

Resources, Guidance, Control and Prevention for Ebola Virus Disease- An Overview

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ABSTRACT

Since the current Ebola Virus Disease (also referred to as Ebola Haemorrhagic Fever) outbreak began in Guinea in December of 2013, the outbreak now involves trans-mission in Guinea, Liberia, Nigeria, and Sierra Leone. Ebola haemorrhagic fever (EHF) is a zoonosis affecting both human and non-human primates (NHP). Ebola virus (formerly officially designated Zaire Ebola virus, or EBOV) was first seen infecting humans in African continent; especially Sudan, Democratic Republic of Congo, Zaire and nearby countries. Fruit bats of the Pteropodidae family are considered to be the natural host of the Ebola virus. The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. The World Health Organization (WHO) reports that this is the largest Ebola Virus Disease (EVD) outbreak ever recorded. EVD outbreaks have a case fatality rate of up to 90%. The research is on-going on development of making vaccine to curb this virus yet licensed success or specific treatment is not achieved.

Keywords: Ebola haemorrhagic fever, EBOV, WHO, NHP, EVD

INTRODUCTION

The disease is caused by infection with Ebola virus, named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, where it was first recognized. The Ebola virus disease (EVD), previously known as Ebola haemorrhagic fever (Ebola HF) is a severe condition caused by a virus belonging to genus Ebola virus, family Filoviridae and order Mononegavirales. The virus is one of two members of a family of RNA viruses called the Filoviridae^[1].

These five viruses are-

Bundibugyo virus (BDBV):

Ebola virus or Zaire Ebola virus (EBOV):

This is most fatal among all five and has the highest case-fatality rate, up to 90% in some epidemics. The first outbreak took place on 26 August 1976 in Yambuku. Mballo Lokela, a 44-year-

old school teacher, became the first recorded case. The symptoms resembled malaria, and subsequent patients received quinine. The initial transmission was believed to be due to reuse of the needle for Lokela's injection without sterilization. Subsequent transmission was also due to lack of barrier nursing and the traditional burial preparation method, which involves washing and gastrointestinal tract cleansing^[2].

Sudan virus (SUDV):

The virus was the second species of Ebola emerging simultaneous with the Zaire virus. It was believed to have originated amongst cotton factory workers in Nzara, Sudan, with the first case reported as a worker exposed to a potential natural reservoir. The carrier is still unknown. The most recent outbreak occurred in May 2004. 20 confirmed cases were

reported in Yambio County, Sudan, with five deaths resulting. The average fatality rates for were 54% in 1976, 68% in 1979, and 53% in 2000 and 2001^[3].

Tai Forest virus (TAFV):

Also referred to as Ivory Coast Ebola virus and Tai Ebola virus; it was first discovered among chimpanzees from the Tai Forest in Côte d'Ivoire, Africa. Studies of tissues taken from the chimpanzees showed results similar to human cases during the 1976 Ebola outbreaks in Zaire and Sudan. As more dead chimpanzees were discovered, with many testing positive to Ebola using molecular techniques. The source of contamination was believed to be the meat of infected Western Red Colobus monkeys, upon which the chimpanzees preyed. One of the scientists performing the necropsies on the infected chimpanzees contracted Ebola. She develops symptoms similar to those of dengue fever approximately a week after the necropsy, and was transported to Switzerland for treatment. She was discharged from hospital after two weeks and had fully recovered six weeks after the infection.

Reston virus (RESTV):

It is not thought to be disease-causing in humans. Discovered during an outbreak of Simian hemorrhagic fever virus (SHFV) in crab-eating macaques from Hazleton Laboratories (now Covance) in 1989. Since the initial outbreak in Reston, Virginia, it has emerged in the Philippines, Siena Italy, and Texas. It is non-pathogenic to humans however hazardous in monkeys^[4].

The first Southern African Centre for Infectious Disease Surveillance (SACIDS) conference on 'One Africa, One Health' served as inspiration for this review to illustrate the concept through a typical emerging infection. Ebola haemorrhagic fever (EHF) is caused by any of above five genetically distinct members. Zaire Ebola virus has been associated with only one human case. Reston Ebola virus has only caused disease in non-human primates (NHP) and was found in swine suffering from porcine reproductive and respiratory disease syndrome.

Zaire, Sudan and Bundibugyo Ebola viruses are responsible for most of the EHF outbreaks^[5]. But ZEBOV constitutes a particularly serious threat to both human and NHPs in sub-Saharan Africa. Ebola haemorrhagic fever has been associated with large human outbreaks, with case fatality rates for ZEBOV as high as 90%. The case fatality rate of EBOV in NHP is unknown but some ecological data suggest that EBOV has contributed to declines of up to 98% of local great ape populations in Gabon and the Republic of Congo. EHF typically appears in sporadic outbreaks coinciding with the rainy season, and is usually spread in humans within a health-care setting^[6].



Fig. 1 Ebola virus^[7].

ETIOLOGY (CAUSES)

Ebola virus belongs to the family Filoviridae, in the order Mononegavirales which includes Rhabdoviridae and Paramyxoviridae. Between people, Ebola disease spreads only by direct contact with the blood or body fluids of a person who has developed symptoms of the disease. Body fluids that may contain Ebola viruses include saliva, mucus, vomit, feces, sweat, tears, breast milk, and urine. Ebola viruses contain single-stranded, non-infectious RNA genomes. *Bolavirus* genomes contain seven genes including **3'-UTR-NP-VP35-VP40-GP-VP30-VP24-L-5'-UTR**. As all filoviruses, ebola virions are filamentous particles that may appear in the shape of a shepherd's crook, of a "U" or of a "6," and they may be coiled, toroid or branched. In general, ebola virions are 80 nanometers (nm) in width and may be as long as

14,000 nm. It contains one molecule of linear, single-stranded, negative-sense RNA of 4.2×10^6 Da.

Person under investigation

A person who has both consistent symptoms and risk factors as follows: 1) Clinical criteria, which includes fever of greater than 38.6 degrees Celsius or 101.5 degrees Fahrenheit, and additional symptoms such as severe headache, muscle pain, vomiting, diarrhoea, abdominal pain, or unexplained haemorrhage; and 2) Epidemiologic risk factors within the past 21 days before the onset of symptoms, such as contact with blood or other body fluids or human remains of a patient known to have or suspected to have EVD; residence in—or travel to—an area where EVD transmission is active*; or direct handling of bats or non-human primates from disease-endemic areas.

Probable case:-

A PUI whose epidemiologic risk factors include high or low risk exposure.

Confirmed case:-

A case with laboratory-confirmed diagnostic evidence of Ebola virus infection.

Exposure risk levels:-

Levels of exposure risk are defined as follows:

* High- risk exposures

A high-risk exposure includes any of the following:

- Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids of EVD patient
- Direct skin contact with or exposure to blood or body fluids of, an EVD patient without appropriate personal protective equipment (PPE)
- Processing blood or body fluids of a confirmed EVD patient without appropriate PPE or standard biosafety precautions.
- Direct contact with a dead body without appropriate PPE in a country where an EVD outbreak is occurring*

* Low-risk exposures

A low-risk exposure includes any of the following:

- Household contact with an EVD patient
- Other close contact with EVD patients in health care facilities or community settings. Close contact is defined as:
 - Being within approximately 3 feet (1 meter) of an EVD patient or within the patient's room or care area for a prolonged period of time (e.g., health care personnel, household members) while not wearing recommended personal protective equipment (i.e., standard, droplet, and contact precautions; see Infection Prevention and Control Recommendations) ebola virus
 - Having direct brief contact (e.g., shaking hands) with an EVD patient while not wearing recommended personal protective equipment
- Brief interactions, such as walking by a person or moving through a hospital, do not constitute close contact

Early recognition is critical for infection control [8]:- Transmission

According to the WHO (World Health Organisation) this disease can be transmitted from close contact with the blood, secretions, organs or other bodily fluids of infected animals (commonly monkeys, gorillas, chimpanzees, baboon and fruit bats). In humans the disease can be transmitted by the following methods [9,10]. Filo viruses are believed to be zoonotic, meaning they are transmitted to humans by animals. The natural reservoirs, or animal hosts, of Ebola and Marburg viruses are not known. The viruses can replicate, or reproduce, in certain types of bats native to the areas where the viruses are found, so some researchers think that these bats could be the natural reservoirs.

Once the virus has been transmitted to a human, it can then be spread through person-to-person contact. People can be exposed to Ebola and Marburg viruses from direct contact with the blood or secretions of an infected person.

Nosocomial transmission, or the spread of disease within a healthcare setting, also occurs, making the

use of protective clothing and the disposal of needles and syringes crucial to preventing the spread of infection.

Symptoms:

If the patient has both exposure and symptoms, immediately isolate the patient and inform others. Once the condition has progressed a person may notice symptoms like:

- Vomiting
- Abdominal (stomach) pain
- Unexplained haemorrhage (bleeding or bruising)
- Conjunctivitis
- Genital swelling
- Increased sensitivity to pain on the skin,
- Rashes all over the body,
- And reddening of the roof of the mouth.

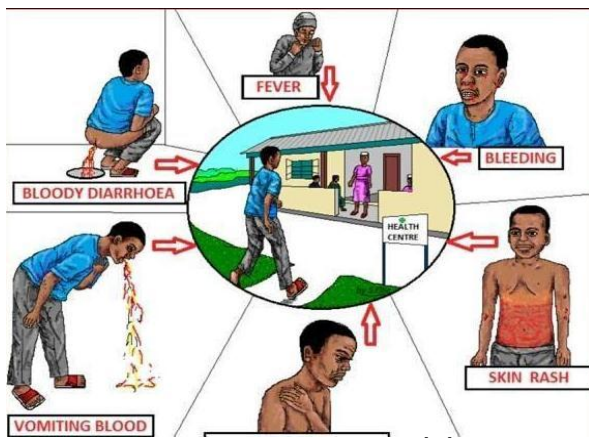


Fig.2: Symptoms of EVD^[14].

Bleeding: All people infected show some symptoms of circulatory system involvement, including impaired blood clotting. In 40–50% of cases, bleeding from puncture sites and mucous membranes (e.g. mouth, gastrointestinal tract, nose, ears, vagina and gums), even reddening of eyes and bloody vomit has also been reported^[11,12,13].



Fig. 3 Ebola is not Airborne^[14].

- Severe headache
- Muscle pain
- Weakness
- Fatigue
- Diarrhoea



Fig.4: Animals susceptible to spread Ebola virus^[14].

DIAGNOSIS^[15,16,17,18]

Diagnosis of Ebola and Marburg haemorrhagic fevers can be difficult because early symptoms are often similar to other infectious diseases, such as malaria and typhoid fever. If they suspect Ebola or Marburg infection, healthcare providers will isolate infected patients. Laboratory tests can confirm infection within a few days of the onset of symptoms. Also diagnosis is confirmed by isolating the virus, detecting its RNA or proteins, or detecting antibodies against the virus in a person's blood. Isolating the virus by cell culture, detecting the viral RNA by polymerase chain reaction (PCR) and detecting proteins by enzyme-linked immunosorbent assay (ELISA) is effective early and in those who have died from the disease.

Usually a physician will be able to diagnose the condition with the symptoms alone, but in order to confirm the diagnosis he/she may prescribe tests like-

- Complete Blood Count (CBC),
- Coagulation studies (a test to check for the amount of time a person's blood needs to clot),
- Viral antigen testing (a test to check for the presence of the viral antigen) and
- Liver function test (LFT).

ISOLATE

If assessment indicates possible Ebola virus infection, take action.

- Isolate the patient in a private room with a private bathroom or covered, bedside commode and close the door
- Wear appropriate personal protective equipment (PPE).
- Limit the healthcare personnel who enter the room
- Keep a log of everyone who enters and leaves the patient's room
- Consider alternative diagnoses, and evaluate appropriately
- Only perform necessary tests and procedures
- Avoid aerosol-generating procedures
- Follow CDC guidelines for cleaning, disinfecting, and managing waste.

THINK EBOLA WHEN YOU APPROACH A PATIENT.

Start the steps for basic infection control before assessing the patient for risks.

Always use standard precautions

- If there are concerns that the patient could meet the criteria for Ebola, immediately separate the patient from others
- Coming into contact with the blood, secretions, organs or other bodily fluids of an infected person.
- Contact with the bodily fluids of an infected person who has passed away.
- Handling the meat from infected animals.
- Exposure to objects (such as needles) that have been contaminated with infected secretions.
- Healthcare workers may contract the disease through transmission as well through contact with infected bodily fluids.

Treatment and Prevention:

Prevention of infection for tourists, visitors and residents:

For tourists, visitors or residents in affected areas, the risk of infection is considered very low if some elementary precautions are followed:

- Avoiding contact with symptomatic patients and/or their bodily fluids
- Avoiding contact with corpses and/or bodily fluids from deceased patients alert others, including public health authorities.
- Notify your facility's infection control program and other appropriate staff
- Contact your state or local public health authorities
- Consult with state or local public health authorities about testing for Ebola
- For a list of state and local health department numbers
- Avoiding any form of close contact with wild animals (including monkeys, forest antelopes, rodents and bats), both alive and dead, and consumption of any type of 'bush meat'
- Washing and peeling fruits and vegetables before consumption
- Strictly practising 'safe sex'
- Strictly following hand-washing routines

Prevention for healthcare workers:

In healthcare settings, the risk level can vary from very low to low. However, the risk is high in the event of mishaps that result in skin penetrations or mucosal exposure to contaminated materials (e.g. needle stick injuries).

Preventive approaches for healthcare workers include:

- Full compliance to vaccinations (notably yellow fever) and malaria prophylaxis as recommended for the target region (including documentation as a vaccination record);
- Sensitisation for viral haemorrhagic fever symptoms before working in endemic countries; and
- Strict implementation of barrier management, use of personal protective equipment, and disinfection procedures, as per specific guidelines^[19,20].

Assess your patient for:

Travel to a country with widespread transmission or uncertain control measures (Guinea, Liberia, Sierra Leone, or Mali) within the last 21 days OR Contact with someone with Ebola within the last 21 days AND had a fever at home, or has a current temperature $\geq 100.4^{\circ}\text{F}$ ($\geq 38^{\circ}\text{C}$).

There are no specific drugs to treat Ebola or Marburg haemorrhagic fevers. If hospitalized, ill people can be given supportive care such as intravenous fluids. During this Ebola time, we cannot care for family and friends that die the way we are used to. While you are waiting for the burial team to arrive, keep a distance of at least 3 feet (1meter) from the body. Do not touch it. Do not touch, wash or clean any dead body. Burying all who die safely is one of the best ways to make sure we have zero cases of Ebola in Liberia.

Burial teams know this kind of safe burial is very difficult for the family and the community. They will talk to the family members about the different ways they can pay respect without touching the body. All burials will be safe, free, and respect the families.



Fig. 5: Burial teams with special protective clothes [21]

Burial teams wear special protective clothes (the overhaul suits) to keep them safe. Burial teams are watched by others and have chlorine sprayers. They spray the chlorine to clean the body and the area the body was in to kill the Ebola virus and keep the family and the community safe.



Fig. 6: Family Decision for Dead person [21].

The family has the right to decide if the personal things of the dead person will be burned, put in the grave with the person, or sprayed with chlorine to clean them.

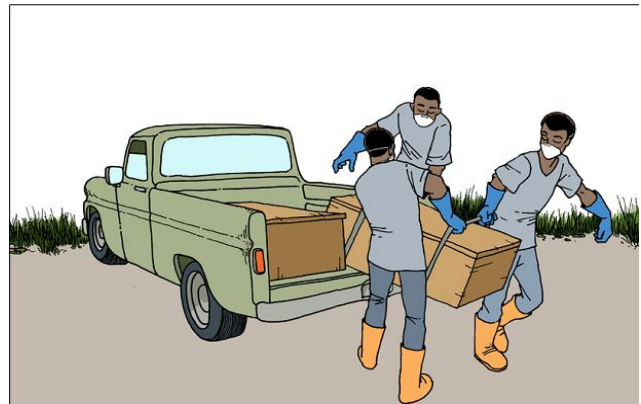


Fig. 7: Deliver the Dead body [21].

The burial teams will deliver the body to the cemetery. No bodies will be burned.



Fig. 8: Don't travel with Burial team [21].

Five members of the family will be able to attend the burial. They will not travel with the burial team. The family can stand 15 feet away. A religious leader can come. The family can choose a gravestone for the family member.

Protect yourself. Protect your family. Protect your community. All burials will be safe, free, and respectful of the body and the grieving family.

RECENT ADVANCES/RESEARCH ON EBOLA ^[22]

Ebola/Marburg Research

The molecular events that affect disease transmission and human response to Ebola and Marburg viruses are poorly understood. Researchers in NIAID's Division of Intramural Research and Vaccine Research Centre as well as NIAID-supported scientists at external institutions are studying all aspects of Ebola and Marburg viruses and how they cause disease. This includes seeking better ways to diagnose and treat Ebola and Marburg fevers, and using applied research to develop diagnostics, vaccines, and therapeutics.

Ebola Vaccine Research

The Vaccine Research Centre (VRC) has developed an Ebola vaccine candidate in collaboration with Okairos, a Swiss-Italian biotech company recently acquired by GSK. The investigational vaccine, which was designed by VRC scientists, contains no infectious Ebola virus material. It is a chimpanzee adenovirus vector vaccine into which two Ebola genes have been inserted. This is a non-replicating viral vector, which means the vaccine enters a cell, delivers the gene inserts and does not replicate further. The gene inserts express a protein to which the body makes an immune response. The investigational vaccine has recently shown promise in a primate model. The VRC vaccine will enter into a phase 1 clinical trial, which could start enrolment as early as fall 2014, pending approval by the FDA. The VRC is also in discussions with governmental and non-governmental partners regarding options for advancing this candidate beyond Phase I clinical evaluation.

NIAID/GSK Experimental Ebola Vaccine Appears Safe, Prompts Immune Response



Fig. 9 NIH Phase 1 Clinical Trial Support Accelerated Development of Candidate Vaccine ^[22]

A 39-year-old woman, the first participant enrolled in VRC 207, receives a dose of the investigational NIAID/GSK Ebola vaccine at the NIH Clinical Center in Bethesda.

Additionally, NIAID's Division of Microbiology and Infectious Diseases is supporting the Crucell biopharmaceutical company's development of a multivalent Ebola/Marburg vaccine using recombinant adenovirus vector platforms. A Phase I clinical trial is planned for late 2015 or early 2016. NIAID is also funding Profectus Biosciences to develop and test a recombinant vesicular stomatitis virus vectored vaccine against Ebola virus. The vaccine is currently in preclinical testing to determine the most promising constructs. In addition, NIAID is working with Bavarian Nordic on development of a recombinant Marburg vaccine candidate that uses the Modified Vaccinia Ankara vector.

Investigators from NIAID's Division of Intramural Research and Thomas Jefferson University are collaborating to develop a candidate Ebola vaccine based on the established rabies virus vaccine that has demonstrated protection against rabies and Ebola infection in animals. This research team is pursuing an inactivated version of this vaccine for

human and veterinary use and a live vaccine for use in wildlife in Africa to help prevent the transmission of Ebola virus from animals to humans.

Ebola Therapeutics Research

NIAID is supporting a number of projects designed to develop Ebola treatments. For example, NIAID supported Mapp Biopharmaceutical, Inc., in its development of a monoclonal antibody “cocktail” called MB-2003, which prevents Ebola virus infection in mice and non-human primates when administered as post-exposure prophylaxis within one to two days of Ebola virus infection. Additionally, NIAID currently is funding development of an optimized anti-Ebola monoclonal antibody product, zMapp, which has superior efficacy compared to earlier cocktails. The zMapp, which is partially derived from MB-2003, is a cocktail of three antibodies against Ebola.

In addition, NIAID is funding BioCryst Pharmaceuticals to develop and test BCX4430, a novel nucleoside with broad spectrum antiviral activity including against Ebola virus. To date, BCX4430 has shown efficacy in animal infection models for Ebola and Marburg viruses. A Phase I trial is expected to begin in late 2014 or early 2015. NIAID

also is supporting other monoclonal antibody-based broadly-protective filovirus immunotherapeutic.

Ebola Diagnostics Research

NIAID is also supporting the development of improved diagnostics for Ebola virus infection. For example, NIAID is funding a Lassa fever recombinant antigen diagnostic. A similar diagnostic is being designed to detect Ebola virus infection. NIAID also is supporting development of multiplex diagnostics, microfluidics-based diagnostics and optofluidic-based diagnostics for Ebola.

CONCLUSION

The current Ebola outbreak is a dominating headline globally. The Ebola virus is transmitted by direct contact with the blood, body fluids and tissues of infected persons. For people who are currently trying to get through this terrible outbreak that will be of little comfort. Ebola haemorrhagic fever epidemics constitute a significant public health concern in Africa and an effective vaccine is needed urgently. The review is aimed at Ebola haemorrhagic fever, its Sources, sign, symptoms, diagnosis, mode of transmission, prognosis, guidance as well as treatment and advances in Research.

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