VHF
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Viral Hemorrhagic Fever (VHF) is a syndrome caused by any of a number of RNA viruses.

The Viral Hemorrhagic Fevers, or VHFs, are comprised of a variety of viral illnesses that share a common feature in their ability to produce a febrile hemorrhagic state in infected patients. There has been no known use of these agents as biological weapons but the concern exists that the use of these very pathogenic viruses is feasible, and given the high degree of attention focused on such diseases as Ebola in the media and in movies, there is a great potential for widespread fear.

The two families of viruses that are of most concern based on feasibility of production and high mortality are the filoviruses, which include Ebola and Marburg viruses; and the arenaviruses, which include the agents of the South American Hemorrhagic Fevers and Lassa Fever virus. Flaviviruses such as dengue and Yellow Fever viruses and bunyaviruses including Congo-Crimean Hemorrhagic Fever virus are also potential bioweapon agents producing VHF.

All of the agents cause sporadic disease or epidemics in areas of endemicity. Routes of transmission are variable, most of the diseases are zoonotic with spread via arthropod bites or contact with infected animals. Person-to-person spread is a major form of transmission for many of the viruses. Filoviruses and Congo-Crimean HF virus are readily transmitted through blood and other body fluids. Nosocomial spread of these diseases to healthcare workers via needle sticks and fluid contact is well-documented and greatly feared in regions with limited healthcare resources. Nosocomial transmission of some arenavirus infections has also been reported. Direct transmission of natural infection between humans via a respiratory route is uncommon for all the VHF's and has been difficult to prove. However, it is likely possible for many, including Ebola HF. All but dengue virus can cause infection as an environmental or laboratory-produced aerosol. Mortality is variable but can be as high as 90% during outbreaks of Ebola.

All of the potential agents of VHF are RNA viruses. This is a photo of an electron micrograph of ebola virus.

Virus enters the body through mucosal surfaces in contact with infectious fluids, needlesticks or via inhalation. Pathogenesis studies of ebola in animals have shown that a high-grade viremia occurs within 2 days of inoculation and that foci of infection occur in multiple organs, particularly the liver, spleen and lungs. Viral shedding from mucosal surfaces occurs but is preceded by fever and other systemic symptoms. Symptoms appear after a variable incubation period, but it ranges from 2 days to 3 weeks, depending on the disease. Involvement of the vasculature and coagulation system leads to disruptions in fluid and clotting homeostasis that can cause vascular leakage with edema, and significant hemorrhage.

Incubation periods are variable and range from 2 days to 3 weeks. Common early symptoms mimic those of other viral diseases such as influenza with fevers, myalgias and malaise. Disease can range from minimally symptomatic to fulminant, and symptomatology varies depending on the specific disease. However, all share the potential for the development of a bleeding diathesis manifested by severe hemorrhage from mucosal surfaces and petechiae. The severity of this hemorrhagic state is variable and may be absent. Bleeding can be further complicated by massive shifts in intravascular volume and edema as a result of disrupted vascular permeability. Shock is the end result in the most severe cases. Thrombocytopenia, leukopenia and hepatitis are common findings in many of the diseases. Diseases most often misdiagnosed as VHF include malaria, typhoid, rickettsial disease, meningococcemia, and any cause of disseminated intravascular coagulation (DIC).

This photo demonstrates cutaneous ecchymosis and edema in a patient with Congo-Crimean Hemorrhagic Fever.

A high index of suspicion is necessary to diagnose a VHF because there are no readily available rapid confirmation tests. An initial diagnosis should be made presumptively on clinical features, especially in an outbreak setting. A confirmed diagnosis can be made retrospectively for most of the VHF agents by serological methods. Virus can be isolated from blood for some of the VHF's, but require a laboratory with capability of highly advanced safety measures (BSL-4). Experimental rapid diagnostic tests such as PCR may be available for some agents at reference laboratories.

For all patients with VHF, supportive therapy is the mainstay of management. Intravascular volume support can be complicated by vascular fragility. Rapid fluid shifts into extravascular spaces require aggressive volume resuscitation, however the pulmonary vasculature is also prone to leakage at this time, increasing the risk of ARDS. Routine attention to electrolyte balance, oxygenation and hemodynamic status must be given. Hemorrhage should be addressed with specific therapy as guided by coagulation studies, and by avoidance of invasive procedures if possible. Sedatives and other hepatically cleared drugs should be used judiciously. Experience with antivirals is limited, however ribavirin has been used successfully as specific antiviral therapy for

CCHF, Lassa Fever and others. It has no activity versus the filovirus or flavivirus hemorrhagic fevers.

Other than oral ribavirin, which has been used investigationally after high-risk exposure to CCHF and Lassa Fever, there is no specific prophylaxis for asymptomatic persons with suspected exposure to VHF agents. Those potentially exposed should be monitored closely for development of VHF symptoms. Even for the few agents with an available vaccine, immunity takes too long to develop for vaccination to be useful as post-exposure prophylaxis.

Yellow Fever is the only VHF with an available licensed vaccine. It has proven to be effective when administered to travelers to endemic areas and serious adverse effects are rare.

All patients should be placed in strict respiratory and contact isolation, including the use of face mask and goggles for close contact. Those with the highest potential for spread because of severe cough, hemorrhage, diarrhea, etc. should also be isolated under airborne precautions in a negative pressure room with requirement for use of a HEPA filtered respirator.