Viral Hemorrhagic Fevers

Investigative Guidelines

December 2024

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify the source of infection for viral hemorrhagic fever (VHF) cases.
2. To identify VHF cases as early as possible to prevent transmission.
3. 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 any known or suspected case of VHF immediately to the local health department (LHD) as an, “uncommon illness of public health significance.”
2. If this is not possible, such cases should be reported to the Oregon Acute and Communicable Disease Prevention (ACDP) section at 971-673-1111.
3. Laboratories must report any potential exposure to an agent that could cause VHF to the Oregon ACDP section at 971-673-1111.

1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed or suspect cases of VHF immediately to ACDP.
2. Consult with ACDP about strategies for enhanced surveillance, contact investigation, and exposure monitoring.
3. Work with local providers and facilities to ensure compliance with infection prevention and control recommendations for patients with suspected or confirmed VHF.
4. Provide education to and monitoring of VHF persons under monitoring (PUMs).
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.

1.4 OPHD Responsibilities

1. Provide consultation to LHD public health, Tribal, and private sector health professionals concerning:
   - Isolation of suspect and confirmed cases;
   - Diagnostic evaluation;
   - Required reporting and surveillance activities;
   - Contact identification and follow-up;
   - Inter-jurisdictional tracking of cases and contacts who move out of county or state jurisdiction;
   - Development and maintenance of adequate tools to coordinate case and contact surveillance, and assure adequacy of response activities;
   - Provision of surge capacity if a VHF outbreak investigation overwhelms resources of LHD.
2. Facilitate expert consultation with infectious disease specialists and CDC as needed.
3. Coordinate specimen collection with the relevant LHD or Tribal jurisdiction 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 the likelihood of an intentional release:
   - Some VHFs are classified as “Category A” bioterrorism agents
   - If effectively disseminated, these viruses could pose a serious public health threat

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

VHFs are a group of zoonotic diseases which can cause a hemorrhagic syndrome in humans. Most VHFs are caused by viruses from four families. All are RNA viruses:

- **Filoviruses**: Filoviruses include Ebola virus (EBOV), Marburg virus (MARV), Sudan virus (SUDV), Bundibugyo virus (BDBV), Taï Forest virus (TAFV), and Ravn virus (RAVN).
- **Bunyavirales order**: Viruses in the Bunyavirales order include primarily arenaviruses (Lassa fever virus, Junín virus, Chapare virus, Lujo virus, Machupo virus, Sabia virus, and Guanarito virus) as well as hantaviruses, Crimean-Congo Hemorrhagic Fever (HF) virus (a nairovirus), and Rift Valley Fever virus (a phenuvirus).
- **Flaviviruses**: Flaviviruses include Yellow Fever virus, Dengue virus, Alkhurma HF virus, Kyasanur Forest Disease virus, and Omsk HF virus.
- **Paramyxoviruses**: Paramyxoviruses include Hendra and Nipah viruses. (1)

2.2 Description of Illness

The signs and symptoms of VHFs may vary, and classically include the abrupt onset of high fever with additional non-specific symptoms such as myalgia, fatigue, and gastrointestinal symptoms. Unexplained bleeding or bruising may occur several days into the infection. Clinicians should consult the CDC Guide for Clinicians Evaluating an Ill Person for VHF or Other High-Consequence Disease for additional information.

Mortality rates for VHFs vary and may approach 90% in low-resource settings.(2)

2.3 Reservoirs

Filoviruses can cause severe illness in people and nonhuman primates. The Egyptian fruit bat is the reservoir for Marburg virus. The reservoir for EBOV is unknown but is believed to be a bat. Viruses in the Bunyavirales order are spread by rodents or insects, such as mosquitos, ticks, or sand flies. Flaviviruses are spread primarily by mosquitoes and ticks.(1)

2.4 Sources and Routes of Transmission

Depending on the virus, initial human cases in VHF outbreaks typically involve exposure to affected reservoir rodents or their droppings (arenaviruses), reservoir bats or infected bushmeat (EBOV, Marburg virus), infected livestock (Rift Valley Fever virus, Crimean-Congo HF virus), ticks (Alkhurma HF virus, Omsk HF virus, Crimean-Congo HF virus) or mosquitoes (Yellow Fever virus, Dengue virus). Some VHF infections including filoviruses spread readily from person to person through contact with an infected person's body fluids.(1) Percutaneous exposure to contaminated body fluids carries a high risk of exposure. Airborne transmission has not been documented.(3)

2.5 Incubation Period

The incubation period varies by virus and ranges from 2 to 32 days.(1)

2.6 Period of Communicability or Infectious Period

In general, the risk for person-to-person transmission increases as symptoms progress. VHF infection has not been reported in persons whose contact with an infected patient occurred only during the incubation period (i.e., prior to symptom onset).(4)

2.7 Epidemiology

VHFs are distributed globally. Clusters and outbreaks occur following spillover from animal reservoirs to humans.(2)

2.8 Treatment

Supportive therapy is the mainstay of VHF treatment. Virus-specific therapies are limited and may be supported by limited clinical data.(2)

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case Definition

Acute onset of fever >38°C/100.4°F, **AND** one or more of the following clinical findings:

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

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

AND one or more 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
- Detection of VHF viral antigens in tissues by immunohistochemistry(5)

3.2 Suspect Case Definition

Meets clinical criteria listed above, **AND** has one or more of the following epidemiologic exposures in the three weeks before symptom onset:

- Contact with blood or other body fluids of a patient with VHF
- Residence in—or travel to—a VHF-endemic area or an area with active transmission
- Work in a laboratory that handles VHF specimens
- Work in a laboratory that handles bats, rodents, or primates from an enzootic area or an area with active transmission
- Sexual exposure to semen from a confirmed acute or recovered case of VHF(5)

3.3 Diagnostic Testing

For information on diagnostic testing, see CDC Guidance on Performing Routine Diagnostic Testing for Patients with Suspected VHFs or Other High-Consequence Disease.

3.4 Services Available at Oregon State Public Health Laboratory

OSPHL offers Zaire Ebola virus testing by PCR and can facilitate testing for other VHFs through CDC. Contact the ACDP Epi on-call for testing approval. Once testing is approved, OSPHL staff (503-693-4100) will provide specific guidance on specimen collection, handling, and transport. CDC offers guidance on VHF Specimen Collection and VHF Clinical Specimen Packaging and Shipping.

4. ROUTINE CASE INVESTIGATION

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

Case investigation of VHFs in Oregon residents will involve close collaboration between ACDP epidemiologists, LHD staff, and the CDC. Not all VHFs are communicable; in the absence of laboratory confirmation that the pathogen is non-communicable, assume communicability and proceed with case and contact investigation as outlined below.(1) Unless absolutely necessary, cases should be investigated remotely (i.e., by phone) due to the potential morbidity and mortality associated with VHF infections.

4.1 Identify the Source of Infection

The case investigation should aim to identify the source of VHF infection. In most cases, the source will be obvious (e.g., an infection prevention breach while caring for an ill patient). In sporadic cases, the source may not be obvious, and identifying risk factors during the incubation period prior to infection, such as contact with wild animals or visiting a cave, will be critical. The VHF case report form will guide the case investigation and should be completed and uploaded to Orpheus as a document.

4.2 Identify and Quarantine Close Contacts

The case investigation should aim to identify all persons with high-risk exposures to a VHF. These close contacts should be quarantined for the duration of the incubation period of the VHF following their last exposure. They should be actively monitored daily during this period and restricted from traveling by commercial transport.(6)

A close contact is any person who has been exposed to a suspect or confirmed case in one or more of the following ways:

- Physical contact with a person who has a confirmed or suspected VHF, without the use of recommended personal protective equipment (PPE)
- Providing health care to a patient with a confirmed or suspected VHF without use of recommended PPE or experiencing a breach in infection control precautions that results in the potential for percutaneous, mucous membrane, or skin contact with the blood or other body fluids of a patient with a VHF while working in a VHF treatment unit or associated facility (e.g., laboratory) or while taking care of a patient with a VHF;
- Physical contact (without using recommended PPE) with a body of a person who died of confirmed or suspected VHF, or any dead body in an area with a declared VHF outbreak, or experiencing a breach in infection control precautions while handling such a dead body
- Living in the same household as a person with confirmed or suspected VHF while that person was symptomatic(6)
- Has touched the blood or body fluids of a case during their illness
- Has touched the clothes or linens of a case
- A baby who has been breastfed by a case(7)

5. CONTROLLING FURTHER SPREAD

5.1 Protective Actions and Personal Protective Equipment

Protective actions include avoiding non-essential travel to areas with known outbreaks of VHF and avoiding high-risk exposures when traveling to areas with known outbreaks.

CDC guidance regarding infection prevention and control including personal protective equipment (PPE) in healthcare facilities includes:

- Infection Prevention and Control Recommendations for Patients in U.S. Hospitals who are Suspected or Confirmed to have Selected Viral Hemorrhagic Fevers
- Guidance for Personal Protective Equipment
- PPE: Clinically Stable Patients Suspected to have VHF
- PPE: Confirmed Patients and Clinically Unstable Patients Suspected to have VHF
- Considerations for Discharging People under Evaluation for Selected VHFs
- VHF Clinical Care for Safely Performing Acute Hemodialysis in Patients in U.S. Hospitals
- Interim Guidance for Environmental Infection Control in Hospitals
- Handling VHF-Associated Waste
- Safe Handling of Human Remains of VHF Patients in U.S. Hospitals and Mortuaries

CDC guidance regarding infection prevention and control including PPE for emergency services includes:

- Interim Guidance for Emergency Services
- Interim Guidance for EMS Systems and 9-1-1 Answering Points
- Interim Guidance for Air Medical Transport

The duration of precautions should be determined on a case-by-case basis, in conjunction with local, state, and federal health authorities. Factors which should be considered include the presence of symptoms, the time since symptom resolution, and available laboratory information.(8)

5.2 Isolation of VHF Cases

People with suspected or confirmed VHF should remain in isolation until they have been determined not to have VHF (if suspected) or to be no longer infectious (if confirmed).(6)

5.3 Returning Traveler Screening and Activation of Person Under Monitoring Approach

CDC has implemented screening for travelers returning from active outbreak areas several times in the past. These screenings may involve the rerouting of commercial flights to specific airports in the U.S. Screening typically occurs upon arrival in the U.S. and may be augmented through follow-up text notifications regarding symptom monitoring through the isolation period.

CDC may also recommend activation of a person under monitoring approach, in which individuals who meet a specific risk threshold are actively monitored by public health for one incubation period following their last exposure.

5.4 Public Health Orders

Quarantine or isolation may be voluntary or under public health orders. State, tribal, local and territorial authorities have primary jurisdiction for isolation and other public health orders within their borders. Federal public health authority primarily extends to international arrivals at ports of entry and to preventing interstate spread of communicable diseases. Federal public health orders may be issued to enforce isolation, quarantine, or conditional release. The list of quarantinable communicable diseases for which federal public health orders are authorized is defined by Executive Order and includes viral hemorrhagic fevers.(6)

6. MANAGING SPECIAL SITUATIONS

We anticipate outbreak- and pathogen-specific recommendations from the CDC and these will be disseminated to public health and clinic partners through a variety of mechanisms including the Health Alert Network.

7. REFERENCES

1. CDC. About Viral Hemorrhagic Fevers. April 15, 2024.
2. Belhadi D, El Baied M, Mulier G, Malvy D, Mentré F, Laouénan C. The number of cases, mortality and treatments of viral hemorrhagic fevers: A systematic review. PLOS Neglected Tropical Diseases. 2022;16(10):e0010889.
3. Siegel JD, Rhinehart E, Jackson M, Chiarello L, Committee HCICPA. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. American journal of infection control. 2007;35(10):S65.
4. Control CfD, Prevention. Update: management of patients with suspected viral hemorrhagic fever--United States. MMWR Morbidity and mortality weekly report. 1995;44(25):475-9.
5. CDC. Viral Hemorrhagic Fever (VHF) 2022 Case Definition. August 30, 2021.
6. CDC. Public Health Management of People with Suspected or Confirmed VHF or High-Risk Exposures. May 15, 2024.
7. Greiner A, Angelo K. CDC methods for implementing and managing contact tracing for Ebola virus disease in less-affected countries. 2014.
8. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Last update: September 2024. 2024.

8. UPDATE LOG

2024. Overall revision to align with updated CDC resources. (Sutton, Moffett)

2023. Updated testing information. (Leman, Henning, Humphrey-King)

2022. Updated treatment and testing information. Minor edits for clarity. Contact interview check list revised to incorporate REAL-D. (Leman)

2019. Updated list of VHFs: reservoirs, routes of transmission, period of communicability, treatment, and information on infection prevention. Minor edits; links to references added.

2014. Typos corrected. Sec. 3.1: temperature component of Ebola case definition and guidance on lab specimen shipment updated. 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