Lympohocytic Choriomeningitis Virus (LCMV)

Organism or Agent: Lymphocytic Choriomeningitis Virus (LCMV)
Exposure Risk: Lymphocytic Choriomeningitis
AKA: Armstrong’s Disease

UCSF Occupational Health Services: 415/885-7580 (Available during work hours)
Exposure Hotline: 415/353-7842 (Available 24 hours)
Office of Environment Health & Safety: 415/476-1300 (Main number; available during work hours)
415/476-1414 or 9-911 (In case of emergency, via the UCSF Police Department; available 24 hours)
EH&S Public Health Officer: 415/514-3531
Biosafety Officer: 415/514-2824

PROTOCOL SUMMARY

In the event of an accidental exposure or injury, the protocol is as follows:

1. Modes of Transmission:
   a. Skin puncture or injection
   b. Ingestion
   c. Contact with mucous membranes (eyes, nose, mouth)
   d. Contact with non-intact skin
   e. Exposure to aerosols containing LCMV
   f. Possible arthropod vector mediated transmission
   g. Bites of infected animals

2. First Aid:
   a. **Skin Exposure**, immediately go to the sink and thoroughly wash the skin with soap and water. Decontaminate any exposed skin surfaces with an antiseptic scrub solution.
   b. **Skin Wound**, immediately go to the sink and thoroughly wash the wound with soap and water and pat dry.
   c. **Splash to Eye(s), Nose or Mouth**, immediately flush the area with running water for at least 5-10 minutes.
   d. **Splash Affecting Garments**, remove garments that may have become soiled or contaminated and place them in a double red plastic bag.

3. Treatment:
   a. In the event of an acute injury resulting from a laboratory incident which requires immediate medical care, the injured employee/student should report to the emergency department for acute medical treatment. The injured individual must take a copy of this entire protocol document to the Emergency Department, including information regarding the specific strain associated with exposure.
b. In the event of exposure, with or without an injury, call the Exposure Hotline in order to get access to medical care for the exposure. The hotline responder will provide guidance to the injured individual on necessary medical treatment and post exposure follow-up.

4. **Follow up is needed in the event of any Laboratory Exposure:**
   a. **After first aid has been administered, immediately inform your supervisor of the exposure.**
   b. In the event of a large spill, contact the emergency response team (9-911) for clean-up.
   c. Contact Occupational Health Services, after first aid is complete, for a follow-up care.
ROLES & RESPONSIBILITIES
AFTER ACCIDENTAL EXPOSURE TO LCMV

1. WORKER’S RESPONSIBILITIES (Employee/Student Initial Self-Care)
   a. First Aid: Perform the recommended first aid and decontamination according to the posted instructions.
   b. Treatment: i) In the event of an acute injury resulting from a laboratory incident which requires immediate medical care, the injured individual should report to the Emergency Department for acute medical treatment. ii) In the event of an exposure, with or without an injury call Exposure Hotline pager in order to get access to medical care for the exposure.
   c. Access to the Exposure Hotline: Call the Exposure Hotline in order to get access to medical care for the exposure. Dial 415/353-7842 and provide your name and contact information to the operator. If there is no call back in 15 minutes, call again. If there is no call back the second time, proceed to the nearest Emergency Department with a copy of this protocol.
   d. Reporting: Inform your laboratory supervisor / principal investigator of the exposure.
   e. Secure the laboratory: Identify the equipment involved in the exposure and the mechanism of exposure. Make sure that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   f. Follow up: Contact Occupational Health Services (OHS) at 415/885-7580 for any needed follow up care.

2. SUPERVISOR’S/PI’S RESPONSIBILITIES
   a. First Aid and Decontamination: Verify that the worker has washed and decontaminated himself/herself. Ensure that appropriate medical treatment has been received.
   b. Secure the laboratory: Confirm that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   c. Laboratory clean-up (as needed): Contact the Office of Environment Health & Safety (EH&S) through the UC Police Department Emergency Dispatch (from a campus telephone 9-911, from a non-campus phone 415/476-1414).
   d. Report the exposure: Call the Biosafety officer during regular hours to discuss the exposure. Prepare a written report for the Biosafety Officer and the Biosafety Committee.
   e. Follow Up: Confirm that the worker has called for an appointment at the UCSF Occupational Health Clinic.
SECTION I – Infectious Agent
Organism or Agent: Lymphocytic choriomeningitis Virus (LCMV)
Synonym or Cross Reference: LCM, lymphocytic meningitis
Characteristics: Arenaviridae; ssRNA, enveloped, 50-150 nm diameter

SECTION II – Recommended Precautions
Containment Requirements: Biosafety level 2 practices safety equipment and facilities for laboratory-adapted LCM strains; biosafety level 3 practices, safety equipment, and facilities for activities involving the manipulation of the neurotropic strains of virus and animal studies involving the same. Work with hamsters infected with any type of strain should be conducted at animal biosafety level 3.
Other Precautions: Special precautions when working with infected hamsters may be indicated (HEPA filtered respirator); virus may pose a special risk during pregnancy because of potential infection of the fetus.

UCCSF Required Personal Protective Equipment: gloves, safety goggles, lab coat,

SECTION III – Handling Information
Spills: Allow aerosols to settle; wearing protective clothing, gently cover spill with paper towel and apply 10% sodium hypochlorite, starting at perimeter and working towards the centre; allow sufficient contact time before clean up (30 min)
Biohazardous Waste: Collect solid waste in double red bags and transport in a rigid container. Decontaminate liquid waste with 10% bleach for a minimum of 30 minutes before disposing down the drain.
Disposal: Decontaminate before disposal; steam sterilization, chemical disinfection, incineration
Storage: Store in sealed containers that are appropriately labeled.

SECTION IV – Health Hazards
Pathogenicity: Biphasic febrile illness, diversity of clinical manifestations - mild influenza-like illness or occasionally, meningeal or meningoencephalomyelitic symptoms, transverse myelitis, a Guillain-Barre-type syndrome; orchitis or parotitis; usually short duration; no chronic infection, infection asymptomatic in one third of individuals; rarely fatal, mortality <1% recovery from severe disease without sequelae in most cases; temporary or permanent neurological damage is possible; pregnancy-related infection has been associated with abortion, congenital hydrocephalus, chorioretinitis and mental retardation. On an emergent basis, the PI should be the best source of information regarding potential health hazards.
Modes of Transmission: Infected mice excrete virus in saliva, urine, milk and feces for up to six months; man is infected through inhalation of infectious aerosolized particles of rodent urine, feces or saliva, food contaminated with virus, contamination of mucus membranes, skin lesions or cuts with infected body fluids.
Incubation Period: 8-13 days; 15-21 days (meningeal symptoms)
Communicability: No evidence of person to person spread; vertical transmission from mother to child is possible.
FOR THE USE OF THE EXPOSURE HOTLINE

SECTION V – Viability

Drug Susceptibility: Evidence of ribavirin susceptibility from in vitro studies
Susceptibility to Disinfectants: Susceptible to 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol, formaldehyde

Physical Inactivation: Sensitive to heat inactivation
Survival Outside Host: Virus survives out of host - mice droppings

SECTION VI – Medical

Surveillance: Self-monitor for flu-like symptoms for three weeks; acute and convalescent sera will be tested through the Exposure Hotline NP; and for immune compromised individuals or pregnant women, there should be a discussion by the hotline responder with an infectious disease specialist.

Any exposed UCSF employee or student should be evaluated at the UCSF-OHS. In general, LCMV titers should be obtained within 1-2 days of exposure, and convalescent follow-up serum titers should obtained. A baseline titer following exposure is critical since 5-10% of the US population has preexisting antibodies. The complement fixation test for LCMV is considered insensitive, and IFA is preferred. ³ An Infectious Disease Consultation should be considered within 24-48 hours for any pregnant or immune compromised worker.

Although there is no specific treatment for LCMV, ribiviran susceptibility has been demonstrated in vitro, and has been used in severe infections. There is anecdotal evidence that of known laboratory strains, the risk of human infection from the Armstrong strain is very low. However, medical evaluation following any exposure should be obtained due the potential for severe sequelae, especially in immune compromised or pregnant individuals.

Any exposed worker who subsequently develops a influenza like illness within 3 weeks of exposure should be referred to an infectious disease specialist. A repeat titer should be obtained 3-4 weeks following exposure.

First Aid/Treatment: No specific treatment; anti-inflammatory drugs may be useful
Immunization: None available
Prophylaxis: None available


SECTION VII – Laboratory Hazards

Laboratory-Acquired Infections: Well documented hazard (46 cases with 5 deaths), especially from infected laboratory rodents (hamsters and mice); cases also reported arising from contaminated cell lines

Sources/Specimen: Blood, CSF, urine, secretions of the nasopharynx, feces; infected tissues from animals or human sources; presence of virus may be ascertained by inoculation of sample into uninfected mice, presence of specific antibodies by ELISA or IFA is considered diagnostic

Primary Hazards: Parenteral inoculation, inhalation, contamination of mucous membranes or broken skin with infected animal tissues or fluids, and exposure to infectious aerosols

Special Hazards: Contaminated tissue cultures represent a potential hazard. Contaminated cell lines passedag in nude mice have resulted in at least 8 laboratory-acquired LCMV infections to personnel working with the mice. Tumors may acquire LCMV as an adventitious virus without obvious effects on the tumor. The virus may survive freezing and storage in liquid nitrogen for long periods. When infected tumor cells are transplanted, subsequent infection of the host and virus excretion may ensue.
SECTION VIII – Emergency Medical Treatment

Treatment Indications: Emergency department treatment will be required for immediate treatment. The treatment needs to consist of the following: 1) decontamination and debridement, 2) wound repair, and 3) follow up with OHS.

Exposure Indications: In the event of an exposure, with or without an injury, the Exposure Hotline must be called.

Decontamination: Ensure that the wound has been adequately decontaminated.

(Format/Content adapted directly from Canadian SDS and the 5th Edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL) with additional information from subsequent portions of the protocol)

SECTION IX – References

Public Health Agency of Canada


Infectious Diseases of Mice and Rats, National Research Council, 1991 pp. 199-205
(http://www.nap.edu/openbook.php?isbn=0309063329)
I. **Risks in Laboratory Workers/Clinical Summary**

- The Arenaviridae family has one genus: arenavirus. There are 18 species of arenavirus and LCMV is considered a prototype virus: an enveloped virus containing two single-stranded RNA segments designated small and large. LCMV is primarily a murine virus, but may infect other rodents and susceptible primates, including man.
- There are numerous reports of human LCMV infection occurring through environmental exposure to mice or laboratory exposure to infected laboratory animals. Up to 5% of the United States human population has serologic evidence of exposure. Laboratory animals susceptible to infection include mice, hamsters, guinea pigs, nonhuman primates, swine and dogs.
- Airborne transmission is well documented.
- Outbreaks in humans have occurred following infection of rodents in animal care facilities.
- Fatal outbreaks in humans have occurred in immunosuppressed recipients of organ transplants from infected donors.
- Many strains of LCMV exist. Some strains are much more hazardous to humans. Established strains include the Armstrong strain and the Traub and WE strains.
- LCMV is an often undiagnosed cause of sporadic or epidemic, acquired or congenital infection in humans.
- The WE strain was isolated from a human after exposure to persistently infected mice. It is considered among the more pathogenic of established strains in case of human exposure.
- Most established strains of LCMV, and neuropathic strains, are considered Biosafety Level 2 (BSL-2) pathogens. New human or field isolates of LCMV are considered Biosafety Level 3 (BSL-3) pathogens.
- Laboratory workers must remember that LCMV can infect rodents. The principal investigator is responsible for identifying strategies to avoid the cross contamination to other experimental colonies.

All UCSF employees who work with LCMV should be aware of the EH&S policy on workers with immune compromise. Please refer to Campus Research Exposure Protocols, Immune Compromised Worker: http://www.occupationalhealthprogram.ucsf.edu/ohpEE.asp#EP

II. CDC/NIH RECOMMENDATIONS FOR LABORATORY EXPOSURE TO LCMV

Lymphocytic choriomeningitis (LCM) is a rodent-borne viral infectious disease that presents as aseptic meningitis, encephalitis, or meningoencephalitis. The causative agent is the LCM virus (LCMV) that was initially isolated in 1933. The virus is the prototypical member of the family Arenaviridae.

LABORATORY INFECTIONS

Laboratory associated infections (LAI) with LCM virus are well documented. Most infections occur when chronic viral infection exists in laboratory rodents, especially mice, hamsters and guinea pigs. Nude and severe combined immune deficient (SCID) mice may pose a special risk of harboring silent chronic infections. Inadvertently infected cell cultures also represent a potential source of infection and dissemination of the agent.

NATURAL MODES OF INFECTION

LCM and milder LCMV infections have been reported in Europe, the Americas, Australia, and Japan, and may occur wherever infected rodent hosts of the virus are found. Several serologic studies conducted in urban areas have shown that the prevalence of LCMV infection among humans ranges from 2% to 10%. Seroprevalence of 37.5% has been reported in humans in the Slovak Republic. The common house mouse, Mus musculus, naturally spreads LCMV. Once infected, these mice can become chronically infected as demonstrated by the presence of virus in blood and/or by persistently shedding virus in urine. Infections have also occurred in NHP in zoos, including macaques and marmosets. The etiologic agent of Callitrichid hepatitis virus is LCMV. Humans become infected by inhaling infectious aerosolized particles of rodent urine, feces, or saliva, by ingesting food contaminated with virus; by contamination of mucous membranes with infected body fluids; or by directly exposing cuts or other open wounds to virus-infected blood. Four recipients of organs from a donor who had unrecognized disseminated LCMV infection sustained severe disease and three succumbed. The source of donor infection was traced to a pet hamster that was not overtly ill.

LABORATORY SAFETY

The agent may be present in blood, CSF, urine, secretions of the nasopharynx, feces and tissues of infected animal hosts and humans. Parenteral inoculation, inhalation, contamination of mucous membranes or broken skin with infectious tissues or fluids from infected animals are common hazards. Aerosol transmission is well documented. Pregnant women infected with LCMV have transmitted the virus to their fetus with death or serious central nervous system malformation as a consequence.

CONTAINMENT RECOMMENDATIONS

BSL-2 practices, containment equipment, and facilities are suitable for activities utilizing known or potentially infectious body fluids, and for cell culture passage of laboratory adapted strains. BSL-3 is required for activities with high potential for aerosol production, work with production quantities or high concentrations of infectious materials, and for manipulation of infected transplantable tumors, field isolates and clinical materials from human cases. Strains of LCMV that are shown to be lethal in nonhuman primates should be handled at BSL-3. ABSL-2 practices, containment equipment, and facilities are suitable for studies in adult mice with strains requiring BSL-2 containment. Work with infected hamsters also should be done at ABSL-3.

SPECIAL ISSUES

Vaccines: Vaccines are not available for use in humans.
Transfer of Agent: Importation of this agent may require CDC and/or USDA importation.
permits. Domestic transport of this agent may require a permit from USDA/APHIS/VS. A DoC permit may be required for the export of this agent to another country.

Adapted directly from CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories, 5th* edition, February 2007. For references, please refer to the document which is available online at:


III. REFERENCES:

Please see individual sections above in addition to:

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5514a4.htm
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5430a3.htm
http://www.cdc.gov/vhf/lcm/