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EBOLA AS TRESPASSER IN LIVING BEING- A REVIEW

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ABSTRACT

EVD or Ebola viral disease is a deadly haemorrhagic disease spread by Ebola virus and was commonly found in the African province. This review article is an attempt to gather information on Ebola by highlighting pathogenesis, transmission, symptoms of the disease and other factors from various sources and compile it. Human and non-primates are commonly affected by this virus and the main carrier of this virus is the fruit bat. It is spread from one person to another by contact with body fluids, blood and tissues of animals. During outbreak the virus spreads quickly within healthcare such as clinicians and other personnel They contain single stranded RNA genomes and contains seven genes. Virus remains in the body of immunologically advantaged sites and these sites are the ones where they survive even after it is cleared from other place in the body, like testes, placenta, CNS especially CSF, interior of eyes etc. Virus evade the immune system by inhibiting the early steps of neutrophil activation Drugs are being developed to treat EVD work by stopping the virus from making copies of itself. Survivors suffer from health issues after recovery from Ebola.

KEYWORDS: EVD, Ebola virus, bat, fever, death.

INTRODUCTION

Ebola is a viral haemorrhagic deadly disease, caused by Ebola viruses (WHO 2014), occurring primarily on the African continent and is also known as EVD or Ebola Virus Disease. EVD mostly affects human and non-human primates like chimpanzees, gorillas etc. This disease was first identified in 1976 at Ebola river, situated in a village at Yambuku

(Democratic Republic of Congo) (WHO 2014). Since then, the virus started infecting people, leading to outbreaks in African countries. Ebola outbreaks occur sporadically in sub- Saharan Africa. WHO reported about 24 outbreaks between 1976-2012 resulting in about 1,590 deaths. Among the 24 outbreaks, the largest epidemic was the one that occurred in West Africa on December 2013, reporting about 28,646 cases and 11,323 deaths (WHO 2019, CDC 2014). After the continuous outbreaks, WHO declared Ebola outbreak, a health emergency (Grady D *et al* 2019).

Classification

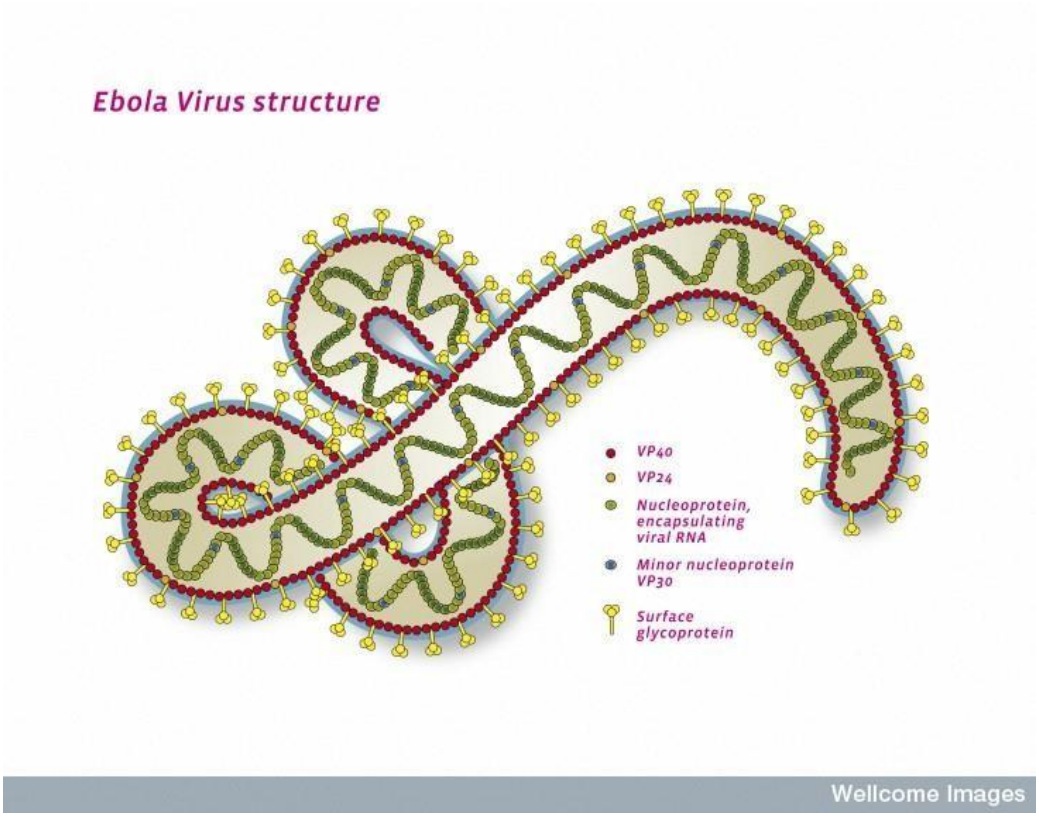
Genera *Ebolavirus* was classified as the species of *Filovirus*, which is now an outmoded species. The various group that are thought to cause Ebola within the genus *Ebola virus* are: -

1. Ebola virus- *Zaire ebolavirus*- ZEBOV.
2. Bombali virus- *Bombali ebolavirus*-BOMV.
3. Bundibugyo virus- *Bundibugyo ebolavirus*- BDBV.
4. Tai Forest virus- *Tai Forest ebolavirus*- TAFV.
5. Reston virus- *Reston ebolavirus*- RESTV.
6. Sudan virus- *Sudan ebolavirus*- SUDV.

Of these only Ebola, Tai Forest, Sudan and Bundibugyo cause disease in humans, Bombali in bats and Reston in other primates and pigs.

Structure

Ebola Virus are generally about 80 nm in diameter and 970 nm in length. They may be cylindrical or tubular and contain a viral envelope, a matrix and nucleocapsid components. Virus appears to be ling, filamentous or sometimes U- shaped, 6- shaped or even circular. They contain a virally encoded glycoprotein (GP) spikes of 7-10 nm. These glycoproteins contain carbohydrate chains known as glycans that are covalently attached to their polypeptide side chains, which is responsible for the entry into new host cells. The outer envelope is derived by the budding of domains of host membrane. They contain single stranded RNA genomes (Pringle CR 2005) and contains seven genes.



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Life cycle

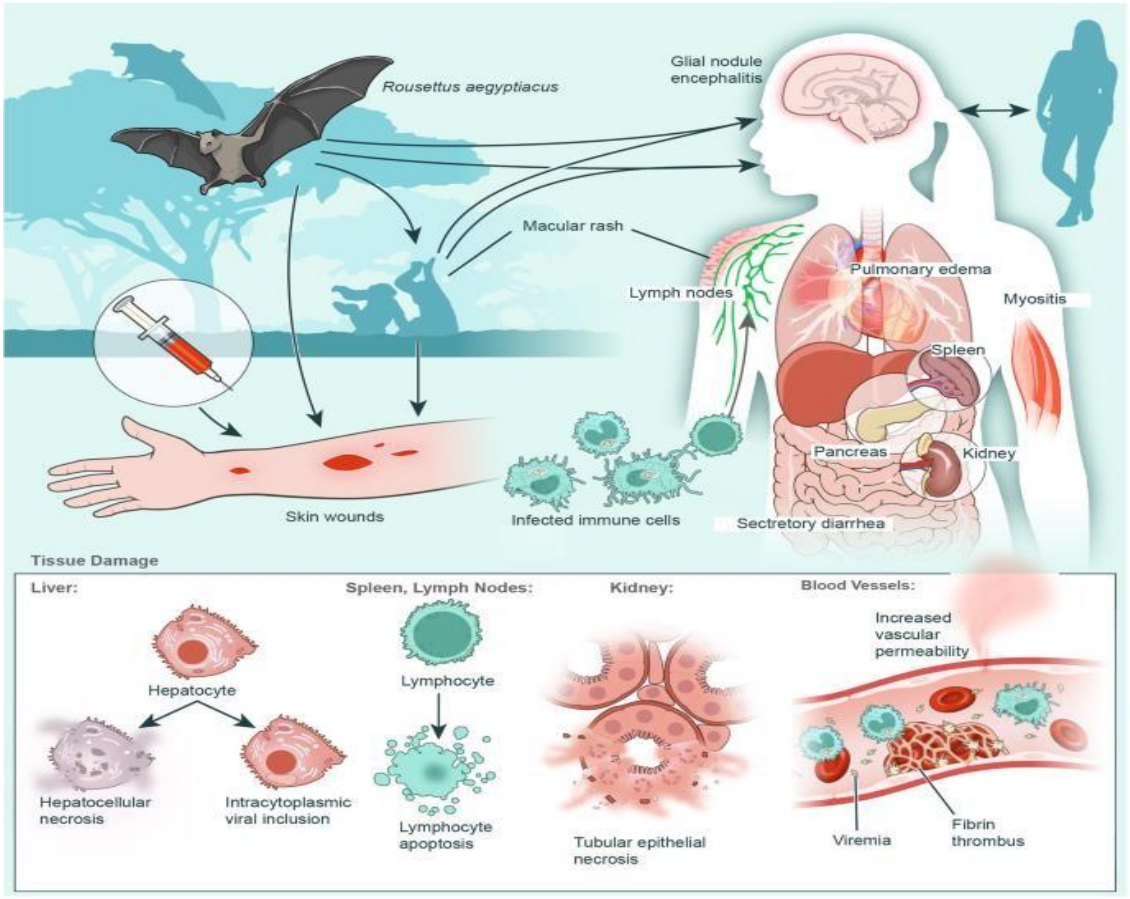
The lifecycle is thought to begin by attaching to a specific surface receptor called C-type lecithins or integrins. The attachment is followed by the fusion of viral envelope with cellular membranes (Misasi J 2014). The virions then travel to the lysosomes and endosomes where the cleavage of the envelope takes place, thus helping it to bind to cellular proteins, thereby fusing with the internal cellular membranes (Misasi J 2014). RNA polymerase which is encoded by the L-gene, uncoats the nucleocapsid partially and transcribes the genes, which are then translated into structural and non-structural proteins. Replication of the genome results in the full-length, positive strand antigenomes which are further transcribed into negative strand virus progeny (Lejnik J 2011). The newly synthesized genomes and structural proteins self-assemble and accumulate inside of the cell membrane. Cellular membrane is gained by the virions from the cell from which they bud. The cycle is then repeated.

Pathophysiology

Ebola viruses can replicate very efficiently in many cells, thereby producing large no. of viruses in monocytes, macrophages, dendritic cells, liver cells, fibroblasts and cells of the adrenal gland (Ansari A 2014) As a result of replication high levels of inflammatory signals

are generated, leading to a septic state.[10] Ebola virus is thought to infect the human cells through breaks in the skin or through contact with mucous membrane (Fink DJ 2014). Further invasion it targets the various immune cells. Virus is further carried to the nearby lymph nodes where further reproduction takes place and then enters the blood stream and lymphatic system further spreading to the whole body (Fink D J 2014). Since virus infects the macrophages, it causes programmed cell death (Chippaux 2014). Later programmed cell death occurs in WBC, especially lymphocytes leading to low concentration in the blood causing a weakened immune system.

After three days of exposure endothelial cells get infected resulting in their break down leading to blood vessel injury. The main cause of this breakdown is due to the synthesis of glycoproteins by the virus, thereby reducing the availability of integrins causing liver damage, resulting in defective blood clotting. Blood volume reduces in patients in such a way that it causes shock and swelling (Kubl A *et al* 2012). Virus evade the immune system by inhibiting the early steps of neutrophil activation. Ebola viral proteins also interferes with the ability to produce and respond to α, β, γ interferons (Ramanan P et al, CDC 2014).



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Transmission

Fruit bats are known to be the natural carrier (WHO 2014) Animals may get infected when they consume fruits partially eaten by the bat. Initially Ebola virus spreads to people only through direct contact with body fluids, blood and tissues of animals such as fruit bat or non-human primate, which is known as spill over event. Spread will also occur from the items recently contaminated with the body fluids (WHO 2014). Ebola virus will spread to other people through direct contact with body fluids (urine, tears, semen, saliva, breast milk), faeces, vomit of the sick or the dead, by touching the body fluids directly or indirectly (infected clothes, bedding and other medical equipment) and virus enters the next host through broken skin or mucous membrane present in the eyes, open wounds, cuts , abrasions, nose or mouth. It is able to survive in a dried state for a few hours (Osterholm *et al* 2015, CDC 2014).

EVD is also transmitted through sexual contact (oral, vaginal, or anal sex) with the sick person or the one who has already recovered from the illness. Virus remains in body fluids like semen from about three months to one year even if they do not have symptoms of illness. Evidence of Ebola spread through vaginal fluids is not yet reported.

Dead bodies are considered to be infectious and hence acre should be taken while performing rituals and also while embalming the body (CDC 2014). Risk infection also occurs in the case of health care workers (Jone R M, Brosseau 2015) especially when they do not work with protective clothing or while handling contaminated objects (Jone R M, Brosseau 2015). The actual risk of airborne transmission in Ebola is very low (Gatherer D 2014).

Ebola is not transmitted through water and food, but can be spread through handling or consumption of wild animals (bush meat) infected with Ebola. Mosquitoes and other insects do not transmit Ebola (Jone R M, Brosseau 2015).

Persistence

Virus remains in the body of immunologically advantaged sites and these sites are the ones where they survive even after it is cleared from other place in the body, like testes, placenta, CNS especially CSF, interior of eyes etc. Researchers are finding, how long the virus stays among the Ebola survivors. During outbreak the virus spreads quickly within healthcare such as clinicians and other personnel. Always the instruments like needles and syringes used must be of disposable type, or must be sterilised properly before use. Ebola viruses can also

survive on surfaces like countertops, doorknobs etc for several hours and several days at room temperature. Disinfection must be performed only using hospital grade disinfectants (CDC 2014).

Symptoms and Signs

Signs and symptoms do not start developing as soon as the person is infected and this period is known as the incubation period. Spread to other people occurs only after they develop symptoms. EVD has the almost the similar symptoms to influenza (flu), malaria or typhoid fever and may be mistaken for these diseases. It is a very rare but severe and deadly disease.

The length of time between exposure to the virus and the (incubation period) development of symptoms appear anywhere from 2 to 21 days and typically 4 and 10 days after contact the virus. The illness progresses from _dry' symptoms like fever (38.3^{o}C or 101^{o} F) (Magil A 2013), aches (head ache, throat (Brown C S et al 2017)), pain (chest, muscular, joint, abdominal) and fatigue and then finally progresses to _wet' symptoms such as diarrhoea and vomiting. Along with these primary symptoms are include unexplained haemorrhaging, bleeding or bruising. Later secondary symptoms include red eyes, skin rash and hiccups (Sharma N Cappell M S 2015, GoeijenbierM *et al* 2014). Severe vomiting and diarrhoea may lead to dehydration (Hoenen T *et al* 2006). Shortness of breath and confusion also occurs (Haas CN 2014). In most of the cases development of maculopapular rash (a flat red area covered with small bumps) is observed seven days after the appearance of symptoms.

Internal and external bleeding is observed in some patients (WHO 2014) and begins after five to seven days of the first symptoms appear (Simpson DI 1977). Sites of needle punctures and mucous membrane bleeding is common in about 45% cases (Medscap 2012), leading to blood loss through stool, vomit, and coughs (Ministry of Health and Longterm care 2014) and decreased blood clotting is also seen. Haematomas, purpura etc are seen around needle injection sites (Feldmann H Geisbert TW 2014). Bleeding into the gastrointestinal tract is yet another complication found as a result of Ebola.

Recovery and Death

Recovery from EVD depends on good supportive clinical care and the patient's immune response. It begins between 7 and 14 days after the symptoms appear. Researches show that survivors of Ebola virus infection have antibodies that can be detected in the blood up to 10 years after recovery (MEDSCAPE 2012). Survivors are thought to have some protective immunity to the type of Ebola that sickened them. Survivors may experience side effects after

their recovery such as ongoing muscular and joint pain, muscle aches, eye and vision problems, liver inflammation, decreased appetite (WHO 2015). Some of them may experience long term complications.

In case death occurs, it will be often from typically six to sixteen days from the first appearance of symptoms and is considered to be often due to low blood pressure as a result of fluid loss Patients are often in coma towards the end of their life.

Diagnosis

If EVD is suspected after work history, travel, or exposure to wildlife, non-specific diagnostic measures like low platelet count, initial decrease in WBC followed by increase in WBC, disseminated intravascular coagulation, bleeding time etc are taken into account (Kortpeter MG *et al* 2011). Virions may be identified by their unique filamentous shapes with electron microscopy (Goldsmith CS Miller SE 2019). Further specific diagnosis like isolating the virus by cell culture and detecting proteins or antibodies by ELISA are performed in the early stages (CDC 2014). Real time PCR is also done for detecting viral RNA (CDC 2014). The most common and reliable diagnostic measure during an outbreak of EVD is real time PCR and ELISA **(**Grolla A,*et al* 2005**)**. A rapid antigen test which gives result in 15 minutes was approved by WHO (WHO 2015) and is able to confirm about 925 of affected cases.

Prevention

When travelling or living in a region where Ebola virus is present or after an outbreak, there are a no. of ways to be protected from the spread of EVD.

- Avoid contact with blood and body fluids (such as urine, faeces, saliva, sweat, vomit, breast milk, semen, and vaginal fluids) of persons who are ill.
- Avoid contact with semen from a man who has recovered from EVD, until testing verifies the virus is gone from the semen.
- Items that may have come in contact with an infected person‘s blood or body fluids (such as clothes, bedding, needles, and medical equipment) should be avoided.
- Care should be taken while performing funeral or burial rituals that require handling the body of someone who died from EVD.
- Avoid contact with bats and nonhuman primates ‘blood, fluids, or raw meat prepared from these animals (bushmeat).
- Prevent contact with the raw meat of an unknown source.
- Practice hand hygiene. Proper hand hygiene methods are: -

- Use alcohol-based hand sanitizer when hands are not visibly soiled. These products usually contain 60-95% ethanol or isopropanol and should not be used when hands are visibly soiled with dirt, blood, or other body fluids.
- Use soap and water when hands are visibly soiled with dirt, blood, or other body fluids and as an alternative to alcohol-based hand sanitizer. Antimicrobial soaps are not proven to offer benefits over washing hands with plain soap and water.
- Use mild (0.05%) chlorine solution where hand sanitizer and soap are not available. But repeated use of 0.05% chlorine solution can cause skin irritation.

After returning from an area affected by Ebola, health should be monitored for 21 days and medical care should be sought immediately if symptoms develop.

Treatment

When treated early as soon as the onset of symptoms, basic interventions can significantly improve the chances of survival which include-providing fluids and electrolytes (body salts) through infusion into the vein (intravenously), providing oxygen therapy to maintain oxygen status and using medication to support blood pressure, reduce vomiting and diarrhoea and managing fever and pain.

Vaccine

During the 2018 eastern Democratic Republic of the Congo outbreak, four investigational treatments were initially available to treat patients with confirmed Ebola. For two of those treatments, called regeneron (REGN-EB3) and mAb114, overall survival was much higher. These two antiviral drugs currently remain in use for patients with confirmed Ebola. Drugs that are being developed to treat EVD work by stopping the virus from making copies of itself.

The U.S. Food and Drug Administration (FDA) approved the Ebola vaccine rVSV-ZEBOV (tradename ―Ervebo‖) on December 19, 2019. The rVSV-ZEBOV vaccine is a single dose vaccine regimen that has been found to be safe and protective against only the *Zaire ebolavirus* species of ebolavirus. This is the first FDA approval of a vaccine for Ebola.

Another investigational vaccine was developed and introduced under a research protocol in 2019 to combat an Ebola outbreak in the Democratic Republic of the Congo. This vaccine leverages two different vaccine components (Ad26.ZEBOV and MVA-BN-Filo) and requires

two doses with an initial dose followed by a second ―booster‖ dose 56 days later. The second vaccine is also designed to protect against only the *Zaire ebolavirus* species of Ebola.

Survivors

After the two large outbreak of Ebola in 2014 and 2018, now there are more survivors. The large number of survivors provides a better chance to better understand the effect of Ebola virus. Survivors suffer from health issues after recovery from Ebola (Qureshi A I *et al* 2015).

The most common complications are

- Stomach pain.
- Weight gain.
- Loss of appetite (Nanyonga M *et al* 2016).
- Headches.
- Muscle and joint pain.
- Tiredness.
- Eye and vision problems like light sensitivity, redness, blurred vision.
- Hair loss.
- Memory loss.
- Hearing problems.
- PTSD- post traumatic disorder.
- Impotence, decreased or lost interest in sex.
- Inflammation of testicles.
- Changes in menstruation.
- Inflammation of the Pericardium (Epstein L 2015, Mohammed A 2015, Clark 2015, Kibadi 1999, Bwaka *et al* 1999, Chancellor *et a*l 2016, Mahadevan S *et al* 2015).

Infection control

- People caring the infected persons should wear protective clothing which does not leave skin exposed. Persons handling contaminated objects also must take care (CDC 2014). It is recommended that training should be given to medical personnel for proper use of suit up and removing of PPE and in addition a person who is appropriately trained should be watching each step of these procedures to ensure donning and doffing is done properly (CDC 1998). The infected person should be in barrier isolation and all the wastes should be properly disinfected.
- Ebolaviruses can be eliminated with heating at 60^0C for 30-60 minutes. Lipid solvents

such as alcohol -based products, detergents, sodium hypochlorite, calcium hypochlorite at appropriate concentrations may be used to disinfect surfaces (CDC 2014).

- General public should be educated about the risk factors of infection and preventative methods should be introduced like regular hand washing using soap and water (Public health agency of Canada2001). Bushmeat, which is an important source of protein should be handled and cooked thoroughly before consumption (CDC 2014).

  Maintenance of proper protective barrier while performing burial rituals is required (WHO 2014).
- Transportation crews must follow certain isolation procedure, in case anyone exhibit symptoms resembling EVD (Harden B 2000). In laboratories where tests are carried out, containment of BSL-4 is required and the researchers must be properly trained in it (WHO 2014).
- Control of outbreaks requires rapid detection, isolation of the sick and contact tracing which is important to contain an outbreak. Contact tracing involves finding everyone who had close contact with the infected individuals and monitoring them, isolating them if tested positive and then tracing the contacts‘contacts (OSHA 2014, Frieden T R et al 2015).

CONCLUSION

Ebola virus disease has caused so much disruption because of its high mortality and because of its clinical manifestations. EVD has emerged as a significant global public health menace due to multiple disease outbreaks in the last 25 years. Recent advancements are being carried out in the form of effective Ebola virus vaccine and anti- Ebola virus drugs. However, rapid geographic dissemination, nonspecific clinical presentation, lack of vaccine, and specific diagnostic test are the possible challenges to combat this dreaded public health menace. However, the current pandemic has not occurred because Ebola virus has mutated but, rather, because a lack of information, inadequate public health practices, eases of travel, insufficient infection control and poor health care education.

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