

Viral Hemorrhagic Fevers

Report Immediately

1. DISEASE REPORTING

A. Purpose of Surveillance and Reporting

1. To identify potential foci of infection of Viral Hemorrhagic Fever agents which may exist in the United States (such as non-human primates or laboratory specimens).
2. To identify sources of transmission and geographical areas of risk outside of the United States.
3. To determine the magnitude of risk to humans and animals.
4. To stop transmission from all such sources and geographical areas.
5. To identify cases as early as possible to prevent transmission to other persons or animals.
6. To identify cases and clusters of human illness that may be associated with a bioterrorist event.

B. Laboratory and Physician Reporting Requirements

1. Physicians are required to report known or suspected cases of VHF **immediately** to the local health department (LHD) as an "unusual disease or condition of public health significance."
2. If this is not possible, the physician should report to the Oregon Acute Communicable Disease Program (ACDP) at 503/731-4024 (after hours 503/731-3040).
3. Report any potential exposure to an agent which could cause VHF.

C. Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed, probable, or suspect cases or illness suggestive of VHF immediately to ACDP.
2. Consult with ACDP about strategies for enhanced surveillance and contact investigation and monitoring.
3. Educate and consult with local providers and facilities to ensure compliance with respiratory and contact isolation procedures in medical care of case patients.
4. Assure all contacts potentially exposed to the VHF case patient are identified, educated, and placed under adequate surveillance for the period when symptoms are most likely to arise.
5. Complete the reporting forms, surveillance and follow-up forms, and otherwise document investigation, outreach, active surveillance, and completeness of containment efforts.
6. Consult with ACDP prior to closing case and contact investigation activities for each suspected or confirmed VHF case (Oregon Administrative Rules 333-019-0000, Authority of Public Health Agencies to Investigate Reportable Diseases).

D. State ACDP Responsibilities

1. Provide consultation to LHD public health and private sector health professionals concerning:
 - a. isolation of cases and potential cases;
 - b. diagnostic evaluation, treatment, and clinical monitoring;
 - c. required reporting and surveillance activities;
 - d. contact identification and follow-up;
 - e. inter-jurisdictional tracking of cases and contacts who move out of county or state of Oregon jurisdiction;
 - f. development and maintenance adequate information systems to provide needed case and contact surveillance, and assuring adequacy of response activities;
 - g. providing surge capacity if a VHF outbreak and contact investigation overwhelm resources of the LHD.

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2. Facilitate expert consultation with infectious disease specialists and CDC as needed.
3. Coordinate specimen collection with the LHD and Oregon State Public Health Laboratory (OSPHL), to assure confirmation of suspected VHF cases, and early identification of disease in symptomatic contacts and others.
4. Evaluate bioterrorist potential:
 - a. 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;
 - b. If acquired and properly disseminated, these viruses could cause a serious public health challenge in terms of ability to limit the numbers of casualties and establish control of transmission during an attack.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Viral hemorrhagic fever agents (VHFs) include numerous zoonotic diseases, all of which cause a hemorrhagic syndrome in humans. Because of its extremely high fatality rate and the importation of the virus into the United States in non-human primates, Ebola hemorrhagic fever has been most publicized in the United States. VHFs are known to be caused by viruses from four families:

- Filoviruses: Ebola and Marburg;
- Arenaviruses: Lassa, Junín (Argentine VHF), Machupo (Bolivian VHF), Sabiá (Brazilian VHF) Guanarito (Venezuelan VHF);
- Bunyaviruses: Crimean-Congo HF, Rift Valley fever, Hantavirus;
- Flaviviruses: Dengue, Yellow Fever, Omsk HF, Kyasanur HF.

B. Description of Illness

The onset of viral hemorrhagic fever is usually sudden. The duration of illness can vary from a few days to a couple of weeks. Patients present with a brief prodrome characterized by nonspecific signs, including fever, headache, fatigue, weakness, irritability, dizziness, muscle aches, nausea and vomiting. As disease progresses, symptoms may include rash, diarrhea, swelling around the eyes, flushing, and redness of the eyes, low blood pressure, sustained fever, and sweats. As signs become more serious, the patient becomes prostrate and may develop a sore throat, and pain in the chest or abdomen, as well as petechiae and ecchymoses (bruises). Bleeding occurs from mucous membranes (including nosebleeds, bleeding gums, bloody vomit, bloody urine, blood in stools and sputum), and the patient will often go into shock, with multi-organ dysfunction. Encephalopathy, hepatitis, tremors, and reduced white blood cell and platelet levels are frequently seen. Renal failure may occur.

Differential diagnoses include a variety of viral and bacterial diseases: influenza, hepatitis, staphylococcal or other bacterial sepsis, toxic shock syndrome, rubella, measles, and hemorrhagic smallpox, among others. Non-infectious diseases which present with bleeding also must be excluded (e.g., hemolytic uremic syndrome, leukemia). Mortality rates for VHFs vary depending on the agent and strain, and can be from 10% to 90%. In Lassa VHF, nerve deafness occurs in 25% of patients, with only half recovering hearing after 1–3 months.

C. Reservoirs

Many wild and domestic animals, ticks, and mosquitoes are known to carry some of the VHF agents, although the reservoirs have not been identified for all VHF agents. Rodents are known to be the carriers of Lassa, Junín, Machupo, Guanarito, Sabiá, Crimean-Congo hemorrhagic and Rift Valley fever viruses. Mosquitoes, ticks and animals (including foxes, hares, and groundfeeding birds) are known to carry bunyaviruses that cause VHF (Rift Valley, Crimean-Congo viruses).

Primates are the only non-human animals known to have been affected by Ebola and Marburg hemorrhagic fever viruses. However, because these infections are associated with a rapid and often fatal illness in these animals, they are not considered reservoirs.

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Once certain VHF viral infections establish themselves in human populations, rapid person-to-person spread may occur.

D. Sources and Routes of Transmission

The mode of transmission for index cases of VHF in any outbreak is animal-, tick- or mosquito-to-human. Once humans are infected with a VHF agent, person-to-person transmission may occur. Infection is acquired through contact with infectious blood or secretions from infected persons or animals. Individuals have acquired VHFs through sexual contact. Bedding or other fomites may serve as a source of infection. Medical equipment that has not been properly cleaned or sterilized has been responsible for the spread of some VHFs. In rare cases laboratory workers have been infected through handling of specimens. For most VHFs, direct physical contact with infectious blood or secretions is thought to be required for transmission. Airborne transmission from person to person appears to be rare, but cannot be ruled out.

E. Incubation Period

The incubation periods for VHFs range from 2 to 21 days, with an average of 3 to 10 days.

F. Period of Communicability or Infectious Period

Infected individuals are generally considered infectious for a variable period preceding the onset of symptoms and throughout the course of clinical symptoms. Consider isolation. All persons, including health care personnel and laboratory personnel who have close contact with a case (or with high-risk close contacts of a case) within 21 days of the patient's onset of symptoms, are to be placed under medical surveillance or isolation. Virus may remain in the blood and secretions for months after an individual recovers. Patients convalescing from filoviral and arenaviral infections are advised to refrain from sexual activity for three months after clinical recovery. Contaminated bedding, clothing and medical equipment may remain infectious for several days.

G. Epidemiology

Viruses of VHFs are primarily infectious agents in wild animals, birds, mosquitoes and ticks. Individual VHFs occur in different geographic regions, specifically in Africa (Ebola, Marburg, Lassa) or the Americas (New World arenaviruses such as Junín, Machupo). Outbreaks, when they occur, tend to be sporadic. Outbreaks of Ebola virus hemorrhagic fever in imported non-human primates used for research have occurred in the U.S. In one instance, individuals working with infected primates developed antibody to Ebola, suggesting exposure, but the individuals did not become clinically ill. There is speculation that this particular strain of Ebola virus (called Ebola Reston) may be unable to cause clinical disease in humans.

H. Treatment

There is no effective treatment for most diseases caused by VHF agents other than supportive care. Maintain fluid and electrolyte balance, circulatory volume, and blood pressure. Mechanical ventilation, renal dialysis, and anti-seizure treatment may be required. Injections, aspirin, and all anticoagulants are contraindicated, and steroids are not indicated. While laboratory confirmation of the specific agent is pending, supportive ribavirin therapy should be initiated immediately. A 10-day course of ribavirin is helpful with arenavirus and bunyavirus infections, but this drug has not been shown to be useful against filovirus or flavivirus infections.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

A. Confirmed Case Definition

A confirmed case of VHF requires that the specific VHF virus be isolated from specimens or specific IgM antibody be present. Confirmation by lab results also includes:

- a. A four-fold or greater rise in serum IgG level between acute and convalescent serum samples;
- b. detection of specific VHF antigen in tissues;
- c. positive post-mortem histopathology.

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B. Presumptive Case Definition

Because VHF viruses are difficult to detect outside a Biosafety level 4 laboratory, presumptive or probable VHF case diagnosis relies on clinical signs and symptoms compatible with viral hemorrhagic fever agents.

C. Suspect Case Definition

A suspect VHF case definition is based on signs and symptoms found during an outbreak of viral hemorrhagic fever. In a non-outbreak situation, early signs are non-specific. Suspicion of VHF usually requires progression in severity and advanced clinical signs such as increasing pain in abdomen, chest, throat, with bruising and bleeding from mucosal membranes.

D. Services Available at the Public Health Laboratory

The Oregon State Public Health Laboratory (OSPHL) does not provide direct testing of clinical specimens for VHFs, which requires a Biosafety Level 4 lab (CDC or USAMRIID). Specimens for VHF agent testing should be sent to CDC through the OSPHL Virology Section at 503/229-5504. The OSPHL staff will provide guidance on what specimens to send and how to send them. Since the CDC is the principal testing laboratory for VHFs in the United States, any lab-confirmed cases found in an Oregon resident would be reported to CDC, which in turn would notify Oregon ACDP. Information on Oregon residents exposed or diagnosed in Oregon or elsewhere would be received by ACDP and communicated to the LHD in the community where the case resides.

4. ROUTINE CASE INVESTIGATION

The most important action for a LHD or health care clinician if a suspect or confirmed case of VHF is reported, or any potential exposure to an agent which could cause VHF, is to call the State ACDP epidemiologist *immediately*, any time of the day or night. Daytime phone numbers of the DHS Acute and Communicable Disease Program: 503/731-4024, after hours and weekends 503/731-4030.

Case investigation of VHF in Oregon residents will occur through close and joint collaboration between the State ACDP epidemiologists and the LHD staff. If a bioterrorist event is suspected, the ACDP, LHD, county and state Emergency Preparedness agencies will coordinate to provide instructions on how to proceed. Working closely with the State ACDP epidemiologists, the LHD Communicable Disease staff will be involved in the investigation any VHF case living within their communities.

Contacts at risk for VHF infection need to be identified, located, interviewed, and assessed for symptoms of illness. Local health department staff need to do a rapid screening of contacts for symptoms of illness, using checklist (see final page) and monitoring baseline temperature, for decision-making about medical referral.

A. Investigation activities

1. Use Tyvac suits and N-95 masks for respiratory protection.
2. Complete the case report form. Most of the information required on the form can be obtained from the healthcare provider or the medical record. For each VHF case or suspect, record "Viral Hemorrhagic Fever" as the disease being reported. For initial suspects and cases, and in early phase of symptoms, lab results may not be available. When possible, record the type of VHF (*e.g.*, Ebola, Marburg, Lassa, Junín, Machupo, Sabiá, Guanarito, Crimean-Congo hemorrhagic fevers or Rift Valley fever).
3. Record demographic and clinical information about the suspected or probable case patient. Interviews most likely will be done with close household members as the patient may be too ill to provide adequate information. Use the case report form to collect the following data for each case:
 - a. name, age, race/ethnicity, address, phone numbers;
 - b. parent/guardian information, if applicable;
 - c. clinical data, including signs and symptoms, date of onset, date of diagnosis, duration;
 - d. status (hospitalized, at home, deceased).

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4. List information about the healthcare providers attending the case patient:
 - a. the name and phone number of the hospital where the case is or was hospitalized;
 - b. the name and phone number of the attending physician;
 - c. the name and phone number of the infection control official at the hospital;
 - d. if the patient was seen by a healthcare provider before hospitalization, or seen at more than one hospital, obtain these names and phone numbers as well;
 - e. name of any person or agency involved in transporting the patient while symptomatic.
5. Determine exposure history (“likely period of infectiousness”). Use the incubation period range for VHF (2–21 days, varying by etiologic agent). See final page.
6. Identify, assess, and monitor all contacts who spent time with the infected case, particularly all those with physical contact with the ill patient. Institute surveillance of VHF contacts for a period of 14–21 days after the last date of exposure to the case patient (time period depends on lab confirmation of the specific agent).
 - a. For Ebola and Marburg filoviruses: contact persons who have had any direct physical contact with the patient’s infected blood, secretions, organs or semen. Airborne transmission has not been documented, but cannot be ruled out. Nosocomial infections have occurred from contaminated needles and syringes.
 - b. For New World arenaviruses: Lassa VHF has been transmitted to contacts through infected aerosols or direct physical contact with infected blood, excreta, or other body fluids, or through sexual activities. Contact persons to patients with Machupo virus have been infected through direct personal contact (touching).
 - c. Because airborne transmission of VHF agents cannot be ruled out from available evidence, identify all persons who spent time in the same close air space with the ill patient, in each of the patient’s social settings. Ask about household and other sleeping places, worksites, and places of leisure activities (church, clubs, sports teams, frequently-visited households of friends, etc.).
 - d. For travel history, identify contacts during any method of travel that occurred 2–21 days before the onset of symptoms. Determine the date(s) and geographic area(s) traveled to. List all persons who had close contact with the case patient during travel during the infectious period (carpool, bus, airplane, bicycle).
7. Educate contact individuals who have had possible exposure about VHF transmission and the need for self-monitoring for symptoms suggestive of VHF infection (ability to monitor temperature twice daily for 21 days). Make plans for medical care should symptoms develop.
 - a. Asymptomatic contacts should monitor temperatures twice daily during the surveillance period. The LHD should have telephone or home visit monitoring of this temperature surveillance.
 - b. If a contact develops a body temperature over 101°F, place the contact in the hospital with strict isolation precautions.
 - c. Interview symptomatic contacts for their close contacts.
 - d. Interview, assess and monitor secondary contacts to VHF cases.
 - e. Asymptomatic contacts may continue their routine daily activities, but are advised not to travel outside of the home community during the surveillance period.
 - f. Visitors should be discouraged in households where close contacts are under surveillance for clinical symptoms after exposure to a VHF patient.

5. CONTROLLING FURTHER SPREAD

A. Personal Preventive Measures

All persons at risk of VHF infection because of occupational or household contact with VHF patients need instruction on frequent and thorough hand hygiene, the use of gloves and other personal protective barrier equipment including respiratory protection to prevent exposure to blood

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and body fluids, and safe methods of waste disposal. In addition, healthcare workers in hospital settings need education and monitoring for adherence to respiratory precautions when providing care to VHF patients.

To avoid cases of naturally-occurring exposure to VHF agents:

- Avoid traveling to areas with known outbreaks of VHF;
- Notify any laboratory workers who may be required to handle specimens suspected of containing the agents of VHFs, to practice enhanced precautions to avoid exposures;
- Persons working with imported non-human primates (NHPs) should know the signs of VHF in NHPs; and immediately report any cases of suspect or confirmed VHF in NHPs to the DHS Acute and Communicable Disease program.

For more information regarding international travel and VHFs, contact the CDC's Travelers Health Office at 1-877/394-8747 or through the internet at http://www.cdc.gov/travel/diseases/viral_hemorrhagic.htm

B. Isolation of VHF cases

VHF cases and suspects must be isolated and all persons caring for them must observe strict contact and airborne precautions.

1. Healthcare professionals are at risk from accidental percutaneous and mucous membrane exposures to blood and body fluids. Universal precautions must be strictly observed. Pay special attention to the use of barrier/contact precautions in care of the patient by direct contact, and control of all items soiled by or touching the VHF patient.
2. Airborne precautions such as negative pressure isolation rooms, and use of respirators by staff and visitors are recommended.
3. Period of Isolation of Patient
 - a. Patients should be isolated until they are clinically well, and then monitored for at least three weeks.
 - b. Because blood and secretions may contain virus for anywhere from weeks to months after VHF illness, recovering patients must be educated and monitored for infectiousness (specific lab monitoring of specimens to determined by expert clinician consultation).
 - c. Recovering VHF patients should refrain from sexual activity for three months after clinical recovery.

C. Follow-up of Cases

Patients recovering from Viral Hemorrhagic Fever disease should be monitored clinically during convalescence. Patients with Lassa VHF virus infections are at risk of deafness and hearing acuity and should be monitored during recovery.

D. Protection of Contacts of a Case

There is no immunization or prophylaxis for contacts of cases. Healthcare workers and other contacts of known or suspected cases of VHF should practice standard (including respiratory) precautions together with physical contact precautions to reduce their chances of acquiring VHF. Individuals who have had any contact with infectious patients should be monitored by their healthcare provider for the maximum incubation period for the specific agent.

E. Vaccines and Antiviral Prophylaxis

There are no effective vaccines available against the Viral Hemorrhagic Fever agents, except for the Yellow Fever vaccine. Yellow Fever vaccine is not useful for preventing disease from other VHF agents. A live attenuated vaccine against Machupo virus (Argentine HF) has been developed by USAMRIID that is safe and effective, and may provide some cross-protection with Sabiá virus (Bolivian HF), but the vaccine is in limited supply, and used under Investigational Drug protocols.

Ribavirin is the only available antiviral medication which has been found effective in treatment of the arenaviruses. It is not effective against the filoviruses (Ebola, Marburg).

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There is some evidence that the use of ribavirin for post-exposure prophylaxis will delay onset of VHF disease, but not prevent it. High-risk contacts exposed to VHF patients should be closely monitored for signs of illness, including developing a fever of 101°F or greater. Ribavirin should be administered promptly, unless the causative agent is known to be a filovirus.

CDC guidelines recommend ribavirin for high-risk contacts of Lassa fever patients.

F. Environmental Measures

Depending on the VHF agent identified, vector control for specific reservoir animals should be enhanced during a VHF outbreak. Consult with the State ACDP public health veterinarian for specific recommendations. Households where VHF patients have been identified, or recovering patients are living, must receive targeted teaching about personal hygiene, waste disposal, and limiting exposure to possibly infected materials or animals.

G. Infection Control

With the lack of effective therapy or preventive vaccines against VHF agents, efforts to prevent transmission rely on careful and vigilant infection control measures.

1. Isolation

Suspected VHF cases must be immediately reported to the infection control professional within a health care facility, and isolated promptly.

- a. Isolate the patient in a negative-pressure room alone, or, if not possible, use group rooms housing VHF patients in the same wing or area of the facility.
- b. Allow only a limited number of staff into patient room, and with full protective equipment.
- c. Keep the door to the room closed at all times.
- d. No visitors, except for a limited number of family members, with full protective equipment.

2. Personal Protective Barrier Precautions

- a. Strict hand hygiene plus double gloves;
- b. impermeable gowns, shoe and leg coverings;
- c. eye protection (goggles), and face shields.

3. Respiratory precautions

- a. Use high-efficiency particulate protection, such as an N-95 respirator.
- b. Powered air-purifying respirators (PAPRs) may in theory be more efficacious than N-95 disposable respirators, to guard against small-particle aerosols. However, N-95 masks, in combinations with face shields and goggles, have been found protective in the healthcare setting.
- c. Use a negative-pressure room, relative to outside hallway air pressure, with 6 to 12 room air exchanges per hour. If a negative-pressure room is not available, room air should be exhausted to the outdoor air.
- d. In outbreak and mass casualty situations, negative pressure may not be possible. All other infection control barrier methods have been found sufficient to prevent transmission of disease to health care workers.

4. Surveillance of health care workers and laboratory personnel potentially exposed to VHF

Monitor health care workers and laboratory workers with possible exposure to VHF agents for 21 days after exposure to a symptomatic patient (or infectious material from the patient). If a staff member develops fever, follow guidelines for prophylaxis. Treat with ribavirin if known arenavirus exposure.

5. Post-mortem practices

Contact with corpses has been found to be a source of transmission in some VHF outbreaks. Mortuary personnel need to be alerted to any suspect or confirmed VHF case. It is recommended that only trained personnel handle bodies of deceased VHF fever patients, using infection control procedures as during transport of ill persons. Autopsies should be discouraged, or performed only by specially trained persons, wearing maximum respiratory protection equipment, in negative-pressure rooms, to guard against aerosols generated. No embalming should be done, while prompt burial or cremation is recommended.

5. SPECIAL SITUATIONS

A. Bioterrorism Potential

Viral Hemorrhagic Fevers are not endemic to the U.S. (except Hantavirus). Studies have demonstrated successful infection of nonhuman primates by aerosol preparations of Ebola, Marburg, Lassa, and New World arenaviruses. CDC has classified the VHF agents as Category A bioweapon agents. In a case of VHF detected domestically in a person who does not have any risk factors for the disease, bioterrorism should be considered as a potential cause.

6. VIRAL HEMORRHAGIC FEVER ILLNESS CHECKLIST

Onset of viral hemorrhagic fever is usually sudden. Symptoms include:

- Fever
- Weakness
- Irritability
- Dizziness
- Fatigue
- Headache
- Muscle aches
- Nausea / vomiting

Other symptoms may include:

- Rash
- Swelling around the eyes
- Flushing
- Sweats
- Painful abdomen
- Petechiae
- Nosebleeds
- Bleeding gums
- Bloody urine
- Blood in the sputum
- Diarrhea
- Redness of the eyes
- Low blood pressure
- Sore throat
- Chest pain
- Ecchymoses (bruises)
- Bleeding from mucous membranes
- Bloody vomit
- Blood in stools
- Renal failure

Incubation Periods of VHF Agents	Usual	Range
Filoviruses		
Ebola	2–21 days	
Marburg	3–9 days	
Arenaviruses		
Lassa	6–21 days	
Junín (Argentine VHF)	7–16 days	
Machupo (Bolivian VHF)	7–16 days	
Sabiá (Brazilian VHF)	7–16 days	
Guanarito (Venezuelan VHF)	7–16 days	
Bunyaviruses		
Crimean-Congo HF	1–3 days	1–12 days
Rift Valley fever	3–12 days	
Hantavirus	2–4 weeks	a few days to few months
Flaviviruses		
Dengue	4–7 days	3–14 days
Yellow Fever	3–6 days	
Omsk HF	3–8 days	
Kyasanur HF	3–8 days	