

## **VIRAL HEMORRHAGIC FEVER** (VHF)

### **REPORTING INFORMATION**

- **Class A:** *Report immediately via telephone* the case or suspected case and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report immediately via telephone to the local public health department in which the reporting health care provider or laboratory is located. Local health departments should report immediately via telephone the case or suspected case and/or a positive laboratory result to the Ohio Department of Health (ODH).
- Reporting Form(s) and/or Mechanism:
  - *Immediately via telephone.*
  - For local health departments, cases should also be entered into the Ohio Disease Reporting System (ODRS) within 24 hours of the initial telephone report to the ODH.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset, and all the fields in the Epidemiology module.

### **AGENTS AND DISEASES**

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of enveloped RNA viruses. In general, the term "viral hemorrhagic fever" is used to describe a severe multi-organ system syndrome (multisystem in that multiple organ systems in the body are affected). Characteristically, the overall vascular system is damaged, and the body's ability to regulate itself is impaired. 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.

The three most common VHFs are Ebola virus disease, Lassa fever and Marburg hemorrhagic fever. Please see the IDCM chapters on [Ebola virus](#), [Lassa fever](#), [Marburg virus](#) and [Crimean-Congo hemorrhagic fever](#) disease for specific guidance.

### **CASE DEFINITION**

#### **Clinical Description**

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

- A fever > 40°C (104°F)
- One of 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 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

### **Criteria for Epidemiologic 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 10 weeks of that person's onset of symptoms

### **Case Classification**

Suspect: Case meets the clinical and epidemiologic linkage criteria.

Confirmed: Case meets the clinical and laboratory criteria.

Comment: VHF refers to viral hemorrhagic fever caused by Ebola, Lassa, Lujo, or Marburg virus, a new world arenavirus, or Crimean-Congo hemorrhagic fever.

## **SIGNS AND SYMPTOMS**

Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion. Patients with severe cases of VHF often show signs of bleeding under the skin, in internal organs, or from body orifices like the mouth, eyes, or ears. However, although they may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patient cases may also show shock, nervous system malfunction, coma, delirium, and seizures. Some types of VHF are associated with renal (kidney) failure.

## **DIAGNOSIS**

Diagnosing specific viral hemorrhagic fevers in the first few days of illness can be difficult because the initial signs and symptoms — high fever, muscle aches, headaches and extreme fatigue — are common to many other diseases.

Whole blood or serum may be tested for virologic (PCR, antigen detection, virus isolation) and immunologic (IgM, IgG) evidence of infection. Tissue may be tested by immunohistochemistry, PCR, and virus isolation. Postmortem skin biopsies fixed in formalin and blood collected within a few hours after death by cardiac puncture can be used for diagnosis. Samples should be sent for testing to a reference laboratory with biosafety level 3 and 4 capability.

## **EPIDEMIOLOGY**

### **Occurrence**

VHF viruses are distributed throughout the world. Each virus is associated with one or more nonhuman hosts, restricting natural occurrence of VHF to the areas inhabited by these species. Viruses causing hemorrhagic fevers are initially transmitted to humans when the habitats of the infected reservoir hosts and humans overlap. Risk of VHF is associated with human incursion into such areas. In general, humans are incidental

("dead-end") hosts for these enzootic diseases.

### **Mode of Transmission and Source**

The viruses carried in rodent reservoirs are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents. The viruses associated with arthropod vectors are spread most often when the vector mosquito or tick bites a human, or when a human crushes a tick. However, some of these vectors may spread virus to animals, livestock, for example. Humans then become infected when they care for or slaughter the animals.

Some viruses that cause hemorrhagic fever can spread from one person to another, once an initial person has become infected. Ebola, Marburg, Lassa and Crimean-Congo hemorrhagic fever viruses are examples. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids. For example, contaminated syringes and needles have played an important role in spreading infection in outbreaks of Ebola hemorrhagic fever and Lassa fever.

### **Incubation Period**

Incubation period can be as long as 21 days.

## **PUBLIC HEALTH MANAGEMENT**

### **Case**

#### Investigation

Obtain information about the patient's occupation, history of travel outside the United States, contact with wild animals or lab animals, contact with a suspected or confirmed case of viral hemorrhagic fever, or close contact with an ill individual who traveled to a viral hemorrhagic fever-endemic area.

#### Treatment

Patients should receive supportive care consisting of maintenance of appropriate fluid and electrolyte balance, oxygenation and blood pressure, as well as treatment of any other complicating infections.

#### Isolation

Ohio Administrative Code (OAC) 3701-3-13 (DD) states:

"Viral hemorrhagic fever (VHF): a person with confirmed or suspected viral hemorrhagic fever shall be placed in airborne isolation until no longer considered infectious."

Clinicians evaluating suspect cases should use standard (e.g., hand hygiene), airborne (e.g., N-95 respirator) and contact (e.g., gowns and gloves) precautions.

### **Contacts**

#### Investigation

Currently there is no post exposure prophylaxis available for individuals exposed to these agents. Investigation of contacts and source of infection: Identify all close contacts in the three weeks after the onset of illness. Initiate quarantine and active surveillance of contacts by having contacts take and maintain record of body temperature twice a day for 3 weeks after last exposure. If temperature is greater than 101°F (38.3°C), hospitalize patient immediately and initiate appropriate isolation precautions. Specific treatment such as Ribavirin is most effective if given within 6 days of illness onset.

For further information, see <https://www.cdc.gov/vhf/index.html>

**What are viral hemorrhagic fevers?**

Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of viruses. 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). Characteristically, the overall vascular system is damaged, and the body's ability to regulate itself is impaired. 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.

**How are hemorrhagic fever viruses grouped?**

VHFs are caused by viruses of five distinct families: arenaviruses, filoviruses, bunyaviruses, flaviviruses and paramyxoviruses. Each of these families share a number of features:

- They are all RNA viruses, and all are covered, or enveloped, in a fatty (lipid) coating.
- Their survival is dependent on an animal or insect host, called the natural reservoir.
- The viruses are geographically restricted to the areas where their host species live.
- Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.
- Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.
- With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs.

In rare cases, other viral and bacterial infections can cause a hemorrhagic fever; scrub typhus is a good example.

**What carries viruses that cause viral hemorrhagic fevers?**

Viruses associated with most VHFs are zoonotic. This means that these viruses naturally reside in an animal reservoir host or arthropod vector. They are totally dependent on their hosts for replication and overall survival. For the most part, rodents and arthropods are the main reservoirs for viruses causing VHFs. The multimammate rat, cotton rat, deer mouse, house mouse, other field rodents and the African fruit bat are examples of reservoir hosts. Arthropod ticks and mosquitoes serve as vectors for some of the illnesses. However, the hosts of some viruses remain unknown – Ebola virus is a well-known example.

**Where are cases of viral hemorrhagic fever found?**

Taken together, the viruses that cause VHFs are distributed over much of the globe. However, because each virus is associated with one or more particular host species, the virus and the disease it causes are usually seen only where the host species live(s). Some hosts, such as the rodent species carrying several of the New World arenaviruses, live in geographically restricted areas. Therefore, the risk of getting VHFs caused by these viruses is restricted to those areas. Other hosts range over continents, such as the rodents that carry viruses which cause various forms of hantavirus pulmonary syndrome (HPS) in North and South America, or the different set of rodents that carry viruses which cause hemorrhagic fever with renal syndrome (HFRS) in Europe and Asia. A few hosts are distributed nearly worldwide, such as the common rat. It can carry Seoul virus, a cause of HFRS; therefore, humans can get HFRS anywhere where the common rat is found. While people usually become infected only in areas where the host lives, occasionally people become infected by a host that has been exported from its native habitat. For example, the

first outbreaks of Marburg hemorrhagic fever, in Marburg and Frankfurt, Germany, and in Yugoslavia, occurred when laboratory workers handled imported monkeys infected with Marburg virus. Occasionally, a person becomes infected in an area where the virus occurs naturally and then travels elsewhere. If the virus is a type that can be transmitted further by person-to-person contact, the traveler could infect other people. For instance, in 1996, a medical professional treating patients with Ebola virus disease (EVD) in Gabon unknowingly became infected. When he later traveled to South Africa and was treated for EVD in a hospital, the virus was transmitted to a nurse. She became ill and died. Because more and more people travel each year, outbreaks of these diseases are becoming an increasing threat in places where they rarely, if ever, have been seen before.

### **How are hemorrhagic fever viruses transmitted?**

Viruses causing hemorrhagic fever are initially transmitted to humans when the activities of infected reservoir hosts or vectors and humans overlap. The viruses carried in rodent reservoirs are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents. The viruses associated with arthropod vectors are spread most often when the vector mosquito or tick bites a human, or when a human crushes a tick. However, some of these vectors may spread virus to animals, livestock, for example. Humans then become infected when they care for or slaughter the animals. Some viruses that cause hemorrhagic fever can spread from one person to another, once an initial person has become infected. Ebola, Marburg, Lassa and Crimean-Congo hemorrhagic fever viruses are examples. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids. For example, contaminated syringes and needles have played an important role in spreading infection in outbreaks of Ebola virus disease and Lassa fever.

### **What are the symptoms of viral hemorrhagic fever illnesses?**

Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion. Patients with severe cases of VHF often show signs of bleeding under the skin, in internal organs, or from body orifices like the mouth, eyes, or ears. However, although they may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patient cases may also show shock, nervous system malfunction, coma, delirium, and seizures. Some types of VHF are associated with renal (kidney) failure.

### **How are patients with viral hemorrhagic fever treated?**

Patients receive supportive therapy, but generally speaking, there is no other treatment or established cure for VHFs. Ribavirin, an antiviral drug, has been effective in treating some individuals with Lassa fever or HFRS. Treatment with convalescent-phase plasma has been used with success in some patients with Argentine hemorrhagic fever.

### **How can cases of viral hemorrhagic fever be prevented and controlled?**

With the exception of yellow fever and Argentine hemorrhagic fever, for which vaccines have been developed, no vaccines exist that can protect against these diseases. Therefore, prevention efforts must concentrate on avoiding contact with host species. If prevention methods fail and a case of VHF does occur, efforts should focus on preventing further transmission from person to person, if the virus can be transmitted in this way. Because many of the hosts that carry hemorrhagic fever viruses are rodents, disease prevention efforts include

- Controlling rodent populations;
- Discouraging rodents from entering or living in homes or workplaces;
- Encouraging safe cleanup of rodent nests and droppings.

For hemorrhagic fever viruses spread by arthropod vectors, prevention efforts often focus on community-wide insect and arthropod control. In addition, people are encouraged to use insect repellent, proper clothing, bednets, window screens, and other insect barriers to avoid being bitten.

For those hemorrhagic fever viruses that can be transmitted from one person to another, avoiding close physical contact with infected people and their body fluids is the most important way of controlling the spread of disease. Barrier nursing or infection control techniques include isolating infected individuals and wearing protective clothing. Other infection control recommendations include proper use, disinfection, and disposal of instruments and equipment used in treating or caring for patients with VHF, such as needles and thermometers.

In conjunction with the World Health Organization, the CDC has developed practical, hospital-based guidelines, titled "[Infection Control for Viral Haemorrhagic Fevers in the African Health Care Setting](#)". The manual can help healthcare facilities recognize cases and prevent further hospital-based disease transmission using locally available materials and few financial resources.

### **What needs to be done to address the threat of viral hemorrhagic fevers?**

Scientists and researchers are challenged with developing containment, treatment, and vaccine strategies for these diseases. Another goal is to develop immunologic and molecular tools for more rapid disease diagnosis, and to study how the viruses are transmitted and exactly how the disease affects the body (pathogenesis). A third goal is to understand the ecology of these viruses and their hosts in order to offer preventive public health advice for avoiding infection.

From the CDC website:

<https://www.cdc.gov/vhf/index.html>