

VIRAL HEMORRHAGIC FEVERS

Bioterrorism Agent Profiles for Health Care Workers

Causative Agent:

Arenaviridae – Junin virus (Argentine hemorrhagic fever), Machupo virus (Bolivian hemorrhagic fever), Guanarito virus (Venezuelan hemorrhagic fever), Sabia virus (Brazilian hemorrhagic fever), Lassa virus (Lassa fever)

Bunyaviridae – Rift Valley fever virus, Crimean-Congo hemorrhagic fever virus, Hantaan and related viruses of the hantavirus genus (hemorrhagic fever with renal syndrome)

Filoviridae – Ebola virus, Marburg virus

Flaviviridae – Dengue virus, Yellow fever virus, Omsk hemorrhagic fever virus, Kyasanur Forest disease virus

Routes of Transmission: Dependent on the specific virus. Routes transmission include the bite of an infected tick or mosquito, inhalation of aerosol generated from infected rodent excreta, contact with infected animal carcasses, or person-to-person transmission by close contact with infectious body fluids.

In the laboratory all the viral hemorrhagic fever agents, except dengue virus, are infectious by aerosol.

Incubation Period: The overall incubation period ranges from 2 to 21 days.

Clinical Effects: There is great diversity in the symptoms of these illnesses and infection by these viruses does not necessarily lead to viral hemorrhagic fever disease. Common presenting symptoms and complaints include high fever, headache, malaise, arthralgias, myalgias, nausea, abdominal pain, and nonbloody diarrhea. Clinical examination may reveal fever, hypotension, relative bradycardia, tachypnea, conjunctivitis, and pharyngitis. Rash and cutaneous flushing are typical manifestations, though the specific characteristics of the rash differ by disease. Full blown viral hemorrhagic fevers can evolve to progressive hemorrhagic diathesis, such as petechiae, mucous membrane and conjunctival hemorrhage; hematuria; hematemesis; and melena, disseminated intravascular coagulation, and circulatory shock.

Arenaviruses progress to illness gradually, while filoviruses are characterized by an abrupt onset of disease.

Lethality: The mortality rate varies greatly among these diseases, from 0.5% for Omsk hemorrhagic fever to 90% for Ebola (subtype Zaire).

Transmissibility: Some viral hemorrhagic fevers can be spread person to person. These are: Argentine hemorrhagic fever, Bolivian hemorrhagic fever, Venezuelan hemorrhagic fever, Brazilian hemorrhagic fever, Lassa fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndrome, Ebola hemorrhagic fever, and Marburg hemorrhagic fever.

Primary Contamination & Methods of Dissemination: A likely method of dissemination as a biological weapon would be through aerosolization.

Secondary Contamination & Persistence of Organism: Some of the viral hemorrhagic fever viruses can remain present in bodily fluids for long periods after clinical recovery. Because of this continued risk of contagion patients convalescing from an arenaviral or a filoviral infection should abstain from sexual activity for three months following clinical recovery.

Decontamination & Isolation:

Patients – Strict hand hygiene plus use of double gloves, impermeable gowns, face shields, eye protection, leg and shoe coverings, and N95 respirators are recommended. The majority of person-to-person transmission of filoviruses and arenaviruses has been due to direct contact with infected blood and bodily fluids.

Equipment, clothing & other objects – Environmental surfaces in patients' rooms and contaminated medical equipment should be disinfected with 0.5% hypochlorite solution (1 part household bleach + 9 parts water = 0.5% solution). Contaminated linens and clothes can be placed in double bags and washed without sorting in a normal hot water cycle with bleach. Alternatively, they may be autoclaved or incinerated.

Outbreak Control: All individuals who have been potentially exposed to a hemorrhagic fever virus should be placed under medical surveillance for 21 days and instructed to record their temperatures twice daily and report any symptoms they are experiencing, including any temperature 101° F or higher.

Laboratory testing: Laboratory detection consists of antigen-capture enzyme-linked immunosorbent assay (ELISA), IgM antibody detection by antibody-capture ELISA, RT-PCR, and viral isolation. The most useful of these for the clinical setting are antigen detection (by ELISA) and RT-PCR. If viral hemorrhagic fever is suspected, the laboratory should be notified so that they can avoid procedures that could aerosolize the virus.

Therapeutic Treatment: Treatment is mainly supportive and should include maintenance of fluid and electrolyte balance, circulatory volume, and blood pressure. Early vasopressor support with hemodynamic monitoring should be considered since some viral hemorrhagic fevers have a propensity for pulmonary capillary leaks and vigorous fluid resuscitation of hypotensive patients can contribute to pulmonary edema without reversing hypotension. Mechanical ventilation, renal dialysis, and antiseizure therapy may be required. Intramuscular injections, aspirin, nonsteroidal anti-inflammatory drugs, and other anticoagulant therapies that would aggravate a bleeding disorder should be avoided.

There are no antiviral drugs approved by the US Food and Drug Administration for treatment of viral hemorrhagic fevers. Ribavirin, a nucleoside analog, has some in vitro and in vivo activity against Arenaviridae and Bunyaviridae but no utility against Filoviridae or Flaviviridae. Ribavirin is available via compassionate use protocols.

Prophylactic Treatment: The prophylactic use of oral ribavirin has been suggested for high-risk contacts (those who have had direct exposure to body fluids) of patients with either Congo-Crimean hemorrhagic fever or Lassa fever.

Yellow fever is the only licensed vaccine for any of the viral hemorrhagic fevers, but it is not efficacious for post exposure disease prevention. Under an investigational new drug application vaccines are available for Argentine hemorrhagic fever and Rift Valley fever. A vaccine for Kyasanur Forest disease is also in existence.

Differential Diagnosis: Differential diagnoses should include illnesses that cause severe sepsis and hemorrhage, including influenza, viral hepatitis, staphylococcal or gram negative sepsis, toxic shock syndrome, meningococemia, salmonellosis and shigellosis, rickettsial diseases (such as Rocky Mountain spotted fever), leptospirosis, borreliosis, psittacosis, dengue, hantavirus pulmonary syndrome, malaria, trypanosomiasis, septicemic plague, rubella, measles, hemorrhagic smallpox, idiopathic or thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, acute leukemia, and collagen-vascular diseases.

References:

Chin J. Control of Communicable Diseases Manual, Seventeenth Edition, American Public Health Association; 2000.

Borio L, Inglesby T, Peters CJ, et al. Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management, JAMA. 2002; 287: 2391-2405.
Available at <http://jama.ama-assn.org/content/vol287/issue18/index.dtl>

Kortepeter M, Christopher G, Cieslak T, et al. Medical Management of Biological Casualties Handbook, U.S. Army Medical Research Institute of Infectious Diseases, U.S. Department of Defense; 2001:54-61
Available at <http://www.usamriid.army.mil/education/bluebook.htm>

Jahrling PB. Viral Hemorrhagic Fevers. In: Zajtchuk R, Bellamy RF, eds. Medical Aspects of Chemical and Biological Warfare. Washington, DC: Office of the Surgeon General, U.S. Department of the Army; 1997:591-602.
Available at <http://www.nbc-med.org/SiteContent/HomePage/WhatsNew/MedAspects/contents.html>

For more information call (602) 364-3289

Frequently Asked Questions About Viral Hemorrhagic Fevers

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 four distinct families: arenaviruses, filoviruses, bunyaviruses, and flaviviruses. 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, and other field rodents 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 and Marburg viruses are well-known examples.

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

Frequently Asked Questions About Viral Hemorrhagic Fevers

(continued from previous page)

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.

People usually become infected with hemorrhagic fevers only in areas where the specific host lives. However, people can be infected by an animal or insect exported from its native habitat. For example, Marburg virus outbreaks occurred in Yugoslavia, and in Marburg and Frankfurt, Germany when laboratory workers handled infected imported monkeys. Also, human travel can spread hemorrhagic fever beyond its natural habitat. In 1996, a health care worker in Gabon unknowingly became infected with Ebola hemorrhagic fever (Ebola HF). He later traveled to South Africa, required hospitalization, and fatally infected a nurse. As world-wide travel increases, so does the risk of spread of unusual infections such as hemorrhagic fevers.

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 hemorrhagic fever 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 anti-viral 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 the animals or insects that carry the infection.

If a case of human VHF does occur, efforts should focus on preventing further transmission. 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 insects, prevention efforts often focus on community-wide insect control such as spraying and eliminating breeding places. In addition, people are encouraged to use personal protective measures, such as insect repellent, proper clothing, bednets, window screens, and other insect barriers to avoid being bitten.

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

The World Health Organization and CDC have developed practical, hospital-based guidelines, titled Infection Control for Viral Haemorrhagic Fevers In the African Health Care Setting. This manual can help health-care facilities with few financial resources to recognize cases and prevent further hospital-based disease transmission using locally available materials.

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.

For more information call (602) 364-3289