PUBLIC HEALTH REFERENCE SHEET
Hemorrhagic Fever, Viral (VHF)

Name	Varies. Includes but is not limited to: Junin virus (Argentine hemorrhagic fever (AHF)), Machupo virus, Guanarito virus, Sabia virus, Lassa virus, Lujo virus, Crimean-Congo hemorrhagic fever virus, Omsk hemorrhagic fever virus, Kyasanur Forest Disease virus, Ebola virus, Marburg virus
Reservoir & Transmission	Varies by the virus; most zoonotic; some associated with bites from ticks or mosquitoes Transmission occurs when humans contact urine, fecal matter, saliva, or other body excretions from an infected animal host (bat, rodent, livestock). For vectorborne viruses, transmission occurs from a bite from an infected insect host (tick, mosquito). Some VHFs can spread from person-to-person through close contact with infected people or body fluids.
Incubation Period	1–3 weeks
Common Symptoms	Acute onset illness with a fever >104ºF or >40ºC and any of the following: severe headache, muscle pain, erythemous maculopapular rash on the trunk with fine desquamation 3 to 4 days after rash onset, vomiting, diarrhea, abdominal pain, thrombocytopenia, bleeding not related to injury. Other symptoms depend on virus type.
Gold Standard Diagnostic Test	Requires testing at a highly specialized reference laboratory ELISA from blood; or culture from blood or tissues; or RNA detected by PCR, sequencing, or NAAT from blood or tissue; or histopathologic identification of viral antigens from tissues
Risk Groups	Individuals engaging in animal research, healthcare workers
Geographic Significance	Varies depending on the causative agent. Risk areas include Africa, Eastern Europe, Central Asia, the Middle East, and South America.

What are viral hemorrhagic fevers?
Viral hemorrhagic fevers (VHFs) are a group of diseases that are caused by several distinct families of ribonucleic acid (RNA) viruses, which change over time at a high rate. VHF refers to a condition that affects multiple organ systems, damages the overall cardiovascular system, and reduces the body's ability to function. VHF virus families include Arenavirus, Flavivirus, Filovirus, Nairovirus, and Phenuivirus. Almost all VHF viruses are classified as Biosafety Level 4 (BSL-4) pathogens.

VHF **excludes** dengue hemorrhagic fever, hantavirus hemorrhagic fever, Korean hemorrhagic fever, chikungunya, yellow fever, and Rift Valley Fever.

What is the occurrence of viral hemorrhagic fevers?
The number of viruses known to cause disease in humans around the globe is ever-increasing, and the way VHF viruses spread is likely to shift due to globalization, international travel, and climate change.

How are viral hemorrhagic fevers transmitted?
- The viruses carried in rodent reservoirs are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents.

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- 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. Some of these vectors may spread the virus to animals (e.g., livestock), then humans can become infected when they care for or slaughter the animals.
- Ebola, Marburg, Lassa, and Crimean-Congo hemorrhagic fever viruses are associated with person-to-person transmission. Secondary transmission of the virus can occur directly, through close contact with blood or body fluids of infected people or indirectly, through contact with objects contaminated with infected body fluids (e.g., syringes and needles contributed to outbreaks of Ebola hemorrhagic fever and Lassa fever).

Who is at risk for viral hemorrhagic fevers?
The likelihood of contracting any VHF is considered extremely low, even for international travelers. However, exposure can occur when traveling to an affected area, especially if in direct contact with the blood or body fluids of infected people or animals, or objects contaminated with infected body fluids. A case is suspected in an individual that has any of the following within the 3 weeks before onset of symptoms:

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

What are the signs and symptoms of viral hemorrhagic fevers?
Signs and symptoms vary by the type of VHF. Nonspecific symptoms may include fever, headache, malaise, muscle aches, or sore throat. Clinical features common among VHFs include retro-orbital pain, joint pain, eye redness, abdominal pain, vomiting, and/or diarrhea. The clinical description is an acute onset illness with a fever >104°F or >40°C and any of the following: severe headache, muscle pain, erythemous maculopapular rash on the trunk with fine desquamation 3 to 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), or thrombocytopenia.

What are potential complications of viral hemorrhagic fevers?
Severe cases of VHF may show signs of bleeding under the skin, in internal organs, or in the mouth, eyes, or ears. Some types of VHF are associated with renal failure. Severely ill patient cases may develop shock, nervous system malfunction, delirium, seizures, coma, or death.

The prognosis varies by disease. Many of these diseases can cause outbreaks and are associated with high morbidity and mortality, with case fatality rates as high as 80%–90% in developing countries.

How are viral hemorrhagic fevers diagnosed?
Almost all VHF viruses are classified as BSL-4 pathogens and must be handled in special facilities designed to contain them safely. Consult with the CDC's guidance for laboratory testing: https://www.cdc.gov/vhf/ebola/laboratory-personnel/index.html

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A confirmed case meets the clinical description with any of the following:

- VHF positive antigen by ELISA from blood
- VHF identified by culture from blood or tissue
- VHF nucleic acid (RNA) detected (e.g., PCR, sequencing, NAAT) from blood or tissue
- Histopathologic identification of VHF viral antigens from tissue

Consult with the CDC for assessing VHF risk in a returning traveler.
https://www.cdc.gov/vhf/abroad/assessing-vhf-returning-traveler.html

For any questions about current outbreaks of VHFs, call the CDC's Emergency Operations Center at 770-488-7100 or email: spather@cdc.gov.

How are viral hemorrhagic fevers treated?

Treatment is supportive care. Isolate the patient in a private room or area with a private bathroom, limit healthcare personnel, and use personal protective equipment as indicated.

- For Lassa virus, the anti-viral drug Ribavirin has been shown to improve treatment outcomes when given early in the disease course.
- For AHF, treatment with convalescent-phase plasma has been used with success in some patients.

How can viral hemorrhagic fevers be prevented?

A vaccine for AHF is not approved by the U.S. Food and Drug Administration. Vaccines are not available for other VHF diseases. These viruses may be destroyed with physical (heat, sunlight, gamma rays) and chemical (bleach, detergents, solvents) methods. Prevention efforts focus on avoiding contact with host species.

Rodent control: For hemorrhagic fever viruses spread by rodents, disease prevention efforts include controlling rodent populations; keeping rodents from entering or living in homes or workplaces; and using safe cleanup of rodent nests and droppings.

Arthropod control: For hemorrhagic fever viruses spread by arthropod vectors, disease prevention efforts often focus on community-wide insect and arthropod control. Use insect repellant, proper clothing, bed nets, 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 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.

What are some public health considerations?

- Be aware that VHF are stable when aerosolized and thus classified as category A bioweapons agents and are associated with severe morbidity and mortality in infected individuals.
- Immediately notify infection control program and staff.
- Immediately notify local and state health department.
- Immediately notify the Defense Centers for Public Health.

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- Call the CDC's Emergency Operations Center at 770-488-7100.
- Specify the etiologic/causative agent.
- Document relevant travel and deployment history occurring within the incubation period.

References:

Defense Health Agency. 2022. *Armed Forces Reportable Medical Events: Guidelines and Case Definitions.* https://www.health.mil/Reference-Center/Publications/2022/11/01/Armed-Forces-Reportable-Medical-Events Guidelines

Heymann, David L. ed. 2022. *Control of Communicable Diseases Manual*. 21st Edition. Washington, DC: APHA Press.

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