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Report on Ebola Virus

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ABSTRACT

Ebola is a disease of human and other primates caused by *Ebola viruses*. The virus spreads by direct contact with body fluids such as blood of an infected human or other animals. This may also occur through contact with an item recently contaminated with bodily fluids. Spread of the disease through the air between primates including humans, has not been documented in either laboratory or natural conditions. Semen or breast milk of a person after recovery from *Ebola virus* disease may still carry the virus for several week or months. Fruit bats are believed to be the normal carrier in nature, able to spread the virus without being affected by it. Another disease such as malaria, cholera, typhoid fever, meningitis and other virus hemorrhagic fevers may resemble *Ebola virus* disease. Blood samples are tested for viral RNA, viral antibodies or for the virus itself to confirm the diagnosis. No specific treatment or vaccine for the virus is available although a number of potential treatments are being studied. Supportive efforts, however, improve outcome. This includes oral rehydration therapy (drinking slightly sweetened and salty water) or giving intravenous fluids as well as treating symptoms.

INTRODUCTION

Ebola virus disease (EVD), formerly known as *Ebola* hemorrhagic fever, is a severe, often fatal illness in humans. *Ebola virus* can be spread by direct contact with body fluids such as blood of infected human or other animals. *Ebola* first emerged in 1976 in Sudan and Zaire. The name *Ebola* comes from Ebola River in Zaire. The first outbreak of *Ebola virus*, *Ebola*-Sudan (EBOS), infected over 284 people, with a mortality rate of 53%. A few months later, the second *Ebola virus* emerged from Yambuku, Zaire, *Ebola*-Zaire (EBOZ). EBOZ, with the highest mortality rate of any of the *Ebola viruses* (88%), infected 318 people. Despite the tremendous effort of experienced and dedicated researchers, *Ebola's* natural reservoir was never identified. The third strain of *Ebola*, *Ebola* Reston (EBOR), was first identified in 1989 when infected monkeys were imported into Reston, Virginia, from Mindanao in the Philippines. Fortunately, the few people who were infected with EBOR (seroconverted) never developed *Ebola* hemorrhagic fever. The last known strain of *Ebola*, *Ebola* Cote d'Ivoire (EBO-CI) (Fig-1) was discovered in 1994 when a female ethologist performing a necropsy on a dead chimpanzee from the Tai Forest, Cote d'Ivoire, accidentally infected herself during the necropsy. Between 1976 and 2013, the World Health Organization reports 24 outbreaks involving 1,716 cases. The largest outbreak to date was the epidemic in West Africa, which occurred from December 2013 to January 2016 with 28,616 cases and 11,310 deaths. It was declared no longer an emergency on 29 March 2016. Another outbreak in Africa began in May 2017 in the Democratic Republic of the Congo.[1-5]

Fig. 1 Map of *Ebola* outbreaks in Africa

Ebola virus, *Marburg virus* and *Cuevavirus*. The first two are the most virulent viruses. *Ebola virus* has 5 species:

1. Zaire (EBOV-Z),
2. Sudan (EBOV-S),
3. Reston (EBOV-R),
4. Tai forest (EBOV-TF) formerly Cote d'Ivoire *Ebola virus*
5. Bundibugyo (EBOV-B) [6,7]

EBOLA VIRUS SENSITIVITY TO PHYSICAL AND CHEMICAL AGENT

Ebola viruses are classified as both biosafety level 4 and category A list pathogens. Currently, there are no approved options available for either treatment or post-exposure prophylaxis. *Filoviruses* infectivity is quite stable at room temperature but is largely inactivated by 30-minute incubation at 60^0C. Current methods of inactivating *filoviruses* are limited to high doses of ultraviolet light and gamma irradiation, formalin treatment, lipid solvents, b-propiolactone, photo-induced alkylating probe 1, 5-iodonaphthylazide, and commercial hypochlorite and phenolic disinfectants.[8-9]

VIRUS STRUCTURE

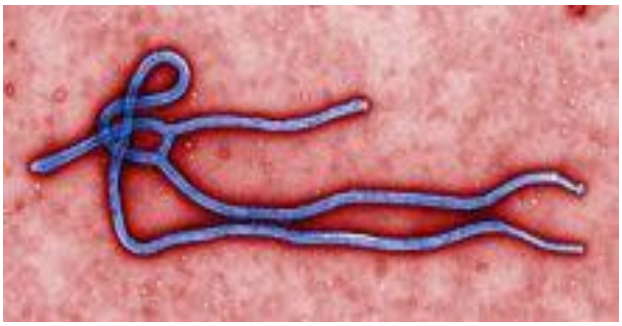

Fig. 2 Structure of *Ebola virus*

Filoviridae, of which *Ebola virus* is a member, is a family of viruses that contain single, linear, negative-sense ssRNA genomes. The family name was derived from the Latin word filum, which alludes to the thread-like appearance of the virions when viewed under an electron microscope (Fig. 2). *Filoviruses* have been divided into two genera: *Ebola*-like

viruses with species Zaire, Sudan, Reston, Cote d'Ivoire and Bundibugyo; and Marburg-like viruses with the single species Marburg. All of these are responsible for hemorrhagic fevers in primates that are characterized by often fatal bleeding and coagulation abnormalities. The tubular *Ebola* virions are generally 80 nm in diameter and 14000 nm long. [10]

REPLICATION

Ebola virus replication and transcription take place in the cytoplasm of the infected cells. The viruses encode their own *RNA-dependent RNA polymerase*, which recognizes the encapsidated negative-strand RNA genome as a template for replication and transcription. The first step in viral replication is attachment to the host cell membrane and penetration into the cell. This process is not completely understood, but it is known that glycoprotein (GP) spikes are involved in entry of virions into the host cell and are used in the mechanisms similar to macropinocytosis. The other proposed mechanisms of cell entry include: clathrin-mediated endocytosis or glycoprotein-facilitated receptor binding. The glycoprotein is cut into GP1 and GP2 proteins. The GP1 takes part in the attachment of the virus particle to the cell membrane, while the GP2 participates in viral fusion with the cell membrane. Viral membrane fuses with cell vesicle membrane to allow the release of the nucleocapsid into the cytoplasm. It is believed that the further steps of replication occur in the cytoplasm, analogously to paramyxoviruses and rhabdoviruses. Encapsidated, genomic RNA is used then as a template for transcription into seven polyadenylated, monocistronic mRNAs and translated by the cellular translation machinery into individual viral proteins. Transcription is regulated by conserved transcription start and stop signals located at the viral gene borders. The gene start signals are parts of RNA secondary structures, and it has been proposed that VP30 binds to the RNA at the first gene start signal to initiate transcription. In addition, VP30 was shown to be important for reinitiation of transcription of subsequent genes. VP30 activity is regulated via its phosphorylation state: phosphorylation of VP30 inhibits viral transcription while viral replication is increased. Because of its essential function in these processes, VP30 is a potential interesting candidate as antiviral therapy target. Subsequently, when a positive-sense full-length genome is replicated, it is concomitantly encapsidated by newly synthesized NP molecules. Other structural nucleocapsid proteins (polymerase cofactor — VP35, and the viral *RNA polymerase* L) participate in the synthesis of the viral genome. The presence of matrix VP24 together with NP and VP35 is required for assembly of viral nucleocapsids, and silencing of VP24 expression prevents the release of viruses. Moreover, in the VP24-deficient

viral particles VP30 transcription and translation are diminished. Further, the most abundantly expressed matrix protein VP40 plays an important role in the formation of new virus particles, and is associated with the endosomal pathway and virus budding from the cell. The mechanisms of this process are not fully understood but it is known that a mutation in the sequences encoding the VP40 leads to inhibition of virus release from the infected cell.[11, 12]

SIGNS AND SYMPTOMS

- Fever
- Severe headache
- Sore throat
- Rash
- Muscle pain
- Difficulty in breathing
- Weakness
- Fatigue
- Diarrhea
- Vomiting
- Abdominal pain
- Unexplained hemorrhage
- Symptoms of impaired kidney and liver function
- Laboratory tests find low white blood cell and platelet counts as well as elevated liver enzyme levels.

Symptoms may occur from 2 to 21 days after exposure to *Ebola*, but the average is 8 to 10 days.

Recovery from *Ebola* depends on good supportive clinical care and the patient's immune response. People who recover from *Ebola* infection develop antibodies that last for at least 10 years. Once someone recovers from *Ebola*, they can no longer spread the virus. However, *Ebola virus* has been found in semen for up to 3 months. People who recover from *Ebola* are advised to abstain from sex or use condoms for 3 months. It is not known if people who recover are immune for life or if they can become infected with a different species of *Ebola*.[3,13]

CAUSES

Ebola is caused by *Ebola virus*. *Ebola* is considered a zoonosis, a disease which can be transmitted to humans from animals. How this transmission occurs at the onset of an outbreak in humans is unknown. In Africa, people have developed *Ebola* after handling infected animals found ill or dead, including chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines. Person to person transmission occurs, if someone infected with *Ebola virus* becomes symptomatic. As it can take between 2 and 21 days for symptoms to develop, a person with *Ebola* may have been in contact with hundreds of people, that's why an outbreak can be hard to control and may spread rapidly.[13]

EPIDEMIOLOGY

Ebola virus disease remains a plague in Africa, with an increase in the number of outbreaks and cases since 2000. As a classic zoonosis, *Ebola virus* is believed to persist in a reservoir species in endemic areas. Apes, man, and perhaps other mammalian species are regarded as end hosts of *Ebola virus*. Bats are currently thought as potential reservoir species. After direct contact with the virus in dead or infected wildlife and the subsequent person-to-person transmission, *Ebola virus* enters the body through mucosal surfaces or skin abrasions. *Ebola virus* disease symptoms usually appear after a 2 to 21days incubation period. Patients initially show nonspecific flu-like symptoms, such as fever, chills, malaise, muscle pain, and headache. A macropapular rash associated with varying severity of erythema often appears around day 5 and serves as a characteristic feature. Extensive viral replication causes systemic, vascular, and neurologic manifestations, and necrosis occurs in the liver, spleen, kidneys, and gonads. In fatal cases, death occurs usually between 6 and 16 days after infection, and multiple organ failure and severe syndrome might resemble the fatal septic shock.[6,13]

PATHOPHYSIOLOGY OF EBOLA VIRUS DISEASE

At the entry site into the body, MARV and *Ebola virus* are capable to infect macrophages and other cells of the phagocytes system. Macrophages *in vitro* are highly susceptible to infection and produce a large number of viral particles, and hence serve as a vehicle to deliver the virus to a variety of organ systems such as liver, endothelium, spleen, lymph nodes, kidney, adrenal gland, and pancreas. *Ebola virus* belongs to the *Filovirus* family, characterized by membrane enveloped filamentous particles in the shape of as hepherd‟s crook or in the shape of a "U" or a "6". It is comprised of three components namely viral envelope, matrix and nucleocapsid. The viral envelope is derived from cell membrane of the host during the budding process and it is here that underlying viral encoded glycoprotein's (GP) insert during transcriptional editing. Marked leukopenia with a left shift and atypical lymphocytes can be observed on peripheral smears of infected patients. Since lymphocytes are not assumed to be host targets for the virus, a substantial reduction in the number of lymphocytes is supposed as a result of bystander apoptosis, showing the death of a large number of lymphocytes triggered by mediators which are released from virus-infected target cells and/or secretion of viral GP. Impaired production of pro-inflammatory cytokines and impaired stimulation of T cells also play a role in this phenomenon.

After entry into the human body, *Ebola virus* mainly affects:

Lymph nodes:

Here it leads to infection of macrophages and dendritic cells and results in the lymphocytes depletion and host immune response impairment.

Liver:

In liver, it leads to the infection and necrosis of hepatocytes through the damage of the endothelial cells that are responsible for the formation of the lining of the blood vessels and leads to difficulty in coagulation of the infected individual‟s blood. As the platelets would not be able to coagulate, this result in hypovolemic shock or decrease in blood pressure and death may also occur.

Adrenal gland:

Causes infection and necrosis of adrenal cortical cells. As a result, synthesis of steroids is impaired. In most outbreaks, *Ebola virus* is introduced into human populations via the handling of infected animal carcasses. In these cases, the first source of transmission is an animal found dead or hunted in the forest, followed by a person-to-person transmission from index case to family members or health-care staff. Animal-to-human transmission occurs when people come into contact with tissues and bodily fluids of infected animals, especially with infected nonhuman primates. The transmission has been reported in Côte d‟Ivoire where an ethologist was infected through handling an infected, dead chimpanzee in the Taï Forest. It was confirmed that the deaths of chimpanzees were indeed due to *Ebola virus*. In Gabon and the Republic of the Congo, outbreaks in humans were associated with extensive deaths of chimpanzees and gorillas. In contrast, the animal source of infection during the DRC, Uganda and Sudan outbreaks has never been detected.

Ebola is one of the zoonotic viruses that can lead to a highly fatal disease in human beings. Humans are also one of the accidental hosts and can be infected through close contact with blood and bodily fluids of another infected case (including humans and animals), either by direct contact or indirectly from a contaminated environment. It seems those mosquitoes and other insects do not play a role in the virus transmission and also it is not spread through the air. *Ebola virus* has high transmissibility and virulence so that less than 10 viral particles are enough for becoming infected. The incubation period range is from 2-21 days (average 5-6). Fortunately, the disease is not transmissible until the patient becomes symptomatic, but it continues to be contagious, even postmortem. Family and healthcare providers caring the *Ebola* patients are at the highest risk of becoming infected because of their possible contact with contaminated blood or body fluids. So the virus can easily spread if reasonable preventive precautions are not taken.

EBOV and MARV are regarded as re-emerging and highly infectious pathogens. Outbreaks have been associated with human sporadic cases, involve high rates of case-fatality and cause social and economic disruption. The substantial clinical appearance of both EBOV and MARV with severe hemorrhaging in most cases has also contributed to the high transmission rate and the fear of epidemic and imported cases. According to the US CDC, EBOV and MARV have been classified as Category a bioterrorism agent due to their highly infectious nature and potential use in biological weapons.[13,14]

TRANSMISSION OF *EBOLA VIRUS*:

Ebola is a disease transmitted from wild animals to humans most likely through hunting and collection of sick or dead wild animals and handling or consumption of uncooked bushmeat. Although the source of infection for non-human primates often remains unclear, most evidence indicates direct infection from one or more natural hosts. In rural areas fruit bats are a popular source of forest meat for humans and are prepared by hand to be dried, smoked and/or cooked. Infection could also be transmitted to humans by consumption of forest fruits contaminated with bat saliva or feces. It is recommended that in affected countries contact with wild animals, including bats, rodents or monkeys should be avoided and that communities in contact with these animals practice basic hygiene measures such as regular hand washing at all times. The hunting of susceptible wild animal species listed above for food in affected countries should be avoided.

Human to human transmission occurs through contact with body fluids of an infected person. It is thought that the current epidemics throughout West Africa originated from a single animal-human transmission event that occurred in the forest at the border between Guinea, Sierra Leone and Liberia.[15, 16]

DIAGNOSIS

When *Ebola virus* disease is suspected in a person, his or her travel and work history along with an exposure to wildlife are the important factors to be considered with respect to further diagnosis. To establish diagnosis viral RNA by PCR or viral antigen by immunoenzymatic methods (ELISA) should be carried out in the blood or other body fluids. It must be stressed that *Ebola virus* RNA can be detected 3 days after the infection, so in cases in which patient present to the doctor early and *Ebola virus* disease is strongly suspected, the test should be repeated.[3,17,18]

Laboratory tests used in diagnosis include (Table No1)

Table 1: Table showing Diagnostic tests available

Sr. no.	Timeline of Infection	Diagnostic tests available
1	Within a few days after symptoms begin	-Antigen- ELISA testing - IgM ELISA - Polymerase chain reaction (PCR) - Virus isolation
2	Later in disease course or after recovery	- IgM and IgG antibodies
3	Retrospectively in deceased patients	- Immunohistochemistry testing - PCR - Virus isolation

PREVENTION

Following are some preventive measures taken to avoid the spread of *Ebola Virus* Disease:

- The best way to avoid catching the disease is by not traveling to areas where the virus is found.
- If you are in areas where *Ebola* is present, avoid contact with bats, monkeys, chimpanzees, and gorillas since these animals spread Ebola to people.
- Health care workers can prevent infection by wearing masks, gloves, and goggles whenever they come into contact with people who may have Ebola.
- Remember, there is no licensed vaccine available for *Ebola virus* disease. [18,19]

TREATMENT

There are no specific treatments for *Ebola Virus* Disease, though researchers are working on it. Treatment includes an experimental serum that destroys infected cells.

Doctors manage the symptoms of *Ebola* with:

- Oxygen
- Fluids and electrolytes
- Blood transfusions

- Blood pressure medication
- Treatment for other infections.[20,21]

CONCLUSION

Ebola virus disease (EVD), formerly known as *Ebola* hemorrhagic fever, is a severe, often fatal illness in humans. The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks. The first EVD outbreaks occurred in remote villages in Central Africa, near tropical rainforests, but the most recent outbreak in West Africa has involved major urban as well as rural areas. Early supportive care with rehydration, symptomatic treatment improves survival. There is as yet no licensed treatment proven to neutralize the virus but a range of blood, immunological and drug therapies are under development. There are currently no licensed *Ebola* vaccines but 2 potential candidates are undergoing evaluation.

REFERENCES

1. "*Ebola Virus Disease Fact Sheet No.103"*. World Health Organization. September 2014. *Archived* from the Original on 11 August 2014.
2. Brief general history of Ebola- Honors thesis Stanford University.
3. Ebola Virus: New Insights for the Healthcare Professional: 2011 Edition: Scholarly Paper. Scholarly Editions. 2012. ISBN 978-1-4649-1493-5.
4. What is Ebola virus disease? Fast facts for kids. National Institute for Communicable Diseases. Available online at www.nicd.ac.za
5. Breman JG, Heymann DL, Lloyd G. Discovery of Ebola in 1976 and Current Relevance. J Infect Dis 2016; 214 (Suppl 3): S93-S101.
6. Michalek P, Krejcova L, Adam V, Kizek R. Epidemiology and pathogenesis of Ebola viruses. Journal of Metallomics and Nanotechnologies. 2015; 1:48-52.
7. Y.S.Li and S.P. Chen, Evolutionary History of Ebola Virus. Epidemiol Infect. 2014 Jun; 142(6):1138-45.
8. Mitchell SW, McCormick JB. Physicochemical inactivation of Lassa, Ebola, and Marburg viruses and effect on clinical laboratory analyses. J Clin Microbiol. 1984; 20: 486–489.
9. Warfield KL, Swenson DL, Olinger GG et al. Ebola virus inactivation with preservation of antigenic and structural integrity by a photoinducible alkylating agent. J Infect Dis 2007; 196 (Suppl 2): S276–S283.
10. Thippeswamy NB. Ebola Virus Disease: New Horizons in Biotechnology. 2015; PP 007-014.
11. Zawilinska B, Kosz-Vnenchak M, General introduction to the Ebola virus biology and disease', Folia Medica Cracoviensia, 2014; 54(3): 57-65.
12. Elke Muhlberger, Filovirus Replication, and Transcription', NIH Public Access, 2007, March; 2(2): 205–215.
13. Wambani et al. Ebola virus disease: A biological and epidemiological perspective of a virulent virus, J Infect Dis Diagn, 2016, 1(1): 1-6.
14. Sukul A, Haque S, Hasan MM, Uddin F. Ebola virus pathogenesis: implications for diagnosis and prevention. Int J Pharmacol Toxicol 2016; 6 (2): 74-81.

15. Saeidi M, Moghaddam HT, Kiani MA, Noras M. A short overview of Ebola outbreak. Int J Pediatrics. 2014; 2 (4-1, N-10):287-294.
16. Ebola Virus Disease. World organization for Animal Health. Available online from 06 oct 2014.
17. Jasik MB, Piatek A, Garlicki A. Ebola virus disease - Pathogenesis, Clinical Presentation and Management. Folia Medica Cracoviensia. 2014; Volume LIV, 3: 49–55.
18. "Ebola Virus Disease", National Center for Emerging and Zoonotic Infectious Diseases. CDC. 8 November 2015.
19. Prevention of the Spread of Ebola Virus Disease in the Community and Health Facility Health advice in the workplace on prevention of Ebola virus disease, a center for health protection.Centre for health protection. 2014: 01-06.
20. Ayten Kadanali, Gul Karagoz. An overview of Ebola virus disease. Infect Dis Microbiol. 2015; 2(1):81-86.
21. Ebola Virus: Symptoms, Treatment, and Prevention - WebMD. Available from [01Oct 2016].