

Viral Hemorrhagic Fevers

REPORT IMMEDIATELY

1. DISEASE REPORTING

1.1. Purpose of Surveillance and Reporting

1. To identify potential foci of infection of viral hemorrhagic fever (VHF) agents in the United States (such as laboratory specimens or ill, non-human primates, or clusters of illness around an imported case).
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.

1.2 Laboratory and Physician Reporting Requirements

1. Laboratories and 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 Prevention Section (ACDP) at 971-673-1111.
3. Report any potential exposure to an agent that could cause VHF.

1.3 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, 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).

1.4 State ACDP Responsibilities

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

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4. Evaluate likelihood of an intentional release:
 - VHFs are classified as “Category A” bioterrorism agents. (See below.)
 - If acquired and effectively disseminated, these viruses could pose a serious public health threat. Limiting transmission and numbers of casualties would be challenging.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1. Etiologic Agent

VHFs include numerous zoonotic diseases, all of which cause a hemorrhagic syndrome in humans. Because of its extremely high fatality rate and the occasional 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. All are RNA, enveloped viruses.

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

2.2 Description of Illness

Though signs and symptoms vary, viral hemorrhagic fever is usually characterized by onset of high fever, headache, muscle aches, and fatigue. The duration of illness can range from a few days to a couple of weeks. As the disease progresses, symptoms may include petechiae, bruising, swelling around the eyes, flushing, shock, sustained fever, and sweats. Bleeding occurs from mucous membranes and may present as nosebleeds, bleeding gums, bloody vomit, bloody urine, blood in stools and sputum. 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.

The differential diagnosis includes 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 that 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.

2.3 Reservoirs

Many wild and domestic animals, ticks, and mosquitoes are known to carry VHF agents, although the reservoirs have not been identified for all VHF agents. Rodents are known to be 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 rapid and often fatal illness in these animals, they are not considered reservoirs. Fruit bats, on the other hand, may be a reservoir for ebola.

2.4 Sources and Routes of Transmission

The mode of transmission for initial cases of VHF in any outbreak is animal-, tick- or mosquito-to-human. Once certain VHF viral infections establish themselves in human populations (notably Ebola, Marburg, Lassa, and Crimean-Congo hemorrhagic fever), person-to-person spread may occur.

With these communicable viruses, infection can occur due to direct contact with infectious blood or secretions from infected persons or contaminated fomites. Individuals have acquired VHFs through sexual contact. 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 communicable VHFs, direct physical contact with infectious blood or secretions appears to be required for transmission. Airborne transmission has never been documented.

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2.5 Incubation Period

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

2.6 Period of Communicability or Infectious Period

To be honest, the evidence isn't great. No VHF infection has been reported in persons who had contact with a case only during the incubation period (that is, before onset of fever). Viral load, and risk for transmission, appears greatest during the later stages of illness. It seems prudent, however, to assume that individuals ill with VHF are infectious throughout the clinical course. All persons, including healthcare and laboratory personnel, who have had close contact with a case's potentially infected secretions (or with high-risk symptomatic contacts of a case) in the absence of appropriate infection control precautions should be placed under medical surveillance with fever watch for 21 days after last exposure. 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.

2.7 Epidemiology

Viruses causing VHF are primarily infectious agents in wild animals, birds, mosquitoes and ticks. Various VHF agents are enzootic 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 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.

2.8 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, dialysis, and anti-seizure treatment may be required. Injections, aspirin, and all anticoagulants are contraindicated, and steroids are not indicated. Ribavirin may be helpful with arenavirus and bunyavirus infections, but this drug has not been shown to be useful against filovirus or flavivirus infections. As of 2013, medications for treatment of marburg and ebola virus infections were in phase one trials.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case Definition

To meet the definition for a confirmed case of VHF, a person would have to have fever $>40^{\circ}\text{C}$ (38.6°C for ebola), plus one or more of the following:

- Severe headache, muscle pain, vomiting, diarrhea, abdominal pain, bleeding not related to injury, thrombocytopenia, or a red maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset.

For arenaviruses, the following are also qualifying signs and symptoms: pharyngitis, retrosternal chest pain, and proteinuria.

In addition, a confirmed case must have at least one of the following laboratory findings:

- Detection of VHF viral antigens by enzyme-linked immunosorbent assay (ELISA),
- 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, or
- Detection of VHF viral antigens by immunohistochemistry

3.2 Suspect Case Definition

A suspect VHF case must meet the clinical criteria listed above in addition to having experienced one or more of the following exposures in the three weeks before onset of symptoms:

- Contact with blood or other bodily fluids of a patient with VHF,
- Residence in—or travel to—a VHF-endemic area,
- Work in a laboratory that handles VHF specimens,

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- Work in a laboratory that handles bats, rodents, or primates from enzootic areas, or
- Exposure to semen from a confirmed acute or convalescent case of VHF within 10 weeks of that person's onset of symptoms

3.3 Services Available at the Public Health Laboratory

OSPHL does not currently conduct testing for VHFs. If testing is needed, contact the ACDP Epi on-call to arrange this. Testing may be done through CDC or another public health laboratory. Once CDC approves testing, OSPHL staff (503-693-4100) will provide guidance on what specimens to send, as well as where and how to send them.

4. ROUTINE CASE INVESTIGATION

If a suspect or confirmed case of VHF is reported, or there is any potential exposure to an agent which could cause VHF, call the ACDP epidemiologist immediately, any time of the day or night, at 971-673-1111.

Case investigation of VHF in Oregon residents will involve close collaboration between ACDP epidemiologists and LHD staff. If a bioterrorist event is suspected, we will be inundated by people from CDC so fast it will make your head swim. Working closely with ACDP and, more than likely, CDC, the LHD Communicable Disease staff will be involved in the investigation of any VHF case living within their communities. As noted previously, some VHFs (ebola, marburg, lassa, Crimean-Congo) are communicable. Some aren't. In the absence of lab confirmation that the illness is caused by a non-communicable virus, we should assume communicability and proceed with contact investigation as outlined below.

Contacts at risk for VHF infection must be identified, located, interviewed, and assessed for symptoms of illness. Local health department staff will do rapid screening of contacts for symptoms of illness. (See checklist on final page.) They can also advise each contact to monitor his or her temperature and can review key symptoms to guide decision-making about medical referral.

4.1 Investigation activities

1. Use a gown and gloves if entering the room of an ill patient. Additionally, use a face shield, a surgical mask, and eye protection (goggles) if you will be within 3 feet of the patient. Consider additional barriers, such as an impermeable gown, leg or shoe coverings, if there is a substantial amount of blood or other bodily fluids in the patient area you are entering.
2. Complete the case report form. See <https://public.health.oregon.gov/DiseasesConditions/DiseasesAZ/vhvf/Documents/vhf-case-report-form.pdf>. 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, Junin, Machupo, Sabiá, Guanarito, Crimean-Congo hemorrhagic fevers or Rift Valley fever). As noted previously, some VHFs (ebola, marburg, lassa, Crimean-Congo) are communicable. Some aren't. In the absence of lab confirmation that the illness is caused by a non-communicable virus, we should assume communicability and proceed with contact investigation as outlined below.
3. Record demographic and clinical information about the suspected or confirmed 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:
 - name, age, race/ethnicity, address, phone numbers;
 - parent/guardian information, if applicable;
 - clinical data, including signs and symptoms, date of onset, date of diagnosis, duration;
 - status (hospitalized, at home, deceased).
4. List information about the healthcare providers attending the case patient:
 - name and phone number of the hospital where the case is or was hospitalized;
 - name and phone number of the attending physician;
 - name and phone number of the infection control official at the hospital;
 - 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;

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- name of any person or agency involved in transporting the patient while symptomatic.
5. Document all activities, including travel, during the 21 days prior to symptom onset. This can provide clues to how, where, and when the case may have been exposed
 6. Also document activities of the case patient between onset of symptoms and when the patient enters medical isolation. This will help to identify, assess, and monitor all contacts who spent time with the infected case. Monitoring is particularly important for all those who had physical contact with the ill patient. Institute surveillance of VHF contacts for a period of 21 days after the last known exposure to the case patient.
 - For Ebola and Marburg filoviruses, institute fever watch for all persons who had any direct physical contact with the ill patient's blood, secretions, organs or semen. Airborne transmission has not been documented. Nosocomial infections have occurred from contaminated needles and syringes.
 - Identify all persons who spent time in the same close air space (within 3 feet) with the ill patient, in each of the patient's social settings, and alert them to the need for fever watch. (See #7 below.) Ask about household and other sleeping places, worksites, and places of leisure activities (church, clubs, sports teams, frequently visited households of friends, etc.).
 - For travel history, identify any contacts ill with symptoms suggesting viral hemorrhagic fever during any travel that occurred in the 21 days before the onset of symptoms to assess where and when infection might have occurred. 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 (car, bus, airplane, etc.).
 7. Educate possible contacts about VHF transmission and the need to self-monitor for fever, as well as for symptoms suggestive of VHF infection, for 21 days after the most recent exposure to the case patient. Make plans for immediate medical evaluation should symptoms develop, but have them alert the provider that they are coming, to avoid exposure to others.
 - Asymptomatic contacts should monitor temperatures twice daily during the surveillance period. The LHD should establish telephone or home visit monitoring of this temperature surveillance.
 - If a contact develops a body temperature over 101°F, place the contact in the hospital with strict isolation precautions.
 - Interview any symptomatic contacts for their close contacts.
 - Interview, assess and monitor secondary contacts to VHF cases.
 - Asymptomatic contacts may continue their routine daily activities, but are advised not to travel outside of the home community during the surveillance period.
 - 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

5.1 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 and body fluids, and safe methods of waste disposal. In addition, healthcare workers in hospital settings need education and monitoring for adherence to standard, contact, and droplet precautions when providing care to VHF patients. Several strategies could help prevent exposure to VHF agents:

- Discourage non-essential travel 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 ACDP (971-673-1111).

5.2 Isolation of VHF cases

Confirmed and suspect VHF cases must be isolated, and all persons caring for them must observe strict standard, contact, and droplet precautions.

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- Healthcare professionals are at risk from accidental percutaneous and mucous membrane exposures to blood and body fluids. They should pay special attention to the use of barrier/contact precautions in care of the patient, and in cleaning or disposal of anything the patient may have touched or contaminated.
- Airborne precautions, with use of N95 or powered air purifying respirators (PAPRs) should be considered for care of VHF patients with severe pulmonary involvement, or when aerosol-generating procedures (endotracheal intubation, sputum induction, bronchoscopy, airway suctioning, or positive pressure ventilation by face mask) are performed.
- Patients with VHF who have respiratory symptoms should wear a surgical mask whenever transported through areas where others may not have appropriate personal protective equipment.

4. Period of Isolation of Patient

- Patients should be isolated until they are clinically well, and then monitored for at least three weeks.
- 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 should be determined by expert clinician consultation).
- Recovering VHF patients should refrain from sexual activity for three months after clinical recovery.

5.3 Follow-up of Cases

Patients recovering from VHF should be monitored clinically during convalescence. Patients with Lassa VHF infections are at risk of deafness, and hearing acuity should be monitored during recovery.

5.4 Protection of Contacts of a Case

Healthcare workers and other contacts of confirmed or suspected cases of VHF should practice standard, contact, and droplet precautions to reduce their risk of acquiring VHF. All persons, including healthcare and laboratory personnel, who have had close contact with a case's potentially infected secretions (or with high-risk symptomatic contacts of a case) without using appropriate personal protective equipment should be placed under medical surveillance with fever watch for 21 days after last exposure.

5.5 Vaccines and Antiviral Prophylaxis

Other than use of ribavirin in those with high-risk body fluid exposures to Lassa fever, there is no immunization or prophylaxis for contacts of cases that could be used post-exposure to decrease their risk of developing illness. Vaccine to prevent infection with VHF agents is available for yellow fever and Argentine hemorrhagic fever.

As noted above, ribavirin has been recommended as post-exposure prophylaxis for contacts with high-risk (i.e. body fluid) exposures of Lassa fever patients.

5.6 Environmental Measures

Depending on the VHF agent involved, it may be useful to enhance vector control for specific reservoir animals 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.

5.7 Infection Control

With the lack of effective therapy or preventive vaccines against most 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 healthcare facility, and isolated promptly.

- Isolate the patient in a private room, with a private bathroom, or, if not possible, use group rooms housing VHF patients in the same wing or area of the facility.
- Allow only a limited number of staff into patient room, and with full protective equipment.
- Keep the door to the room closed at all times.
- No visitors, except for a limited number of family members, with full protective equipment for universal, contact, and droplet precautions.
- Patients with respiratory symptoms should wear a surgical mask any time they move through an area in

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which others around them may not have appropriate personal protective equipment.

2. Personal Protective Barrier Precautions
 - Strict hand hygiene plus double gloves;
 - gowns; consider impermeable gowns, shoe and leg coverings if there is substantial risk of blood or other bodily fluid exposure;
 - goggles and surgical mask or face shield if within 3 feet of patient.
3. Surveillance of healthcare workers and laboratory personnel potentially exposed to VHF
Monitor healthcare 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 fever or other symptoms develop, arrange prompt medical evaluation.
4. Surveillance of healthcare workers and laboratory personnel potentially exposed to VHF
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.

6. SPECIAL SITUATIONS

Long story short: Any case of VHF we investigate is a special situation. Just give us a call. We'll work through it together.

7. REFERENCES

1. CDC. Interim Guidance for Managing Patients with Suspected Viral Hemorrhagic Fever in U.S. Hospitals, May 19, 2005. <http://www.cdc.gov/ncidod/dvrd/spb/pdf/vhf-interim-guidance.pdf>
2. Bausch DG, CM Hadi, SH Khan, JJJ Lertora. Review of the Literature and Proposed Guidelines for the Use of Oral Ribavirin as Postexposure Prophylaxis for Lassa Fever. *Clinical Infectious Disease* 2010;51(12):1435-1441.

UPDATE LOG

2014: Typos corrected. Sec. 3.1: temperature component of ebola case definition updated. Sec. 3.3: guidance on lab specimen shipment updated. Sec. 4.1: language on obtaining history of possible exposure to VHF during travel clarified. (Leman)

2013: Updated infection control guidance, ACDP contact information. Updated case definition. Updated information on treatment and prophylaxis. Revised *Contact Symptom Checklist*. Edits throughout to improve clarity. (Leman)

2004: Original Document

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Contact Interview Checklist

Name: _____
Last First MI

Orpheus # of Epi-linked Case _____

Sex Female Male Ethnicity: Latino? yes no unknown

Race AI/AN Asian Black Pacific Islander white
 Refused unknown Other _____

Date of Birth _____
m d y

Most recent exposure date _____
m d y

Nature of Exposure: Body fluid contact W/in 3 ft. while case was ill Neither of these
 Healthcare worker Laboratorian Family member
 Other

Any of these signs and symptoms?

- | | |
|--|---|
| <input type="checkbox"/> Fever | <input type="checkbox"/> Fatigue |
| <input type="checkbox"/> Weakness | <input type="checkbox"/> Headache |
| <input type="checkbox"/> Irritability | <input type="checkbox"/> Muscle aches |
| <input type="checkbox"/> Dizziness | <input type="checkbox"/> Nausea / vomiting |
| <input type="checkbox"/> Rash | <input type="checkbox"/> Diarrhea |
| <input type="checkbox"/> Swelling around eyes | <input type="checkbox"/> Redness of eyes |
| <input type="checkbox"/> Flushing | <input type="checkbox"/> Low blood pressure (shock) |
| <input type="checkbox"/> Sweats | <input type="checkbox"/> Sore throat |
| <input type="checkbox"/> Any bleeding/bruising in absence of injury? | |

On-going exposure likely? yes no

Education on standard, contact, and droplet precautions given, if on-going exposure predicted.