*epi*TRENDS

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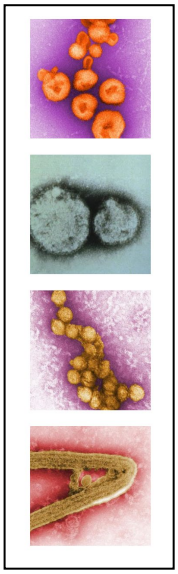
Viral Hemorrhagic Fevers

Viral hemorrhagic fevers are viral illnesses that can lead to a syndrome of fever and bleeding in humans (and other mammals). Two current outbreaks of Marburg virus have renewed interest in the topic.

Background

Several families of viruses have members associated with viral hemorrhagic fever (VHF). All are RNA viruses, making them susceptible to standard viral disinfectants and environmental deactivation. The viral families and some of well-known human illnesses they can cause include the following:



Arenavirus: Lassa fever, Lujo hemorrhagic fever

Bunyavirus: hantavirus

Paramyxovirus: Hendra, Nipah

Nairovirus: Crimean-Congo hemorrhagic fever

Phenuivirus: Rift Valley fever

Flavivirus: Kyasanur Forest disease

Filovirus: Ebola, Marburg

Although sometimes causing similar illnesses, the arthropod-transmitted flaviviruses causing dengue and yellow fever are usually considered separately and are not included as viral hemorrhagic fevers. Washington Department of Health maintains separate guidelines for those conditions and for hantavirus (see Resources).

Each agent has one or more specific animal reservoirs, often a known or suspected bat or rodent, with periodic spill-over to a human. Single human cases may occur, or sustained person-to-person transmission can result in an outbreak. Virus is present in all body fluids (blood, feces, semen, breast milk), and in fluids contaminating clothing, bedsheets, medical equipment, or personal protective equipment (PPE). Viral particles can enter a non-infected person through the eyes, nose, mouth, or broken skin, and can be sexually transmitted. The infectious dose for some viruses (such as Ebola virus) is very low, likely 1-10 particles, so even apparently minor exposures can result in disease transmission. VHF does not spread through casual contact.

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For Ebola and Marburg (and likely for other VHF agents), the risk of transmission is highest when patients have vomiting and diarrhea or other severe symptoms, as well as during active childbirth. After death, when a body begins to release fluids and decompose, is perhaps the most dangerous period of all. Contagiousness continues for days even when bodily fluid have dried, so people participating in funeral and burial practices can be at high risk for infection.

Clinical Features

Symptoms of VHF may overlap with many other conditions occurring in a region. Sudden fever, chills, and headache early in the disease are also consistent with malaria or COVID-19. Severe diarrhea can occur with typhoid and other enteric infections. Multiple viral infections can cause a rash. A miscarriage with bleeding can happen with or without VHF. Some VHFs such as Lassa fever can cause subclinical or asymptomatic infections; Ebola and Marburg infections are rarely, if ever, asymptomatic. Not all infections result in hemorrhage, multi-organ failure, and shock, so case fatality ratio (CFR) calculation is challenging, particularly with limited laboratory testing; CFR estimates range anywhere from 0% to 90%. Survivors may have long-term effects involving the eyes and joints, in addition to psychological stresses from the stigma of the disease and the loss of family members.

The case definition requires laboratory results (PCR, immunohistochemistry, ELISA, viral isolation) which may not be readily available in all settings.

Many VHFs have limited vaccines and treatments. For Ebola outbreaks due by *Zaire ebolavirus*, there are two licensed vaccines. Vaccines are in development for other species of Ebola virus, including *Sudan ebolavirus,* as well as for *Marburgvirus.* Treatments for VHF include several experimental monoclonal antibodies (MABs). Treatment is otherwise supportive, often requiring intensive fluid volume and electrolyte replacement, pressors to maintain blood pressure, oxygenation, nutritional support, and anti-emetic and anti-diarrheal agents.

Epidemiology

The first VHF outbreaks in humans were recognized in the 1960s and 1970s. Ebola outbreaks in particular were identified every few years over the past three decades. The table has major Ebola virus outbreaks since today's Democratic Republic of the Congo (DRC) had the first outbreak:

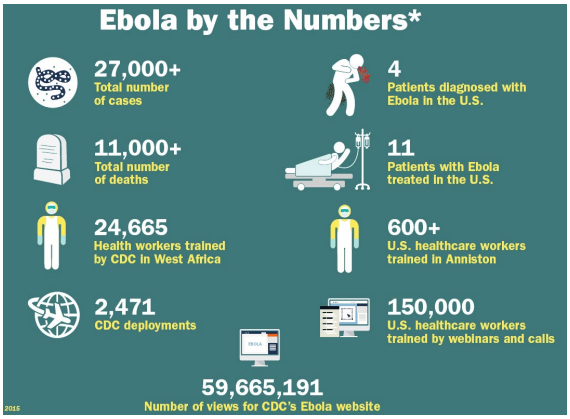
Year	Country	Cases* / CFR	Species
1976	Zaire (DRC)	318 / 88%	*Zaire ebolavirus*
1976	Sudan (S Sudan)	284 / 53%	*Sudan ebolavirus*
1995	Zaire (DRC)	315 / 79%	*Zaire ebolavirus*
2000	Uganda	425 / 53%	*Sudan ebolavirus*
2002	Republic of Congo	143 / 89%	*Zaire ebolavirus*
2007	DRC	264 / 71%	*Zaire ebolavirus*
2007	Uganda	149 / 25%	*Bundibugyo ebolavirus*
2014-2016	Parts of West Africa	28,646 / 40%	*Zaire ebolavirus*
2018-2020	DRC	3,470 / 66%	*Zaire ebolavirus*
2020	DRC	130 / 42%	*Zaire ebolavirus*
2022	Uganda	164 / 33%	*Sudan ebolavirus*

* Counts include varying proportions of laboratory confirmed vs. clinically diagnosed cases

The largest VHF outbreak occurred in West Africa during 2014-2016 in Guinea, Liberia, and Sierra Leone. The response in affected countries was to provide rapid isolation and diagnosis of cases, rapid contact tracing, screening of departing travelers, and education to the public about prevention, such as altered practices during funerals. A very large majority of cases involved known household contact or exposure in a health care setting. A few cases were diagnosed in other countries including in Senegal, Mali, Spain, the United States, the United Kingdom, and Italy among travelers, with little or no subsequent transmission within those countries.

Disruption of the health care system including illnesses and deaths among front line health care workers likely contributed to many collateral deaths during the 2014-2016 outbreak. Treatment became less available for conditions such as tuberculosis, pneumonia, diarrhea, AIDS, and malaria. Preventative services such as routine vaccinations for deadly childhood illnesses were also halted, to devastating effect in the years following the outbreak. Complications of childbirth, trauma, and chronic health conditions were also more likely to receive less care than usual as health care and public health resources were shifted to controlling the outbreak.

Response in the United States involved issuing notices not to travel to affected areas (and if travel was deemed essential to take measures to avoid other infections such as malaria or enteric diarrhea during travel to reduce diagnostic confusion), screening travelers leaving affected areas, monitoring travelers arriving to this country from affected areas including offering free phones, educating health care providers, preparing health care facilities to assess and to treat potential cases, increasing availability of reference laboratory testing, and communicating with the public. Other actions taken at national and international levels addressed traveler screening, providing patient care, and supporting control of the outbreak in the affected countries.



US response to the 2014-2016 Ebola outbreak in West Africa

In February, 2023, Equatorial Guinea declared its first outbreak of Marburg virus, another filovirus. In March, an apparently unrelated outbreak of Marburg was also reported in Tanzania. Guidances are under development but at present there is only a Level 2 Travel Alert (practice enhanced precautions) from the Centers for Disease Control and Prevention for travel to Equatorial Guinea and a Level 1 Travel Alert (practice usual precautions) for travel to Tanzania.

Responding to VHF outbreaks presents many challenges. Affected areas are often medically underserved and need significant allocation of resources. Having sufficient protective equipment available as well as knowing how to don (put on) and doff (remove) this equipment safely can be essential to prevent the loss of health care staff.

Office of Communicable Disease Epidemiology is available for consultation about suspected cases. The person should be placed in isolation while arrangements are made for testing, which can be initiated at the Washington State Public Health Laboratories. Providing health care and taking clinical specimens should be done by staff using personal protective equipment for which they have been trained. Public health and health care interventions should be science-based and not influenced by fear, prejudice, or racism.

Resources

Centers for Disease Control and Prevention

Viral hemorrhagic fever agents: https://www.cdc.gov/vhf/

Ebola virus disease: https://www.cdc.gov/vhf/ebola/index.html

Marburg virus disease: https://www.cdc.gov/vhf/marburg/

Travel health notices: https://wwwnc.cdc.gov/travel/notices

Screening patients: https://www.cdc.gov/vhf/ebola/clinicians/evaluating-patients/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvhf%2Febola%2Fclinicians%2Fevaluating-patients%2Fcase-definition.html

Personal protective equipment: https://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html

Infection control: https://www.cdc.gov/vhf/ebola/clinicians/evd/infection-control.html

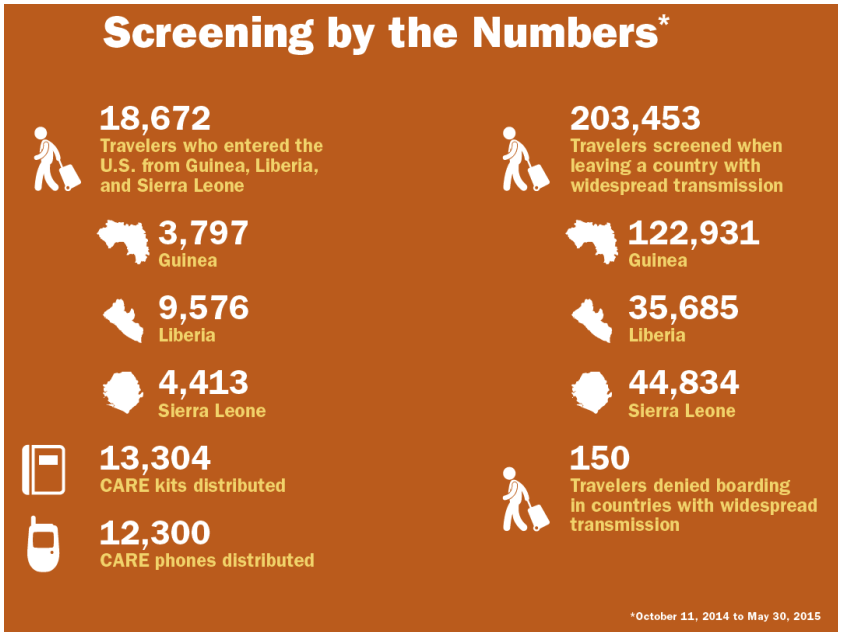
Guidance for laboratories testing routine clinical specimens: https://www.cdc.gov/vhf/ebola/laboratory-personnel/safe-specimen-management.html

Cleaning and disinfecting healthcare environments: https://www.cdc.gov/vhf/ebola/clinicians/cleaning/index.html

https://emergency.cdc.gov/epic/pdf/Ebola-Slides_Final.pdf

Washington State Department of Health

Surveillance guideline: https://doh.wa.gov/sites/default/files/legacy/Documents/5100/420-126-Guideline-Ebola.pdf?uid=64347c51a03d1



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