

## Virginia Department of Health Viral Hemorrhagic Fever (VHF): Overview for Healthcare Providers\*

<b>Organism*</b>	<b><i>Arenaviridae</i></b> : Lassa virus, Lujo virus, New World arenaviruses (Chapare, Guanarito, Junin, Machupo, and Sabia)	<b><i>Bunyaviridae</i></b> : Crimean-Congo hemorrhagic fever (CCHF) virus, Rift Valley fever (RVF) virus, hantavirus	<b><i>Filoviridae</i></b> : Ebola virus (Sudan, Zaire, Reston, Tai Forest, and Bundibugyo), Marburg virus, Ravn virus	<b><i>Flaviviridae</i></b> : Yellow fever (YF) virus, dengue virus, Alkhurma hemorrhagic fever (AHF) virus, Kyasanur Forest disease (KFD) virus, Omsk hemorrhagic fever (OHF) virus
<b>Reporting to Public Health</b>	Suspected or confirmed cases of VHF require <u>immediate</u> notification to the local health department (LHD). Suspected or confirmed cases of dengue and hantavirus pulmonary syndrome require reporting to the LHD within 3 days. See <a href="https://www.vdh.virginia.gov/health-department-locator/">https://www.vdh.virginia.gov/health-department-locator/</a>			
<b>Occurrence</b>	Lassa: West Africa Lujo: Zambia and South Africa New World arenaviruses: Americas	CCHF: Africa, Eurasia RVF: Africa, Saudi Arabia, Yemen	Africa	YF: Africa, tropical Americas Dengue: Asia, the Pacific, the Americas, Africa, and Caribbean AHF: Saudi Arabia, Egypt KFD: India; OHF: Siberia
<b>Natural Reservoir or Vector</b>	Rodents	CCHF: ticks, livestock are amplifying hosts; RVF: mosquito	Ebola: potentially fruit bats Marburg: fruit bats	YF, dengue: mosquito AHF, KFD, OHF: ticks
<b>Route of Infection</b>	All: Primarily inhalation of aerosols of rodent excreta; ingestion of contaminated food. In addition, Lassa: percutaneous, person-to-person transmission, sexual transmission Lujo: person-to-person transmission	All: Vector-borne, contact with infected animals. In addition, RVF: possible consumption of contaminated raw milk, reported airborne transmission in labs CCHF: person-to-person transmission	Contact with infected persons, body fluids or animals; percutaneous, person-to person, sexual transmission	All: Bite from infected insect. In addition, YF: parenteral or unexplained (possibly aerosol) transmission in labs; vertical transmission from mother to infant KFD: aerosol transmission in lab OHF: contact with infected animal; waterborne and airborne transmission might occur
<b>Risk Factors</b> (in addition to living in/traveling to endemic areas)	Rodent exposure (inhalation of aerosols, direct contact), close contact with infected patients; manipulating specimens in labs	Close contact with infected patients or animals; manipulating specimens in labs	All: Close contact with infected patients or animals; manipulating specimens in labs. In addition, Marburg: visiting bat caves	All: Insect exposure. In addition, AHF: contact with livestock; KFD: exposure to rural, outdoor settings, handling of cattle; OHF: contact with infected animals (e.g., muskrats), manipulating specimens in labs

<b>Case-fatality Rate</b>	Lassa: 1% overall, 15–20% among hospitalized cases Lujó: 80% in 1 outbreak	CCHF: 9–50% in hospitalized cases, 10–40% in outbreaks RVF: <1% overall, ~50% in hemorrhagic cases	Ebola: ~50% overall, 25–90% in outbreaks Marburg: 23–90%	YF: 30–60% for severe cases AHF: 1–20% in hospitalized cases KFD: 3–5%; OHF: <1–3%
<b>Incubation Period</b>	Lassa: 6–21 days New World arenaviruses: 5–21 days	CCHF, RVF: 2–10 days	Ebola, Marburg: 2–21 days	YF: 3–6 days Dengue: 4–7 days AHF: 2–4 days KFD and OHF: 3–8 days
<b>Clinical Description</b>	In general, initial signs and symptoms include fever, headache, muscle pain, erythematous maculopapular rash on the trunk, vomiting, diarrhea, abdominal pain, or bleeding			
<b>Differential Diagnosis</b>	Malaria, influenza, viral hepatitis, bacterial sepsis, toxic shock syndrome, meningococemia, salmonellosis, shigellosis, rickettsial disease, leptospirosis, borreliosis, psittacosis, dengue, trypanosomiasis, septicemic plague, rubella, measles, and hemorrhagic smallpox			
<b>Radiography</b>	Pulmonary edema or hemorrhage, acute respiratory distress, dilated bowels with signs of ileus or dynamic intestinal obstruction			
<b>Specimen Collection and Laboratory Testing</b>	Tests: serology, immunohistochemistry, PCR, antigen-detection enzyme-linked immunosorbent assay, and virus isolation. Testing requires high containment (Biosafety Level 3 or 4). Testing performed at CDC, except for preliminary testing for Ebola virus by PCR (Warrior Panel Multiplex RT-PCR or Ebola Zaire real time PCR) that can be performed at the Division of Consolidated Laboratory Services (DCLS); preliminary positive results require confirmatory testing at CDC. If VHF is suspected, notify LHD immediately to discuss the case and laboratory testing. Specimens may be sent to DCLS after VDH has approved testing. For questions about specimen collection, DCLS Emergency Officer can be reached 24/7 at 804-335-4617.			
<b>Treatment</b>	Ribavirin, supportive care New World viruses: monoclonal antibody therapy has shown efficacy in experimental models	Ribavirin, supportive care	Supportive care Ebola: Inmazole™ and Ebanga™, FDA-approved monoclonal antibodies for <i>Zaire ebolavirus</i>	Supportive care
<b>Postexposure Prophylaxis<sup>†</sup></b>	Lassa: oral ribavirin may be used for high-risk exposure	CCHF: ribavirin has shown some benefit	Not available	Not available
<b>Vaccine</b>	Argentine hemorrhagic fever (Junin virus): investigational vaccine available	RVF: investigational vaccine available	Ebola: ERVEBO® FDA-approved for <i>Zaire ebolavirus</i> . <sup>‡</sup> Other investigational vaccines available	YF: FDA-approved vaccine available KFD: vaccine used in India
<b>Infection Control<sup>§</sup></b>	In general, immediately isolate the patient and implement Standard, Contact and Droplet Precautions for the duration of illness. Hemorrhagic fever specific barrier precautions (Standard, Contract, and Airborne Precautions) are recommended if bioterrorism is suspected or if the epidemiology of virus transmission is unpredictable or unknown. For Ebola, see CDC’s guidance for clinicians: <a href="https://www.cdc.gov/vhf/ebola/clinicians/index.html">https://www.cdc.gov/vhf/ebola/clinicians/index.html</a>			

\*Other hemorrhagic fever viruses exist within these categories. However, the viruses that pose the most serious risk as biological weapons are: arenaviruses (Lassa virus, New World arenaviruses), bunyaviruses (Rift Valley fever virus), filoviruses (Ebola virus, Marburg virus), and flaviviruses (yellow fever virus, Omsk hemorrhagic fever virus, Kyasanur Forest disease virus); dengue virus, Crimean-Congo hemorrhagic fever viruses and hantaviruses are considered less likely to be used as biological weapons (Borio, et al 2002). The role of other hemorrhagic fever viruses as potential weapons is not known.

<sup>†</sup>The Working Group on Civilian Biodefense did not recommend prophylactic antiviral therapy for persons exposed to any hemorrhagic fever viruses (including Lassa virus) in the absence of clinical illness (Borio, et al 2002); instead, the group recommended monitoring the exposed person for 21 days and, if symptoms suggestive of VHF develop or fever (≥101°F) is documented, ribavirin therapy should be initiated unless another diagnosis is confirmed (or the etiologic agent is known to be a filovirus or flavivirus). Borio, et al 2002 available here: <https://jamanetwork.com/journals/jama/fullarticle/194908>

<sup>‡</sup>ERVEBO® is not commercially marketed but is in the Strategic National Stockpile. Available from CDC for preexposure vaccination: <https://www.cdc.gov/vhf/ebola/clinicians/vaccine/index.html>

<sup>§</sup>Source: <https://www.cdc.gov/infectioncontrol/guidelines/isolation/appendix/type-duration-precautions.html> for VHFs caused by Lassa, Ebola, Marburg, or Crimean-Congo fever viruses. Note that Borio, et al (2002) recommends additional airborne precautions because airborne transmission of VHFs cannot be conclusively excluded. For Ebola, CDC has developed extensive infection control guidance: <https://www.cdc.gov/vhf/ebola/clinicians/index.html>. Clinicians should consult with their local health department for additional guidance.