

# Ebola Hemorrhagic Fever

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**Context:** Ebola hemorrhagic fever (EHF) is amongst severe and fatal viral hemorrhagic fevers. In February 2014, a strain of the Ebola virus appeared in Guinea and then in Liberia, Sierra Leone, and Mali. The aim of this study was to review the literature on EHF and discuss its routes of transmission and prevention.

**Evidence Acquisition:** We searched medical databases (PubMed, Scopus) from July 1970 to July 2014. The key words for the literature search were as follows; Ebola hemorrhagic fever, epidemiology, transmission routes, clinical manifestation, treatment and prophylaxis.

**Results:** On the basis of the literature search, the researchers believe that bats are the most likely reservoir. Four of five subspecies of Ebola virus have caused disease in humans. Manifestation of Ebola begins abruptly with a sudden onset of an influenza-like syndrome characterized by general malaise, fever, sore throat, severe headache, joint pain, muscle pain and chest pain. There is no Ebola virus specific treatment. Treatment is usually supportive and includes minimizing invasive procedures, and balancing fluids and electrolytes. Adequate sterilization procedures isolate patients and this is a major step towards prevention of transmission of virus to other people.

**Conclusions:** Ebola viruses are highly contagious. Understanding the epidemiology, clinical presentation, prompt diagnosis, suitable treatment and isolation are the main factors for prevention of death and transmission of virus to other people.

**Keywords:** Ebola Hemorrhagic Fever; Diagnosis; Prevention; Treatment

## 1. Context

Ebola hemorrhagic fever (EHF) is caused by Ebola viruses. The first Ebola virus species was discovered in 1976 in Republic of the Congo near the Ebola River. Since then, outbreaks have been reported, sporadically (1-3). The disease is first acquired by a population when a person comes in contact with the blood or bodily fluids of an infected animal such as a monkey or Fruit bat (1-5). Fruit bats are believed to carry and spread the disease without being affected by the virus. When infection occurs, it can spread from one person to another (1-3). People who survive may be able to transmit the disease sexually for nearly two months (1, 2, 6). Symptoms start two days to three weeks after a person comes in contact with the virus and they include fever, chills, headaches, sore throat, muscle pain, and then nausea, vomiting and diarrhea along with decreased function of the liver and kidneys. At this time some people experience bleeding (1-3, 7-9). To diagnose the patient, other diseases with similar symptoms such as malaria, and other viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, sepsis, hepatitis and blood malignancies should be excluded (1-3, 10, 11). The blood should be examined for antibodies against the virus, or polymerase chain reaction (PCR) should be performed to confirm the diagnosis. Treatment is primarily supportive and includes decreasing invasive

procedures, balancing fluids and electrolytes, administration of procoagulants to control hemorrhaging, pain management and administration of antibiotics to treat secondary infections (12-14). Without an approved vaccine, prevention of Ebola hemorrhagic disease (EHD) predominantly involves behavior modification, proper personal protective equipment and sterilization. The recent outbreak first began in Guinea during March 2014. Since its initial outbreak, the virus has spread to Liberia, Sierra Leone and Mali. Here, we aimed to review the literature on Ebola disease and study its routes of prevention and treatment.

## 2. Evidence Acquisition

We searched medical databases (PubMed, Scopus) from July 1970 to July 2014. The key words were as follows; Ebola hemorrhagic fever, epidemiology, transmission routes, clinical manifestation, treatment and prophylaxis.

## 3. Results

We found data on the epidemiology of EHF, transmission routes, clinical manifestation, diagnosis, treatment and prevention methods as below:

### 3.1. Viruses and Cause of Ebola Hemorrhagic Fever

Ebola hemorrhagic fever is caused by four of the five viruses classified in the genus Ebola virus, family Filoviridae and order Mononegavirales (15, 16). Four from five subspecies of Ebola virus are the etiological agents in humans; Zaire Ebola virus, Sudan Ebola virus, Tai Forest Ebola virus and Bundibugyo Ebola virus. The fifth virus, named Reston virus (RESTV), is thought to not cause disease in humans (15-18). Between 1976 and 1998, no Ebola virus was detected in samples from mammals, birds, reptiles and arthropods of outbreak regions (16, 17). However, the virus was detected in the carcasses of gorillas and chimpanzees during outbreaks between 2001 and 2003, which later became the source of infection for humans. Now, it seems that fruit bats spread the disease without being affected by the virus. Birds, arthropods and Plants have been considered as possible reservoirs yet, fruit bats are the most likely candidates. Thus, of 24 plant species and 19 vertebrate species experimentally inoculated with EBOV, only bats became infected (1-4, 19-21).

### 3.2. Mode of Transmission

Ebola hemorrhagic disease occurs after an Ebola virus is transmitted to a human by contact with an infected animal host. Human-to-human transmission occurs by direct contact with blood or infected fluids from an infected individual (even from of an infected dead person) or by contact with contaminated medical equipment such as needles (1-4, 6, 21). Nosocomial transmission has been reported from African countries due to the lack of implementation of universal precautions (1-4). However, until now, aerosol transmission has not been reported during the last and recent outbreaks. Once a person acquires the infection, the disease can spread from one person to another. People who survive can transmit the virus sexually for about two months (1, 4, 21-25).

### 3.3. Clinical Manifestations

Ebola hemorrhagic disease is a human disease caused by Ebola viruses. Clinical manifestation of EHD begins with a sudden onset of an influenza-like syndrome. Symptoms begin two days to three weeks after the individual comes in contact with the virus (1-4, 7-9). These manifestations include; high fever, chills, sore throat, headaches and muscle pain, followed by nausea, vomiting and diarrhea along with decreasing function of the kidneys and liver. Some patients have hemorrhagic diathesis. People who survive may transmit the disease sexually for nearly two months (1-3, 10, 11). Other diseases with similar presentations such as hepatitis, malaria, Marburg virus disease, and other viral hemorrhagic fevers should be excluded. Respiratory tract involvement is characterized by pharyngitis with sore throat, cough and dyspnea. The central nervous system is also affected and patients experience severe headaches, sometimes agitation, confusion, depression, seizures and even coma. Cutaneous presentations such as:

maculopapular rash, petechiae, purpura and hematomas (more around needle injection sites) have been reported (1-4, 8, 9). Bleeding from mucous membranes and puncture sites is seen in 40-50% of patients. Sources of bleeding include; gastrointestinal tract, nose, gingiva and vagina. Development of hemorrhagic symptoms is indicative of a poor prognosis. Up to 90% of people who had acquired the virus have died. The World Health Organization (WHO) describes Ebola as "one of the world's most virulent diseases (1-4, 8, 23-26). The WHO has reported that the outbreak in Liberia, Guinea, and Sierra Leone has infected 1,323 people and killed more than 729 this year, as of July 27. In August, 2014, the Guinea Ministry of Health reported a total of 485 suspected and confirmed cases of Ebola virus disease (EVD), including 358 fatal cases (27).

### 3.4. Diagnosis

The most important method for diagnosis of EHD is via the medical history of the patient, especially travel and occupational history and exposure to wild animals such as fruit bats. Ebola hemorrhagic fever should be excluded from Marburg virus disease, other viral hemorrhagic fevers, falciparum malaria, typhoid fever, typhus, gram-negative septicemia and relapsing fever (1-4, 10, 11). Other infectious diseases that should be included in the differential diagnosis include: measles, fulminant viral hepatitis, leptospirosis, plague, Q fever, candidiasis, histoplasmosis and visceral leishmaniasis. Non-infectious diseases that can be confused with EHD are acute promyelocytic leukemia, hemolytic uremic syndrome, snake bite, clotting factor disorders, thrombotic thrombocytopenic purpura (TTP) and Kawasaki disease (10, 28-31). During an outbreak, virus isolation and electron microscopy are often not feasible options. The most common diagnostic ways are RT-PCR in conjunction with Enzyme-linked immunosorbent assay (ELISA). Indirect immunofluorescence assays (IFAs) are no longer used for diagnosis of EVD in the field (32-37).

### 3.5. Treatment

There is no Ebola virus specific treatment. Treatment is supportive and includes; balancing fluids and electrolytes, decreasing invasive procedures, administration of coagulants to control hemorrhagic diathesis, pain management and administration of antibiotics to treat secondary infections (1-4, 22, 38, 39). Equine immunoglobulin against Ebola virus (EBOV) was used in Russia to treat a laboratory worker who was accidentally infected with EBOV, but the patient died, anyway. During an outbreak in the Republic of the Congo in 1995, seven of eight patients who had received blood transfusions from convalescent individuals survived (1-4, 6, 21, 22). However, this potential treatment is considered controversial. Recent studies have shown that monoclonal antibodies are effective for preventing morbidity and mortality in nonhuman primates when used as a post exposure prophylactic within 1 or 2 days of contact with the virus (1-3, 39).

### 3.6. Prevention

Ebola virus is highly contagious. Governments often quickly quarantine the area to prevent an outbreak. Airline crews should be educated about the symptoms of Ebola and be told to quarantine anyone who looks infected when an outbreak of Ebola disease progresses as bodily fluids from diarrhea, vomiting, and bleeding are hazardous (22, 38-40). Therefore, patients should be isolated, and observed under strict barrier nursing procedures with the use of a disposable face mask, gloves, goggles, and a gown at all times, especially for all medical staff and also visitors. The aim of all of these techniques is to avoid contact with the blood or other infected secretions of patients, even those who are dead. These recommendations are also advised for Crimean-Congo hemorrhagic fever and other viral hemorrhagic fevers (1, 2, 6, 21, 22, 38, 41-46). Vaccines have protected nonhuman primates. Immunization takes six months. In 2003, a vaccine using an adenoviral vector carrying the Ebola spike protein was tested on crab-eating macaques. Then monkeys were challenged with the virus for twenty-eight days and remained resistant. Another vaccine, in 2005, based on attenuated recombinant vesicular stomatitis virus vector carrying the Ebola glycoprotein was able to protect nonhuman primates. On 6th of December 2011, the development of a successful vaccine against Ebola for mice was reported. It could be freeze-dried and stored for a long time, in wait for an outbreak (1, 2, 4, 47, 48). However, until now, the Food and Drug Administration (FDA) has not approved any vaccines (1-4, 25, 47, 48). At this time, it is reasonable to assume that patient isolation is the main method for prevention of disease and the best treatment is isolation.

### 4. Conclusions

Ebola viruses are highly infectious and contagious. Therefore, understanding the clinical presentation, prompt diagnosis and suitable treatment are major steps towards the prevention of death and transmission of virus to other people. Also, in order to avoid transmission of the virus, adequate sterilization procedures, patient isolation, and use of strict barrier nursing procedures for all medical personnel and visitors are advised.

### Authors' Contributions

Maryam Keshkar Jahromi and Batool Sharifi Mood wrote the paper. Each of the two authors had equal roles in the design and writing of the manuscript.

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