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PREVENTION OF EBOLA VIRUS DISEASE-A REVIEW

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ABSTRACT

Ebola virus is a fatal illness in humans and non primates. Ebola Virus Disease (EVD) outbreak began in Guinea in December of 2013, the outbreak now involves trans-mission in Guinea, Liberia, Nigeria, and Sierra Leone. EVD or Ebola haemorrhagic fever (EHF) is a zoonosis affecting both human and non-human primates (NHP). Ebola virus (formerly known as Zaire Ebola virus, or EBOV) was first seen infecting humans in African continent; especially Sudan, 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 EVD outbreak ever recorded. EVD outbreaks have a case fatality rate of upto 90%. EVD is caused by the sudden onset of weakness, muscle pain, headache, sore throat, fever, vomiting, diarrhoea, liver dysfunction, rashes and also internal-external bleeding. As such no specific treatment foe EVD is available but a number of researches are going on. 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 virus, Ebola hemorrhagic fever, EBOV, Outbreak of Ebola, EVD, prevention.

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 (EHF) 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

1. Bundibugyo virus (BDBV)

BDBV is a close relative of the much more commonly known Ebola virus (EBOV). The name Bundibugyo virus is derived from *Bundibugyo* (the name of the chief town of the Ugandan Bundibugyo District, where it was first discovered). BDBV causes severe disease in humans and (experimentally) in nonhuman primates, the Ebola hemorrhagic fever. BDBV is a Select Agent, World Health Organization Risk Group 4 Pathogen (requiring Biosafety Level 4-equivalent containment), National Institutes of Health/National Institute of Allergy and Infectious Diseases Category A Priority Pathogen, Centers for Disease Control and Prevention Category A Bioterrorism Agent, and is listed as a Biological Agent for Export Control by the Australia Group.

2. Ebola virus or Zaire Ebola virus (EBOV)

This is most fatal among all five and has the highest case-fatality rate, upto 90% in some epidemics. The first outbreak took place on 26 August 1976 in Yambuku. Mabalo 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]

3. 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]

4. 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 Cote 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, uponwhich 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.

5. Reston virus (RESTV)

It is not thought to be disease-causing in humans. RESTV 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

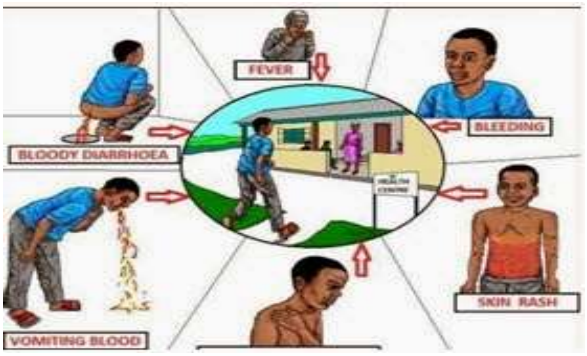


Fig.2: Symptoms of EVD

Symptoms

1. **Bleeding:** All people infected show some symptoms of circulatory system like impaired blood clotting, in 40–50% bleeding from puncture sites and mucous membranes (e.g. mouth, gastrointestinal tract, nose, ears, vagina and gums), reddening of eyes and bloody vomit has also been reported.[7,8,9,10]
2. **Severe headache**
3. **Muscle pain**
4. **Weakness**
5. **Fatigue**
6. **Diarrhoea**
7. **Vomiting**
8. **Abdominal (stomach) pain**
9. **Unexplained haemorrhage (bleeding or bruising)**
10. **Conjunctivitis**
11. **Genital swelling**
12. **Increased sensitivity to pain on the skin,**
13. **Rashes all over the body,**
14. **And reddening of the roof of the mouth.**

Diagnosis[11,12,13,14]

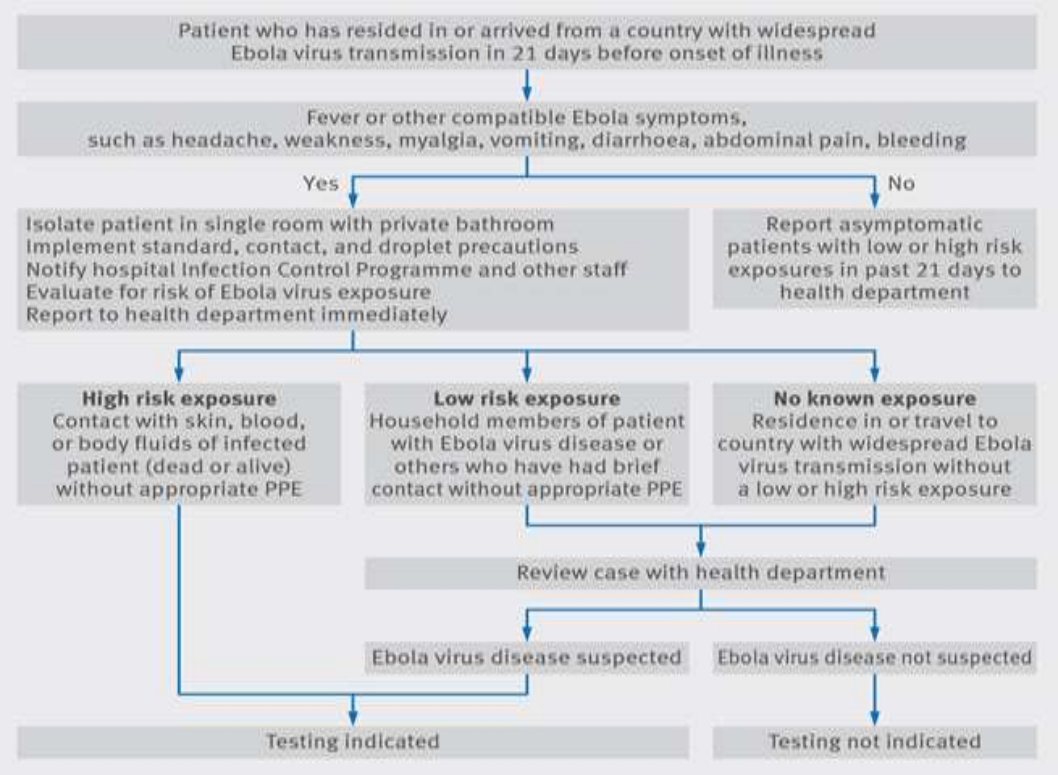
Diagnosis of Ebola and Marburg haemorrhagic fevers can be difficult because early symptoms are often similar to other infectious diseases, such as malaria and typhoid fever. If they suspect Ebola or Marburg infection, healthcare providers will isolate infected patients. Laboratory tests can confirm infection 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. Early recognition is critical for infection control.

Usually a physician will be able to diagnose the condition with the symptoms alone, by the 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.

Table no.1: Diagnosis of Ebola Virus



Diagnostic pathway for the investigation of suspected Ebola virus infection

TRANSMISSION

According to the WHO, 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.[15,16] 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.

New drug - MEAI may curb excess drinking Pfizer's Ibrance got accelerated approval from US FDA Arsenic in drinking water tied to drop in breast cancer deaths.

PREVENTION

There are no vaccinations available as of now, so basic hygiene is of importance and a must be followed in order to prevent the onset of the condition can all serve as precautionary measures.[17-22]

Simple activities like

· Drinking water from a clean source,
· Cooking your meat well,
· Avoid bush meat,
· Maintaining general hygiene,
· Washing your hands well with soaps or detergents,
· Avoid crowded places,
· Sterilizing equipment and wearing protective clothing including masks, gloves, gowns and Goggles.

Follow infection-control procedures,

· Don't handle remains of patients died of Ebola or Marburg disease[13],
· Isolate people who have Ebola symptoms,
· Disinfecting your surroundings,
· Culling of infected animals, with close supervision of burial or incineration of carcasses.
· Yet, not travelling to the areas or countries where the virus is found is the best way to avoid
Ebola and
· If any early symptoms noticed, should visit a doctor immediately.

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

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 ≥100.4°F (≥38°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. 3 Burial teams with special protective clothes[23]

Recent Advances/Research on Ebola[24]

The researchers found that the Ebola virus can't infect cells unless it first attaches to a host protein called Niemann-Pick C1 (NPC1) in membrane compartments called lysosomes deep within cells. "Our study reveals NPC1 to be an Achilles' heel for Ebola virus infection," said co-study leader Kartik Chandran, Ph.D., associate professor of microbiology and immunology and the Harold and Muriel Block Faculty Scholar in Virology at Einstein. "Mice lacking both copies of the NPC1 gene, and therefore devoid of the NPC1 protein, were completely resistant to infection." The other co-study leaders are Steven Walkley, D.V.M., P. Purpura D, Saul R. Korey and John M. Dye.

Ebola virus binds to the host cell's outer membrane, and a portion of host cell membrane then surrounds the virus and pinches off, creating an endosome—a membrane-bound bubble inside the cell. Endosomes carry their viral stowaways deep within the cell and eventually mature into lysosomes—tiny enzyme-filled structures that digest and recycle cellular components.

The viruses captive in the lysosome manage to escape destruction by exploiting components of the cell to gain entry to the cytoplasm, the substance between the cell membrane and the nucleus where the virus can replicate. But the identities of many of these components have remained unknown.

In an earlier study, the Einstein and US AMRIID researchers, together with colleagues at the Netherlands Cancer Institute and Harvard Medical School, found evidence, in tissue culture, that Ebola takes advantage of the NPC1 protein to enter the cell's cytoplasm. NPC1 is embedded within cell membranes, where it helps transport cholesterol within the cell. People lacking NPC1 due to genetic mutations develop a fatal neurodegenerative disorder called Niemann-Pick disease, in which cells become clogged with cholesterol and eventually die.

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

NIH Phase 1 Clinical Trial Vaccine is under progress. 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 Ebolavirus. 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.

The deadly Ebola epidemic in Liberia could likely be eliminated by June if the current high rate of hospitalisation and vigilance can be maintained, according to a new model developed by scientists.

The model, developed by researchers at the University of Georgia (UGA) and Pennsylvania State University, includes such factors as the location of infection and treatment, the development of hospital capacity and the adoption of safe burial practices and is probably the first to include all those elements.

The model projected that, if an 85 per cent hospitalisation rate can be achieved, the Ebola epidemic in Liberia should be largely contained by June 2015.

"That's a realistic possibility but not a foregone conclusion. What's needed is to maintain the current level of vigilance and keep pressing forward as hard as we can," said John Drake, an associate professor in the UGA Odum School of Ecology who led the study published in the journal PLOS Biology. In the study, researchers used a mathematical formulation known as branching processes - a method for keeping track of all possible epidemic outcomes in proportion to their probabilities - calibrated with newly developed methods.

Drake and his colleagues started with information gleaned from earlier Ebola outbreaks. They included data about variables such as the numbers of patients hospitalised health care workers infected, which allowed them to estimate the level of under-reporting; rates of transmission in hospitals, the community and from funerals; and the effectiveness of infection control measures.

Once they had a working model with plausible parameters, they fine-tuned it using data from the World Health Organisation and the Liberia Ministry of Health for the period from July 4 through September 2, 2014. This included information about new cases as well as changes in behaviour and public health interventions during that time, such as the addition of roughly 300 hospital beds and the adoption of safer burial practices.

Liberia continued to add hospital beds after September 2, so in mid-December, Drake and his team updated the model to include information collected through December 1. Using reported data rather than estimates from the earlier version of the model significantly cut down on the range of future possibilities, showing that the response by the Liberian government and international groups had greatly reduced the likelihood of a massive epidemic.

Ebola virus has killed more than 7,800 people, almost all in West Africa, since it broke out a year ago. Sierra Leone, which has overtaken Liberia as the country with the most infections, counted 9,446 cases and 2,758 deaths on December 28.

Liberia has seen a clear decrease in transmission over the past month. As of December 28, the country had recorded 8,018 cases and 3,423 deaths.

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 Bio Cryst 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 filo virus immunotherapeutic.

Ebola Diagnostics Research

NIAID is also supporting the development of improved diagnostics for Ebolavirus 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. This review is aimed at Ebola haemorrhagic fever, its Sources, sign, symptoms, diagnosis, mode of transmission, guidances, prevention as well as treatment and advances in Research.

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