek T, Comer JA, Rollin P, Nichol S, Shieh WJ, Guarner J, Goldsmith C, Greer P, Srinivasan A, Jernigan D, Kehl S, Graham M, Zaki S. Pathology of fatal lymphocytic choriomeningitis virus infection in multiple organ transplant recipients from a common donor. *Mod Pathol* 2005; 18 Suppl 1s:A263-4.
  7. Palacios G, Druce J, Du L, Tran T, Birch C, Briese T, Conlan S, Quan PL, Hui J, Marshall J, Simons JF, Egholm M, Paddock CD, Shieh WJ, Goldsmith CS, Zaki SR, Catton M, Lipkin WI. A new arenavirus in a cluster of fatal transplant-associated diseases. *N Engl J Med* 2008;358:991-8.