

Viral Hemorrhagic Fevers—Machupo and Lassa Fever

(Machupo): Bolivian Hemorrhagic Fever,
South American Hemorrhagic Fever

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Etiology

Lassa virus and Machupo virus are members of the Arenaviridae. Lassa virus belongs to the Old World complex; Machupo virus is a member of the New World complex. Related Old World arenaviruses such as the lymphocytic choriomeningitis virus, Mopeia virus, Mobala virus and Ippy virus, and New World arenaviruses such as Junin virus, Guanarito virus and Sabia virus can also cause hemorrhagic fevers.

Geographic Distribution

Machupo occurs in Bolivia. Related viruses are seen in other South American countries. Lassa fever has been seen in Nigeria, Liberia, Guinea and Sierra Leone and may occur throughout West Africa.

Transmission

Arenaviruses are spread in rodent droppings or urine and are transmitted to humans through broken skin, by ingestion and in aerosols. Lassa virus is shed in the urine and droppings of the reservoir host, the multimammate mouse. In areas where these rodents are eaten, humans may also become infected during food preparation. The Lassa fever virus can be spread from person to person, in bodily fluids such as blood, urine, feces, saliva, vomitus, other secretions, excretions or tissues. Although some sources state that this virus is not spread by casual contact, others suggest that aerosol transmission may occur in a nosocomial setting.

Machupo virus is also excreted by a rodent host, the vesper mouse, and spread in contaminated droppings. Several sources suggest that person-to-person transmission of Machupo virus is uncommon or nonexistent; however, Centers for Disease Control (CDC) information sheets list both Lassa virus and Machupo as arenaviruses that can be transmitted from person to person, as well as nosocomially.

Disinfection

Hypochlorite or phenolic disinfectants are generally recommended for disinfection. Machupo and Lassa viruses are susceptible to 1% sodium hypochlorite, 2% glutaraldehyde and ultraviolet light.

Infections in Humans

Incubation Period

In humans, the incubation period is 7 to 16 days for Machupo and 5 to 21 days (one to three weeks is typical) for Lassa fever.

Clinical Signs

Machupo

The symptoms of Machupo may include fever, malaise, headache, muscle pains and hemorrhages on the margins of the gums. Approximately a third of patients develop delirium, convulsions or serious hemorrhages. Hemorrhages may include petechiae or bleeding from the nose, gums, stomach or intestine.

Lassa Fever

Lassa fever begins with a sore throat, fever, chills, headache, myalgia and malaise, which may be followed by anorexia, vomiting and chest pains. Severe lower abdominal pain and intractable vomiting are common and the face and neck may swell. Hemorrhages develop in approximately 15-20% of patients; they typically occur only on the mucous membranes and are usually fairly mild. Other symptoms may include a maculopapular rash, cough, diarrhea, conjunctivitis, tremors, dizziness or signs of hepatitis. The varied and nonspecific clinical signs can make diagnosis difficult. Complications in a minority of survivors may include alopecia, iridocyclitis, transient blindness and temporary or permanent deafness. Many infections may be mild or asymptomatic.

Viral Hemorrhagic Fevers—Machupo and Lassa Fever

Communicability

Person-to-person transmission of Lassa virus occurs in bodily fluids including blood. Although some sources state that this virus is not spread by casual contact, others suggest that aerosol transmission may occur in a nosocomial setting. Several sources suggest that person-to-person transmission of Machupo virus is uncommon or nonexistent; however, Centers for Disease Control (CDC) information sheets list both Lassa virus and Machupo as arenaviruses that can be transmitted from person to person, as well as nosocomially.

Diagnostic Tests

Machupo

Machupo can be diagnosed by virus isolation; intracerebral inoculation of newborn hamsters is usually used. An antigen-capture ELISAs is available. Immunofluorescence can distinguish old World arenaviruses (Lassa and lymphocytic choriomeningitis viruses) from New World viruses (Junin, Machupo, and Guanarito viruses). Arenaviruses can be identified by surface glycoproteins and neutralization tests. Serology may also be helpful.

Lassa fever

Lassa fever is usually diagnosed by ELISAs that detect virus antigens or virus-specific antibodies (either IgM or IgG). Virus isolation is also used; Lassa virus can be found in numerous tissues including blood, urine and throat washings. Immunohistochemistry may be helpful at necropsy. Reverse transcription-polymerase chain reaction (RT-PCR) assays are available but are mainly used in research.

Treatment and Vaccination

The antiviral drug ribavirin has been used in cases of Lassa fever; treatment is most effective when it is started early in the course of the disease. Some of the New World complex viruses (Junin and Guanarito) also appear to be sensitive to this drug in vitro. Supportive care may be necessary for both Lassa fever and Machupo.

Specific vaccines are not currently available for either Lassa fever or Machupo, but an investigational vaccine against Junin virus may be effective against Machupo. A Lassa fever vaccine is in development.

Morbidity and Mortality

In endemic areas, Lassa fever is mild or asymptomatic in approximately 80% of those infected and the overall mortality rate is 1%. In natural infections, approximately 20% of infected individuals develop severe disease and 15-20% of hospitalized patients die. Infections in pregnant women are generally more serious: mortality rates range from 30 to 50%, and 95% of the pregnancies end in abortion. Occasional epidemics of Lassa fever occur; dur-

ing such outbreaks, the case-fatality rate may be as high as 50%.

Estimates of the mortality rate for Machupo range from 5 to 30%.

Infections in Animals

Species Affected

Machupo virus can infect rodents and non-human primates. Rhesus monkeys, Geoffrey's tamarin, African green monkeys, marmosets, guinea pigs and infant mice develop clinical signs after experimental infection. Infections in the reservoir host, the vesper mouse (*Calomys callosus*), are asymptomatic.

Lassa virus can infect rodents and non-human primates including baboons, rhesus monkeys and squirrel monkeys. Infections in the reservoir host, the multimammate mouse (*Mastomys natalensis*), are asymptomatic.

Incubation Period

The incubation period for Machupo is 6 to 10 days in experimentally infected rhesus monkeys and 3 to 6 days in experimentally infected African green monkeys. The incubation period for Lassa fever is 8 to 18 days in experimentally infected squirrel monkeys.

Clinical Signs

Machupo

The symptoms of Machupo in African green monkeys, rhesus monkeys and marmosets may include anorexia, fever, conjunctivitis, depression, diarrhea, dehydration, hemorrhages and an erythematous skin rash. Surviving animals may develop neurologic signs including tremors, nystagmus, incoordination, convulsions, muscle atrophy, paresis and coma. Infection in the rodent host is asymptomatic.

Lassa fever

In experimentally infected rhesus monkeys, Lassa fever symptoms may include lethargy, anorexia, constipation, fever, conjunctivitis and a skin rash. Baboons often develop symptoms similar to the severe form of Lassa fever in humans; symptoms may include fever, lethargy and hemorrhages. Infection in the rodent host is asymptomatic.

Communicability

Yes. Rodent hosts excrete infectious viruses in urine and feces; primates become infected after contact with excreta. Some New World arenaviruses are spread between adult rodents, probably by bites. Some Old World arenaviruses seem to be transmitted vertically in the rodent hosts.

Viral Hemorrhagic Fevers—Machupo and Lassa Fever

Diagnostic Tests

Machupo

Machupo can be diagnosed by isolating the causative virus from blood and other tissues. This virus is usually isolated by intracerebral inoculation of newborn hamsters. Immunofluorescent staining of infected cells can distinguish old World arenaviruses (Lassa and lymphocytic choriomeningitis viruses) from New World viruses (Junin, Machupo and Guanarito viruses). Arenaviruses can be identified by surface glycoproteins and neutralization tests.

Serology may also be helpful. Serologic tests include indirect immunofluorescent antibody (IFAT), serum neutralization (SN) tests and enzyme-linked immunosorbent assays (ELISAs).

Lassa Fever

Lassa fever can be diagnosed by virus isolation in Vero cells or intracerebral inoculation of weanling mice. Reverse transcription-PCR and antigen-capture ELISAs can detect viral RNA and antigens, respectively. Lassa virus can be found in numerous tissues including blood. Virus has been isolated from nasopharyngeal washings in experimentally infected baboons. In experimentally infected squirrel monkeys, Lassa virus was found in nearly every organ, but particularly high concentrations were found in the lymph nodes, liver, kidneys, adrenal glands and blood.

Serology may also be helpful: in humans, infections can be diagnosed by demonstrating a fourfold rise in antibody titer with indirect immunofluorescence or by detecting virus-specific IgM antibodies.

Treatment and Vaccination

Ribavirin can be helpful in humans infected with Lassa virus. Some of the New World Complex viruses are also sensitive to this drug in vitro. Commercial Lassa or Machupo vaccines are not available for primates.

Morbidity and Mortality

The mortality rate for marmosets, African green monkeys, and rhesus monkeys experimentally infected with Machupo is 80%-100%. In two experiments, mortality in Lassa-virus infected rhesus monkeys was 53-60%. Mortality rates in natural infections are probably lower.

Post-Mortem Lesions

Machupo

In experimentally infected monkeys, gross lesions include necrotic enteritis, bronchopneumonia, hepatic necrosis and hemorrhages in the subcutaneous tissues, lungs, intestine, liver and lymph nodes. Encephalitis has also been seen.

Lassa fever

In experimentally infected monkeys, pulmonary congestion, pleural effusion, pericardial edema, hydropericardium and hemorrhages have been seen.

Internet Resources

Arenaviruses. in *eMedicine*

<http://www.emedicine.com/med/topic166.htm>

Centers for Disease Control and Prevention (CDC)
–Viral Hemorrhagic Fevers Index

<http://www.bt.cdc.gov/agent/vhf/index.asptm>

Material Safety Data Sheets–

Canadian Laboratory Center for Disease Control
<http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu>

Medical Microbiology

<http://www.gsbs.utmb.edu/microbook>

Pathology of Nonhuman Primates from Primate Info Net. Wisconsin Primate Research Center

<http://www.primate.wisc.edu/pin/pola6-99.html>

Primate Info Net. Wisconsin Primate Research Center
<http://www.primate.wisc.edu/pin/>

Proceedings of an international colloquium on Ebola virus infection and other hemorrhagic fevers held in Antwerp, Belgium, 6-8 December, 1977
<http://www.itg.be/ebola/>

The Merck Manual

<http://www.merck.com/pubs/mmanual/>

USAMRIID's *Medical Management of Biological Casualties Handbook*

<http://www.vnh.org/BIOCASU/toc.html>

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Viral Hemorrhagic Fevers—Machupo and Lassa Fever

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