

## CALLITRICHID HEPATITIS/LYMPHOCYTIC CHORIOMENINGITIS VIRUS

Animal Group(s) Affected	Transmission	Clinical Signs	Severity	Treatment	Prevention and Control	Zoonotic
New World nonhuman primates (NHP)- <i>Platyrrhini</i> - of the families Callitrichidae and Callimiconidae; humans and rodents	Horizontal due to ingestion of infected mice with LCMV (including wild rodents) Vertical transmission of LCMV to an aborted nonhuman primate fetus.	Lethargy, jaundice, anorexia, weakness, dyspnea	High fatality rate (morbidity and mortality)	None	Rodent control; avoid feeding primates on mice	Yes

**Fact Sheet compiled by:** Enrique Yarto-Jaramillo

**Sheet completed on:** 3 August 2011; updated 5 September 2012

**Fact Sheet Reviewed by:** Lilian Silva Catenacci; Rosalia Pastor; Pierre Rollin

**Susceptible animal groups:** The house mouse (*Mus musculus*) is the natural host and principal reservoir of LCMV. Several genera of families Callitrichidae, especially *Callithrix* sp., *Saguinus* sp. and Callimiconidae, especially *Callimico goeldii*, are susceptible to the infection with LCMV. In captive golden lion tamarins (*Leontopithecus rosalia*) and pygmy marmoset (*Cebuella pygmaea*), the virus accounted for 43 and 71% of deaths of animals respectively. The humans and wild, laboratory and pet rodents (especially mice, hamsters, gerbils, rats and guinea pigs) are susceptible. Although rodents can potentially become infected, they often do not show any signs of illness.

**Causative organism:** Lymphocytic choriomeningitis virus (LCMV) which is a lipid enveloped single-stranded RNA virus belonging to the family Arenaviridae of the Old World Arenavirus group. It is a virus with high mutation rates and important strain variations. Rodent reservoirs pass the virus to their offspring and shed the virus in urine and oral secretions, which are additional routes of transmission to zoo animals. The other route of transmission to zoo animals is the domestic mice used to feed non-human primates. Animals not eating mice neither became ill nor seroconvert to LCMV even after close contact with sick primates. Thus, direct primate-primate transmission of LCMV was not observed yet, although such a mode of transmission remains a possibility. Vertical transmission of LCMV to an aborted tamarin fetus, however, was demonstrated in a US zoo.

**Zoonotic potential:** Seroconversion with no evidence of clinical disease has been reported in handlers of infected animals, although the infection has been reported to cause substantial neurological disease, especially in immunocompromised humans. In humans, the LCMV causes influenza-like clinical signs, occasionally with neurologic complications. Infection may be asymptomatic in up to one third of patients, although serious complications often occur in intrauterine infection. Less severe cases of adult human infection are likely underreported and often misdiagnosed. It is a potential emerging neuteratogen causing congenital defects in children. In April 2012, the CDC was notified about a patient diagnosed with aseptic meningitis who was an employee at a rodent breeding facility in Indiana and whose testing revealed LCMV. Further testing showed evidence of prevailing or past LCMV infection in 13 out of 52 employees at the same facility. In 2009 the Center for Disease Control and Prevention confirmed a case of LCMV-associated congenital hydrocephalus and choriorretinitis in a child from New York. The mother's history referred exposure to mice during pregnancy. LCMV is recognized as a zoonotic disease associated with exposure to infected hamsters and gerbils.

**Distribution:** LCMV is found worldwide, probably because of its association with its natural Old World host, the house mouse, *Mus musculus*. Although antibodies have also been detected in other rodent species,

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arenaviruses are known to be serologically cross-reactive. Outbreaks have been reported in zoo colonies of callitrichid primates in US and Europe (UK and Germany).

**Incubation period:** In non-human primates, it is from one to three weeks, but deaths which can reach 100% in an outbreak may occur over a period of weeks to months.

**Clinical signs:** In infected primates, clinical findings are acute onset of lethargy, anorexia, weakness, fever, dyspnea and mucus-covered feces. It was also reported abortion and dystocia in captive tamarins and marmosets. Animals having a longer course of the disease may present jaundice and inguinal petechiae. Some authors have reported grand mal seizures or sudden death without prior clinical signs. Clinical laboratory findings: elevated levels of aspartate aminotransferase, alkaline phosphatase and bilirubin, but none of them are specific. Serologic evidence of LCMV in marmosets without clinical signs has been documented.

**Post mortem, gross, or histologic findings:** Gross necropsy findings in NHP may include: hepatitis, hepatomegaly, splenomegaly, pleural and pericardial effusions, lymphadenopathy, jaundice, subcutaneous and intramuscular hemorrhages. Histologic findings include multifocal hepatocyte necrosis with infiltration by lymphocytes and neutrophils and portal vein vasculitis, necrosis of spleen, lymph nodes, adrenal cortex and intestinal tract. Acidophilic bodies (Councilman bodies), that represent apoptotic hepatocytes have been observed in affected liver tissues. Brain tissues may show encephalitis, minimal meningitis and vasculitis.

**Diagnosis:** In NHP clinical signs, clinical findings and husbandry history (exposure to rodent species or history of being fed suckling mice) are consistent with diagnosis. In humans, confirmatory diagnosis is usually by virus isolation in cerebrospinal fluid (CSF); by PCR on tissues or CSF; anti-LCMV IgM and IgG by ELISA in blood, serum, or CSF.

Histopathology, virus isolation, electron microscopy, nucleic acid hybridization analysis, immunofluorescence and immunoblot in liver biopsy and other tissues (spleen, lung, adrenal glands, lymph nodes, intestine, kidneys, urinary bladder, heart and brain) are the reported diagnostic methods for LCMV in NHP. In rodents, few isolates of LCMV have been obtained from wild rodents so little is known about its genetic diversity. Confirmatory diagnosis is by viral isolation or PCR, and antibody detection in the blood/serum by ELISA.

**Material required for laboratory analysis:** Serum for serology, tissue samples (especially liver and brain) frozen at -70°C for PCR or virus isolation. Formalin-fixed tissues for pathology and immunohistochemistry.

**Relevant diagnostic laboratories:**

Virus Reference Laboratories Inc.  
7540 Louis Pasteur Road  
San Antonio, Texas 78229  
Phone: (210) 614 – 7350  
Fax: (210) 614 – 7355

**Treatment:** No effective treatment known, although supportive therapy with fluids to correct hypovolemia and electrolyte imbalances might be of benefit. The antiviral agent ribavirin has been used in infected primates (150mg/kg, intramuscularly, once daily for 6 days), but all of them were in an advanced stage of the disease and a clinical response was not observed.

**Prevention and control:** Avoid feeding callitrichid primates on mice (pinkies), and stringent rodent control programs in zoos and primate centers, particularly in areas housing callitrichids. People using frozen or live rodents to feed other animals should follow safety precautions, including wearing gloves when handling animal products. Washing hands with soap and water after handling animal products is warranted. Once an outbreak has been detected the animal enclosure should be cleaned and disinfected.

**Suggested disinfectant for housing facilities:** A 1:10 bleach solution is effective in killing LCMV.

**Notification:** Due to some reports on human patients contracting the virus from transplanted organs as well as LCMV-associated congenital defects, LCMV is a reportable disease in three U.S states (Wisconsin,

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Massachusetts and Arizona) and one city (New York, New York).

**Measures required under the Animal Disease Surveillance Plan:** Currently none

**Measures required for introducing animals to infected animal:** It appears that most NHP that become clinically infected succumb to the disease. Horizontal transmission has not been reported in people; however vertical transmission can occur.

**Conditions for restoring disease-free status after an outbreak:** Strict pest control and removal and control of all rodents and their droppings, urine and bedding. Disinfection of all premises with 1:10 bleach solution.

**Experts who may be consulted:**

CDC – Viral Special Pathogens Branch

404-639-1115 or 404-639-1510

Dvd1spath@cdc.gov

<http://www.cdc.gov/ncezid/dhcpp/vspb/index.html>

**References:**

1. Lymphocytic Choriomeningitis (LCMV)  
<http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/lcmv.htm> Accessed 19 August 2013.
2. Lymphocytic choriomeningitis virus (LCMV) at a rodent breeding facility in Indiana.  
<http://www.cdc.gov/ncezid/dhcpp/vspb/outbreaks.html> Accessed 19 August 2013.
3. Asper, M., P. Hofmann, C., Osmann, J., Funk, C., Metzger, M., Bruns, F.-J., Kaup, H, Schmitz., and S. Günther. 2001. First outbreak of callitrichid hepatitis in Germany: genetic characterization of the causative lymphocytic choriomeningitis virus strain. *Virology* 284: 203 – 213.
4. Bielitzki, J.T. Emerging viral diseases of nonhuman primates. 1999. *In: Fowler, M.E., and R.E. Miller (eds.) Zoo and Wild Animal Medicine, Current Therapy 4.* Saunders. Philadelphia, Pennsylvania. Pp. 377-382.
5. Blasdel, K.R., S.D. Becker, J. Hurst, M. Begon, and M. Bennett. 2008. Host range and genetic diversity of arenaviruses in rodents, United Kingdom. *Emerg. Infect. Dis.* 14(9): 1455-1458.
6. Catão-Dias, J. L. 2001. Infectious diseases in Order Primates. *In: Fowler, M.E., and Z.C. Cubas (eds.). Biology, Medicine, and Surgery of South American Wild Animals.* Iowa State University Press, Iowa. Pp: 269-272.
7. Fischer, S.A., M.B. Graham, M.J. Kuehnert, C.N. Kotton, A. Srinivasan, F.M. Marty, J.A. Comer, J. Guarner, C.D. Paddock, D.L. DeMeo, W.J. Shieh, B.R. Erickson, U. Bandy, A. DeMaria Jr., J.P. Davis, F.L. Delmonico, B. Pavlin, A. Likos, M.J. Vincent, T.K. Sealy, C.S. Goldsmith, D.B. Jernigan, P.E. Rollin, M.M. Packard, M. Patel, C. Rowland, R.F. Helfand, S.T. Nichol, J.A. Fishman, T. Ksiazek, and S.R. Zaki. 2006. Transmission of lymphocytic choriomeningitis virus by organ transplantation. *N. Engl. J. Med.* 354 (21): 2235.
8. Gog, J., R. Woodroffe and J. Swinton. 2002. Disease in endangered metapopulations: the importance of alternative hosts. *Proc. R. Soc. Lond. B.* 269:671–676.
9. Knust, B., A. Macneil, S.J. Wong, P.B. Backenson, A. Gibbons, P.E. Rollin, and S.T. Nichol. 2011. Exposure to lymphocytic choriomeningitis virus, New York, USA. *Emerg. Infect. Dis.* 17(7): 1324-5.
10. Ludlage, E., and K. Mansfield. 2005. Clinical care and diseases of the common marmoset (*Callithrix jacchus*). *Comp. Med.* 53(4): 369-382.
11. Mello, M.A., C. Toscano, J.A.P.C. Muniz, M.A.N. Torres, O.P. de Oliva, P.F. da Costa Vasconcelos, R. del Rio do Valle, V.L.C. da Silva, V.L.R.S. de Barros, W.K. Svoboda, W.L.A. Pereira, and Z.G.A. Costa., 2005. Manual de Vigilância de Epizootias em Primatas não-humanos. Serie A. Ministry of Health, Secretariat of Health Surveillance, Brasília, Brazil.
12. Montali, R.J., and M. Bush. Diseases of callitrichidae. 1999. *In: Fowler, M.E., and R.E. Miller (eds.) Zoo and Wild Animal Medicine, Current Therapy 4.* Saunders. Philadelphia, Pennsylvania. Pp. 369-376.
13. Montali, R. J., B. M. Connolly, D. L. Armstrong., C. A. Scanga., and K. V. Holmes. 1995.

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- Pathology and immunohistochemistry of callitrichid hepatitis, an emerging disease of captive New World primates caused by lymphocytic choriomeningitis virus. *Am. J. Pathol.* 147: 1441 – 1449.
14. Montali R.J., C.A. Scanga, D. Pernikoff, R. Wessner, R. Ward, and K.V. Holmes. 1993. A common-source outbreak of callitrichid hepatitis in captive tamarins and marmosets. *J. Infect. Dis.* 167: 946–950.
  15. Rensing, S., and A.K Oerke. Husbandry and management of New World species: marmosets and tamarins. 2005. *In: Wolfe-Coote, S. (ed.) The Handbook of Experimental Animals, The Laboratory Primate.* Elsevier, San Diego, California. Pp: 145-162.
  16. Setzer, A.P. 2007. Hepatites virais. *In: Cubas Z.C., J.C.R. Silva, and J.L. Catão-Dias (eds.). Tratado de Animais Selvagens- medicina veterinária.* Roca, Brazil. Pp: 815-825.
  17. Scanga, C. A., K. V. Holmes, and R. J. Montali. 1993. Serologic evidence of infection with lymphocytic choriomeningitis virus, the agent of callitrichid hepatitis, in primates in zoos, primate research centers, and a natural reserve. *J. Zoo Wildl. Med.* 24: 469 – 474.
  18. Stephensen, C. B., J. R. Jacob., R. J. Montali., K. V. Holmes., E. Muchmore., R. W. Compans, E. D. Arms, M. J. Buchmeier, and R. E. Lanford. 1991. Isolation of an arenavirus from a marmoset with callitrichid hepatitis and its serologic association with disease. *J. Virol.* 65: 3995–4000.
  19. Udofin, L.U. 2010. Lymphocytic choriomeningitis. *In: Rabinowitz, P.M., and L.A. Conti (eds.) Human-Animal Medicine, Clinical Approaches to Zoonoses, Toxicants and Other Shared Health Risks.* Saunders, Maryland Heights, Missouri. Pp. 204-209.