Lassa Fever

IMMEDIATELY REPORTABLE DISEASE

Per N.J.A.C. 8:57, healthcare providers and administrators shall immediately report by telephone confirmed and suspected cases of viral hemorrhagic fever to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. The health officer (or designee) must immediately institute the control measures listed below in section 5, “Controlling Further Spread,” regardless of weekend, holiday, or evening schedules. A directory of local health departments in New Jersey is available at http://localhealth.nj.gov.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609-826-5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609-392-2020 during all other days and hours.
THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several different viruses (arenaviruses, bunyaviruses, filoviruses, flaviviruses, etc., Table 1). In general, the term “viral hemorrhagic fever” is used to describe a severe multisystem syndrome (multisystem in that multiple organ systems in the body are affected). VHFs have been recognized by the Centers for Disease Control and Prevention (CDC) as being among the top agents of concern for potential bioterrorist weapons.

Arenaviruses are generally associated with rodent-transmitted diseases in humans and can cause severe illnesses. Many arenaviruses have been isolated in rodents only, but some cause hemorrhagic disease (Chapare, Guanarito, Junin, Lassa, Lujo, Machupo, Sabia).

B. Clinical Description

The VHFs characteristically damage the overall vascular system and impair the body’s ability to regulate itself. These symptoms are often accompanied by hemorrhage (bleeding); however, the bleeding is itself rarely life-threatening. While some types of hemorrhagic fever viruses can cause relatively mild illnesses, many of these viruses cause severe, life-threatening disease.

About 80% of Lassa virus infections are mild or asymptomatic. Mild symptoms include slight fever, general malaise and weakness, and headache. Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and abdominal pain, and respiratory symptoms, including cough and sore throat, may be present. Fever is persistent or spikes intermittently. Inflammation and exudation of the pharynx and conjunctivae are common. In 20% of infected individuals, however, disease may progress to more serious symptoms including hemorrhaging (in gums, eyes, or nose, as examples), respiratory distress, repeated vomiting, facial swelling, pain in the chest, back, and abdomen, and shock. Neurological problems have also been described, including hearing loss, tremors, and encephalitis. Acute illness lasts one to four weeks. Early lymphopenia may be followed by late neutrophilia. Platelet counts are moderately depressed and platelet function is abnormal. The most common complication of Lassa fever is deafness. Various degrees of deafness occur in approximately one-third of infections. In many cases, hearing loss is permanent.

Approximately 15%-20% of patients hospitalized for Lassa fever die from the illness. However, only 1% of all Lassa virus infections result in death. The death rates for women in the third trimester of pregnancy are particularly high. A recent systematic review and meta-analysis of
Lassa fever in pregnancy estimated the relative risk of death in pregnant women compared with non-pregnant women was 2.86 (95% CI 1.77 to 4.63, I²=27.27%, p=0.239).¹

Ribavarin has been used to successfully treat Lassa fever and is most effective when administered early in the course of illness.

C. Reservoirs

The reservoir, or host, of Lassa virus is a rodent known as the “multimammate rat” (*Mastomys natalensis*). An infected rodent can excrete Lassa virus in its urine for an extended time period, possibly for the rest of its life. *Mastomys* rodents breed frequently, produce large numbers of offspring, and are numerous in the savannas and forests of west, central, and east Africa. In addition, they readily colonize human homes and areas where food is stored. All of these factors contribute to the relatively efficient spread of Lassa virus from infected rodents to humans.

D. Mode of Transmission

In countries where the multimammate rat is present, transmission of Lassa virus to humans occurs most commonly through ingestion or inhalation. The rodents shed the virus in urine and droppings and direct contact with these materials, through touching soiled objects, eating contaminated food, or exposure to open cuts or sores, can lead to infection. Person-to-person transmission may occur after exposure to virus in the blood, tissue, secretions, or excretions of a Lassa virus-infected individual. Casual contact (including skin-to-skin contact without any exchange of body fluids) does not spread Lassa virus. Person-to-person transmission is common in health care settings where proper personal protective equipment (PPE) is not available or not used and through contaminated medical equipment, such as reused needles.

E. Incubation Period

6 to 21 days

F. Period of Communicability or Infectious Period

The period of communicability is as long as virus is detected in blood and other bodily fluids. The virus may be excreted in urine for 3-9 weeks after onset of illness. Infection can also spread by sexual contact through semen for up to 3 months after infection. Various published reports

suggest that Lassa virus ribonucleic acid (RNA) may be detected after onset for three to nine weeks in urine, eight weeks in saliva, eight weeks in blood and over three months in semen.\textsuperscript{2,3,4}

G. Epidemiology

VHF\textsuperscript{s} occur naturally in different geographic regions throughout the world, depending on the host and agent. Most VHF\textsuperscript{s} occur on the continents of Asia, Africa, and South America. Humans can become infected in an area where the virus occurs naturally by coming into contact with the host or a vector; also, the host or vector may be exported from its native habitat and pose a risk of infection in an area where the virus normally does not occur. In addition, humans infected in one region and traveling to another region can spread the virus from person to person or to another vector, such as native mosquito populations. Since international travel has been on the rise, VHF\textsuperscript{s} have been identified in places where they have rarely or never been seen before.

Lassa fever was first discovered in 1969 in Nigeria and is endemic in parts of West Africa including Sierra Leone, Liberia, Guinea and Nigeria. Other neighboring countries are also at risk, as the multimammate rat is distributed throughout the region (https://www.cdc.gov/vhf/lassa/outbreaks/index.html). The number of Lassa virus infections per year in west Africa is estimated at 100,000 to 300,000, with approximately 5,000 deaths. Unfortunately, such estimates are crude, because surveillance for cases of the disease is not uniformly performed. In some areas of Sierra Leone and Liberia, it is known that 10%-16% of people admitted to hospitals every year have Lassa fever.

There have only been six cases of Lassa fever in the United States and all have been associated with travel to countries known to have the virus. There have been two imported cases of Lassa fever in New Jersey, in 2004 and 2015.


H. Bioterrorist Potential

VHF are considered to be potential Category A bioterrorism agents. If acquired and properly disseminated, these viruses could cause a serious public health challenge in terms of the ability to limit the numbers of casualties and control other repercussions from such an attack.

2 CASE DEFINITION

The New Jersey Department of Health (NJDOH) Infectious & Zoonotic Disease Program follows the most current VHF case definition as published on the CDC National Notifiable Disease Surveillance System (NNDSS) website.


Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and should not be used by healthcare providers to determine how to meet an individual patient’s health needs.

*The VHF case definition refers to viral hemorrhagic fever caused by either Ebola, Lassa, Lujo, or Marburg virus, a New World arenavirus (Guanarito, Machupo, Junin, Sabia viruses), or Crimean-Congo hemorrhagic fever.*

**CLINICAL CRITERIA:**

An illness with acute onset with ALL of the following clinical findings:

- A fever >104°F (40°C), AND
- One or more of the following clinical findings:
  - Severe headache
  - Muscle pain
  - Erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset
  - Vomiting
  - Diarrhea
  - Pharyngitis (arenavirus only)
  - Abdominal pain
  - Bleeding not related to injury
  - Retrosternal chest pain (arenavirus only)
  - Proteinuria (arenavirus only)
  - Thrombocytopenia
LABORATORY CRITERIA FOR DIAGNOSIS:

One or more of the following laboratory findings:

- Detection of viral hemorrhagic fever (VHF) viral antigens in blood by enzyme-linked Immunosorbent Assay (ELISA) antigen detection
- VHF viral isolation in cell culture for blood or tissues
- Detection of VHF-specific genetic sequence by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) from blood or tissues
- Detection of VHF viral antigens in tissues by immunohistochemistry

EPIDEMIOLOGICAL LINKAGE:

One or more of the following exposures within the 3 weeks before onset of symptoms:

- Contact with blood or other body fluids of a patient with VHF
- Residence in—or travel to—a VHF endemic area
- Work in a laboratory that handles VHF specimens
- Work in a laboratory that handles bats, rodents, or primates from endemic areas
- Exposure to semen from a confirmed acute or convalescent case of VHF within the 10 weeks of that person’s onset of symptoms

CASE CLASSIFICATION

Confirmed
Case meets the clinical and laboratory criteria.

Possible
Case meets the clinical and epidemiologic linkage criteria.

LABORATORY TESTING

Lassa fever is most often diagnosed by using enzyme-linked immunosorbent serologic assays (ELISA), which detect Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies as well as Lassa antigen. RT-PCR can be used in the early stage of disease. The virus itself may be cultured in 7 to 10 days. Immunohistochemistry, performed on formalin-fixed tissue specimens, can be used to make a post-mortem diagnosis. NJDOH will facilitate testing of patients with suspected Lassa fever at CDC.
4 PURPOSE OF SURVEILLANCE AND REPORTING

- To promptly identify imported cases and prevent further transmission within the United States
- To identify sources of transmission and geographical areas of risk outside of the United States
- To identify cases and clusters of human illness that may be associated with a bioterrorist event
- To provide clinicians, travelers, and residents with appropriate preventive health information

5 CASE INVESTIGATION

A. Clinical evaluation

As a matter of routine practice, healthcare facilities should obtain a travel history in triage before completing full patient evaluation so that infection control precautions and patient placement can begin promptly when appropriate. Facilities and providers can stay up-to-date on active travel notices by consulting CDC’s Travelers’ Health website (https://wwwnc.cdc.gov/travel/destinations/list). Locations with previous Lassa outbreaks is available at https://www.cdc.gov/vhf/lassa/outbreaks/index.html.

CDC recommends Emergency Room clinicians use CALM (Consider, Act, Laboratory, Monitor) in assessing a patient with signs, symptoms, and/or diagnostic findings concerning for a possible VHF, such as Lassa. This algorithm is not intended to be a comprehensive guideline and should be used in conjunction with a hospital’s established policies for managing suspect/confirmed VHFs.

- Consider Risk Factors for Viral Hemorrhagic Fever: Assess possible exposures and evaluate if patient has signs and symptoms consistent with Lassa
- Act:
  - Isolate the patient in a private room or separate enclosed area with private bathroom or covered bedside commode.
    - Limit healthcare personnel who enter the room. Only essential healthcare personnel with designated roles should evaluate the patient and provide care to minimize transmission risk.
  - Information relevant health authorities
    - The treating facility should immediately the local health department, hospital’s administration, infection control program, and other appropriate staff of the suspect case.
  - Treat the patient
    - Perform routine/appropriate therapeutic interventions (e.g. placement of peripheral IV, phlebotomy for diagnosis) as indicated by clinical status.
New Jersey Department of Health

- Dedicated medical equipment (preferable disposable, when possible) should be used for the provision of patient care.
- All non-dedicated, non-disposable medical equipment used for patient care should be cleaned and disinfected according to manufacturer’s instructions and hospital policies.
- Limit the use of needles and other sharps as much as possible

- **Laboratory Examination:**
  - Inform the laboratory of the suspect case. Samples from the patient should be managed in accordance with laboratory protocols for handling potential VHF samples.
  - Arrange for testing. The decision for testing will be made in consultation with the New Jersey Department of Health and local health department.

- **Monitor Contacts:**
  - Maintain a log of all people entering the patient’s room. The log should contain full name and contact information for all persons entering patient’s room. Facilities should develop policies for monitoring staff (e.g., healthcare personnel, environmental services, ancillary staff) who have contact with the patient.
  - Visitors should be limited. Exceptions may be considered on a case by case basis for those who are essential for the patient’s wellbeing.
  - Establish procedures for monitoring and managing visitors: Facilities should develop policies for monitoring health care providers (HCP) attending to the patients. Facilities should develop sick leave policies for HCP that are non-punitive, flexible and consistent with public health guidance. Ensure that all HCP, including staff who are not directly employed by the healthcare facility but provide essential daily services, are aware of the sick leave policies.

**B. Persons Under Investigation**

Persons Under Investigation (PUI) are persons with both consistent signs and symptoms and risk factors:

1. Elevated body temperature or subjective fever or symptoms, including severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage; **AND**

2. An epidemiologic risk factor within the 21 days before the onset of symptoms.

**Epidemiologic Risk:** The following epidemiologic risk factors should be considered when evaluating a person for Lassa fever, classifying contacts, or considering public health actions such as monitoring and movement restrictions based on exposure. Individuals at greatest risk of Lassa virus infection are those who live in or visit endemic regions, including Sierra Leone, Liberia, Guinea, and Nigeria and have exposure to the multimammate rat. Risk of exposure may also
exist in other west African countries where Mastomys rodents exist. Hospital staff are not at great risk for infection as long as protective measures and proper sterilization methods are used.

**Epidemiological Assessment Resources:**


- Diagnoses for Consideration in a Returning Traveler with Fever: [https://www.cdc.gov/vhf/abroad/diagnosis-considered-returning-traveler.html](https://www.cdc.gov/vhf/abroad/diagnosis-considered-returning-traveler.html)

**Key Communicable Disease Reporting and Surveillance System (CDRSS) Fields – Specific for Lassa Fever**

<table>
<thead>
<tr>
<th>CDRSS Screen</th>
<th>Required Information</th>
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<tbody>
<tr>
<td>Disease Information</td>
<td>• Document the date reported to State or Local Health Department</td>
</tr>
<tr>
<td></td>
<td>• Household size</td>
</tr>
<tr>
<td>Patient Personal Information</td>
<td>• Document the patient’s preferred language, country of birth, marital status, date first arrived in the United States</td>
</tr>
<tr>
<td></td>
<td>• Document the patient’s contact information</td>
</tr>
<tr>
<td>Clinical Status</td>
<td>• Document date of initial healthcare evaluation, initial diagnosis, hospitalization status, and mortality information</td>
</tr>
<tr>
<td>Contact Tracing</td>
<td>• Enter names of household and other contacts</td>
</tr>
<tr>
<td>Pregnancy Information</td>
<td>• Note if the patient is pregnant. Complete the entire pregnancy information section for pregnant patients.</td>
</tr>
<tr>
<td>Comments</td>
<td>• Document any additional information that cannot be captured in a specific field within CDRSS</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>• Document the patient’s risk factors</td>
</tr>
</tbody>
</table>
CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements

Isolation: Patients with suspected VHFs should be immediately isolated using standard, contact, and droplet precautions. In consultation with NJDOH, suspected or confirmed patients may be transported to a state or regional Ebola Assessment or Treatment hospital. Because blood and secretions can shed virus for up to several months, patient education should be provided prior to discharge.

Quarantine: PUIs who are asymptomatic should be monitored for 21 days after last exposure for the development of fever and/or other symptoms and evaluated medically if symptoms develop. Travel restrictions may be put in place for contacts of a Lassa case based upon their risk level.

B. Contact Tracing of Persons Exposed to Lassa

If a Lassa case is identified in New Jersey, the NJDOH/CDS will work with the LHD and relevant healthcare facilities to identify persons exposed to the case patient and to assess level of risk. NJDOH/CDS will provide a risk assessment questionnaire to identify and interview potential exposures in both community and healthcare settings.

Assessing Exposure Risk of Contacts of a Confirmed EVD Case: Lassa contacts will be categorized into three risk exposure categories: high risk, low (but not zero) risk, and no known exposure. Examples of exposures are defined below.

High risk exposures include any of the following:

- Percutaneous exposure to potentially infectious material: vomitus, excreta, blood or bloody fluids (e.g., needle-stick injuries, exposure through broken skin)
- Direct unprotected contact with potentially infectious material (e.g., touching vomitus with an ungloved hand)
- Mucosal exposure to splashes or droplets of potentially infectious material (e.g., to eyes, nose mouth), mouth-to-mouth kissing, or sexual contact with a symptomatic patient

Low (but not zero) risk exposures include any of the following:

- Sharing a room or vehicle within 3 feet of a potentially infectious patient, without direct contact with potentially infectious material
- Providing routine medical care while using personal protective equipment appropriately
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- Routine cleaning and laundry of contaminated linens and surfaces while using personal protective equipment appropriately

- Transport of a potentially infectious patient without direct contact with potentially infectious material

- Handling of clinical specimens while using personal protective equipment appropriately.

- Casual skin to skin contact without contact with blood or other body fluids

**No known exposure:** No contact with a Lassa case and/or no presence in an area with a Lassa case while infectious

**Monitoring Contacts of a Confirmed Lassa Case**

Community contacts will be entered into the NJDOH CDRSS with symptom reports entered daily by the LHD. Healthcare facility contacts will either be entered into CDRSS or maintained on a facility-specific spreadsheet. If a facility-specific spreadsheet is used, it will be sent to public health authorities daily via encrypted email or a password-protected file. NJDOH/CDS will work with LHDs to monitor community contacts and with healthcare facilities to monitor healthcare worker contacts. All contacts will be monitored for fever and Lassa-compatible symptoms for 21 days from their last exposure to a Lassa case, including on holidays and weekends.

<table>
<thead>
<tr>
<th>Contact Risk Level</th>
<th>Type of Monitoring</th>
<th>Public Health Reporting</th>
</tr>
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<tbody>
<tr>
<td>High Risk</td>
<td>Direct active monitoring: AM and PM temperature and symptom monitoring, with one reading directly observed by LHD or healthcare facility personnel</td>
<td>Once daily, at time of direct observation, or if/when symptoms develop</td>
</tr>
<tr>
<td>Low (but not zero) risk</td>
<td>Self-monitor for fever and other Lassa symptoms for 21 days</td>
<td>Only if/when symptoms develop</td>
</tr>
<tr>
<td>No Known Exposure</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

NJDOH/CDS will coordinate with the CDC’s Division of Global Migration and Quarantine (DGMQ) and LHDs to implement international and domestic travel restrictions, as needed and based on risk exposure categories.

**C. Infection Control**

Infection control measures for Lassa are the same as for a patient with suspected Ebola Virus Disease. CDC recommends a combination of measures to prevent transmission of Lassa in
hospitals including personal protective equipment (PPE). Healthcare personnel might need to take additional infection control steps if a PUI or patient with confirmed Lassa has other conditions or illnesses caused by specific infectious diseases, such as tuberculosis.

Healthcare personnel can be exposed to Lassa virus by touching a patient’s body fluids, contaminated medical supplies and equipment, or contaminated environmental surfaces. Splashes to unprotected mucous membranes (for example, the eyes, nose, or mouth) are particularly hazardous. Procedures that can increase environmental contamination with infectious material or create aerosols should be minimized.

Isolation

Clinicians should immediately isolate any patient with relevant exposure history and signs or symptoms compatible with Lassa or other VHF in a single patient room (containing a private bathroom) with the door closed. Healthcare personnel should follow standard, contact, and droplet precautions. In consultation with NJDOH/CDS, suspected or confirmed patients may be transported to a state or regional Ebola Assessment or Treatment hospital. Because blood and secretions can shed virus for up to several months, patient education should be provided prior to discharge.

Personal Protective Equipment

Healthcare personnel should follow latest CDC guidance for PPE depending on patient condition.

Environmental Cleaning and Disinfection

Lassa is transmitted through direct contact with infected blood or body fluids/substances (urine, feces, vomit) or through exposure to objects (such as needles) that have been contaminated with infected blood or body fluids. The role of the environment in transmission has not been established. However, higher levels of precaution are warranted to reduce the potential risk posed by contaminated surfaces in the patient care environment.

Hospitals

As part of the care of PUIs or patients with confirmed Lassa, hospitals are recommended to:

- Be sure environmental services staff wear recommended PPE to protect against direct skin and mucous membrane exposure of cleaning chemicals, contamination, and splashes or spatters during environmental cleaning and disinfection activities.
- Use a U.S. Environmental Protection Agency (EPA)-registered hospital disinfectant with a label claim for a non-enveloped virus (norovirus, rotavirus, adenovirus, poliovirus) to disinfect environmental surfaces in rooms of PUIs or patients with confirmed EVD.
- Avoid contamination of reusable porous surfaces that cannot be made single use.
• Routinely clean and disinfect the PPE doffing area.

• Discard all linens, nonfluid-impermeable pillows or mattresses, and textile privacy curtains into the waste stream and disposed of appropriately.

D. Managing Special Situations

Outbreak Response

Sporadic cases of VHF are not uncommon in certain countries. If one or more counties experience widespread transmission, additional recommendations may be implemented, including traveler and patient screening, diagnostic testing, and monitoring.

Bioterrorism

If a bioterrorism event is suspected, NJDOH and other response authorities will work closely with local officials to provide additional guidance and instructions.

Pregnancy

Few published studies on Lassa fever in pregnancy exist. Therefore, much remains to be documented regarding clinical management and treatment during pregnancy, adverse maternal and perinatal outcomes, pregnancy-specific mortality rates, and breastfeeding.

E. Preventive Measures

No vaccine for Lassa fever is currently available for use in humans. Research is presently under way to develop a vaccine.

Primary transmission of the Lassa virus from its host to humans can be prevented by avoiding contact with Mastomys rodents, especially in the geographic regions where outbreaks occur. Putting food away in rodent-proof containers and keeping the home clean help to discourage rodents from entering homes. Using these rodents as a food source is not recommended. Trapping in and around homes can help reduce rodent populations; however, the wide distribution of Mastomys in Africa makes complete control of this rodent reservoir impractical. Educating people in high-risk areas about ways to decrease rodent populations in their homes will aid in the control and prevention of Lassa fever.

When caring for patients with Lassa fever, further transmission of the disease through person-to-person contact or nosocomial routes can be avoided by taking preventive precautions against contact with a patient’s secretions (called VHF isolation precautions or barrier nursing methods). Such precautions include wearing protective clothing, such as masks, gloves, gowns, and goggles; using infection control measures, such as complete equipment sterilization; and isolating infected patients from contact with unprotected persons until the disease has run its course.

Other challenges include developing more rapid diagnostic tests.
Environmental Cleaning and Disinfection Resources


International Travel

If you travel to or are in an area affected by a VHF outbreak, make sure to do the following:

- Practice careful hygiene. Wash your hands with soap and water or an alcohol-based hand sanitizer and avoid contact with blood and body fluids (such as urine, feces, saliva, sweat, urine, vomit, breast milk, semen, and vaginal fluids).

- Do not handle items that may have come in contact with an infected person’s blood or body fluids (such as clothes, bedding, needles, and medical equipment).

- Avoid funeral or burial rituals that require handling the body of someone who has died from a VHF.

- Avoid contact with rats, bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals.

- Avoid healthcare facilities where VHF patients are being treated. The United States embassy or consulate is often able to provide advice on facilities.

- Avoid contact with semen from a man who has had Lassa until you know Lassa is gone from his semen.

- After you return, monitor your health for 21 days and seek medical care immediately if you develop symptoms of Lassa.

Additional Information


- CDC: [https://www.cdc.gov/vhf/lassa/index.html](https://www.cdc.gov/vhf/lassa/index.html)

References

