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REVIEW ON EBOLA VIRUS DISEASE: ITS OUTBREAK AND CURRENT STATUS

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ABSTRACT
Ebola virus, formerly designated Zaire Ebola virus, is one of the five known viruses within the genus Ebola virus which cause disease in humans. Ebola Virus Disease (EVD) has become a public health emergency of international concern. The World Health Organization and Centers for Disease Control and Prevention have developed guidance to educate and inform healthcare workers and travelers worldwide. The natural reservoir of Ebola virus is believed to be bats, particularly fruit bats, and it is primarily transmitted between humans and from animals to humans through body fluids. Ebola is RNA virus that belongs to the family filoviridae, genus Ebola virus. The viruses (EBOV) are enveloped, non-segmented, negative-sense, single-stranded RNA viruses. Ebola virus disease (EVD) was first described in the Democratic Republic of Congo (DRC) in 1976. The exact origin, locations and natural reservoir of Ebola virus remain unclear. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person. Hunting and butchering of wildlife (great apes and fruit bats) has been identified in previous outbreaks as a potential source of infection. The onset of Ebola virus disease is sudden and early symptoms includes; fever and headache, followed by vomiting and diarrhea. Patients in the final stage of disease die in the clinical picture of massive bleeding, severe dehydration, hypovolemic shock and multi-organ failure. Ebola virus infections can be diagnosed by detecting antigens with an antigen capture ELISA and by detecting viral RNA with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). No specific treatment has been demonstrated yet to be safe and effective for Ebola virus. Standard treatment currently consists of supportive therapy, including maintenance of blood volume and electrolyte balance, as well as standard nursing care. Prevention and control is mainly based on appropriate precautions to break ways of transmission.

KEYWORDS: Ebola virus disease; viral disease pathogenesis; Ebola viral hemorrhagic fever; Prevention; Zoonotic.

INTRODUCTION[1-12]

Ebola virus disease (**EVD**), also known as **Ebola hemorrhagic fever** (**EHF**) or simply **Ebola** is a viral hemorrhagic fever of humans and other primates caused by Ebola viruses. Signs and symptoms typically start between two days and three weeks after contracting the virus with a fever, sore throat, muscular pain, and headaches. Vomiting, diarrhea and rash usually follow, along with decreased function of the liver and kidneys. At this time, some people begin to bleed both internally and externally. The disease has a high risk of death, killing 25% to 90% of those infected, with an average of about 50%.This is often due to low blood pressure from fluid loss, and typically follows 6 to 16 days after symptoms appear. The virus spreads through direct contact with body fluids, such as blood from infected humans or other animals. Spread may also occur from contact with items 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 EVD may carry the virus for several weeks to months. Fruit bats are believed to be the normal carrier in nature, able to spread the virus without being affected by it. Other diseases such as malaria, cholera, typhoid fever, meningitis and other viral hemorrhagic fevers may resemble EVD. Blood samples are tested for viral RNA, viral antibodies or for the virus itself to confirm the diagnosis.

Control of outbreaks requires coordinated medical services and community engagement. This includes rapid detection, contact tracing of those who have been

exposed, quick access to laboratory services, care for those infected, and proper disposal of the dead through cremation or burial. Samples of body fluids and tissues from people with the disease should be handled with special caution. Prevention includes limiting the spread of disease from infected animals to humans by handling potentially infected bush meat only while wearing protective clothing, and by thoroughly cooking bush meat before eating it. It also includes wearing proper protective clothing and washing hands when around a person with the disease. An Ebola vaccine was approved in the United States in December 2019. While there is no approved treatment for Ebola as of 2019, two treatments (REGN-EB3 and mAb114) are associated with improved outcomes. Supportive efforts also improve outcomes. This includes either oral rehydration therapy (drinking slightly sweetened and salty water) or giving intravenous fluids as well as treating symptoms.

The disease was first identified in 1976, in two simultaneous outbreaks: one in Nzara (a town in South Sudan) and the other in Yambuku (Democratic Republic of the Congo), a village near the Ebola River from which the disease takes its name. EVD outbreaks occur intermittently in tropical regions of sub-Saharan Africa. Between 1976 and 2013, the World Health Organization reports 24 outbreaks involving 2,387 cases with 1,590 deaths.

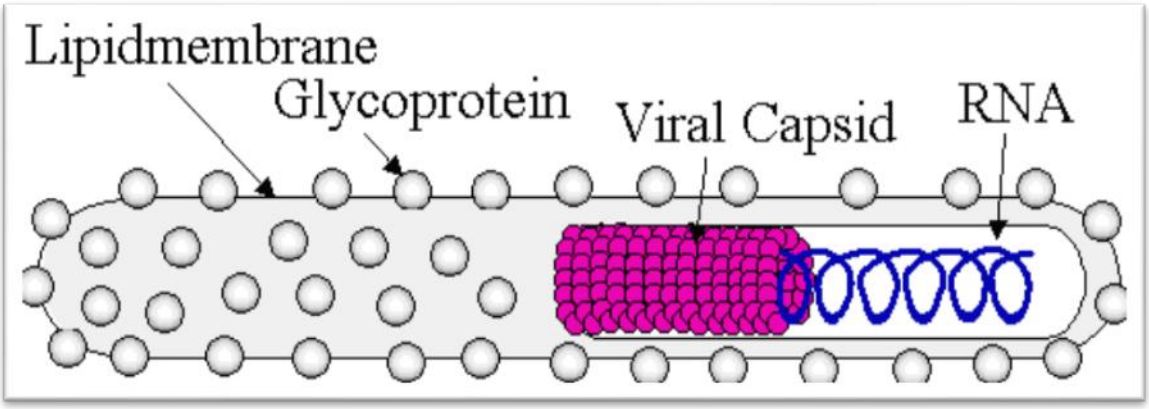

Fig no1:General structure of Ebola virus.

HISTORY OF EBOLA HEMORRHAGIC FEVER[12]

Ebola hemorrhagic fever first appeared in Zaire (currently, the Democratic Republic of the Congo or DRC or Congo) in 1976. The original outbreak was in a village named Yambuku near the Ebola River after which the disease was named. During that time, researchers identified the virus in person-to-person contact transmission. Of the 318 patients diagnosed with Ebola, 88% died. Since that time, there have been multiple outbreaks of Ebola virus, and researchers have identified five strains; four of the strains are responsible for the high death rates. The four Ebola strains are termed as follows: Zaire, Sudan, Tai Forest, and Bundibugyo virus, with Zaire Ebola virus being the most lethal strain. Researchers have found a fifth strain termed Reston in the Philippines. The strain infects primates, pigs, and humans and causes few if any symptoms and no deaths in humans. Most outbreaks of the more lethal strains of Ebola have occurred in sub-Saharan West Africa and mainly in small- or medium-sized towns. Health care professionals Believe bats, monkeys, and other animals maintain the non-human virus life cycle in the wild; humans can become infected from handling and/or eating infected animals. Once an Ebola outbreak is recognized, African officials isolate the area until the outbreak ceases. However, in the last outbreak that began in West Africa in March 2014, some of the infected people reached larger city centers before the outbreak was recognized; this caused further spread. The infecting Ebola virus detected during this outbreak was the Zaire strain, the most pathogenic strain of Ebola. Health agencies are terming this outbreak as an "unprecedented epidemic." This epidemic spread quickly in the West African countries of Guinea and Sierra Leone. In addition, countries of Liberia, Nigeria, Senegal, Uganda, and Mali all reported confirmed infections with Ebola. In addition, a few infections or flare-ups of Ebola virus infection appeared in the United States, Spain, and the United Kingdom; most of the people with Ebola in these countries either were imported infections from West Africa or were newly spread infections from treating patients who originally became infected in Africa. Another outbreak occurred in the DRC in May 2018 in Bikoro, a small town 80 miles from Mbandaka, with 46 reported infections and 26 deaths. Unfortunately, the large city of Mbandaka, with over 1 million people, has recorded at least three people with Ebola. The DRC hopes to isolate or stop the spread of Ebola in the two areas by vaccinating anyone who may have had some physical contact with an infected person with a new chimeric virus vaccine that in 2015 showed good results in Ebola-infected patients.

TRANSMISSIONS[13-17]

Ebola virus is virulent and is highly transmittable. It was introduced to humans by close contact with animals. In humans, the virus primarily spreads through direct contact with the infected person's body fluids (stool, urine, saliva, semen, breast milk, and semen). In a convalescent male, the virus can persist in semen for at

least 70 days. Contaminated objects such as needles, syringes, and contaminated materials can also transmit it indirectly. It is not known to have confirmed air‑borne transmission in humans. The corpse of infected person and carcass of dead infected animals can also be a source of infection.

❖ **Animal Food Products and Ebola Virus**

Transmission Bush meat: The exact nature of animal-to-human transmission of Ebola viruses is not often known. However, harvesting food product is directly related to Ebola virus transmission. Specifically, hunting and butchering of wildlife for food typically referred to as "bush meat," exposes humans to blood and other fluids of potentially infected animals. Studies have found that bush meat is an important source of cash income and a food source in West Africa, particularly during times of economic hard ship. The international market of illegal bush meat poses public health risks as USA and European countries demand for bush meat.

❖ **Livestock**

It is hypothesized that livestock could be a possible Ebola virus reservoir, but no cases have been reported. The Food and Agriculture Organization (FAO) has characterized current knowledge by stating, "Information is extremely limited on the ability of the Ebola virus to infect livestock like cattle, sheep and goats or chickens. Guinea pigs, consumed in several countries, are commonly infected in Ebola virus research. Recent studies have also shown that swine can become infected with the highly pathogenic EBOV. Once the pigs became infected they developed clinical symptoms and transmitted the virus to healthy pigs. There is strong evidence that dogs, which are consumed in some countries including some with EVD outbreaks, can become infected with EBOV naturally.

❖ **Plant Food Products and Ebola Virus Transmission**

Consumption of Contaminated Plant Food Products: There are no known cases of EVD transmission via consumption of plant food products. However, there may be transmission in the same way that an Ebola virus may be transmitted to nonhuman primates through fruit partially eaten by bats. Some experts speculate that Ebola virus could be transmitted via bat saliva or feces on fruit such as mangoes or guava. The concern is great enough that in the Ebola affected nations, United Nation International Children's Emergency Fund (UNICEF) advises not to eat mangoes that "have been bitten by bats".

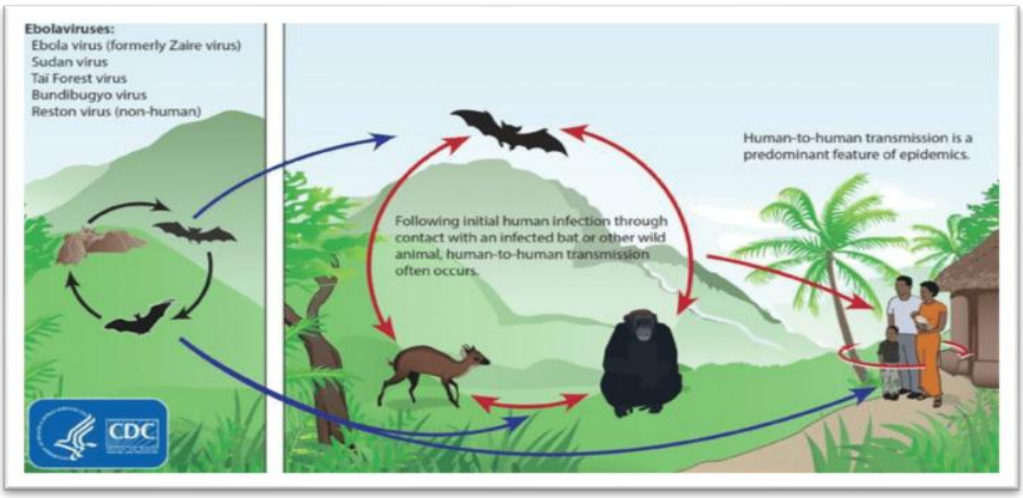

Fig no2: Zoonotic and Transmission of Ebola virus

EBOLA VIRUS SYMPTOMS & SIGNS[18-32]

❖ **Onset**

The length of time between exposure to the virus and the development of symptoms (incubation period) is between 2 and 21 days, and usually between 4 and 10 days. However, recent estimates based on mathematical models predict that around 5% of cases may take greater than 21 days to develop. Symptoms usually begin with a sudden influenza-like stage characterized by feeling tired, fever, weakness, decreased appetite, muscular pain, joint pain, headache, and sore throat. The fever is usually higher than 38.3 °C (101 °F). This is often followed by nausea, vomiting, diarrhoea, abdominal pain, and sometimes hiccups. The combination of severe vomiting and diarrhea often leads to severe dehydration. Next, shortness of breath and chest pain may occur, along with swelling, headaches, and confusion. In about half of the cases, the skin may develop a maculopapular rash, a flat red area covered with small bumps; five to seven days after symptoms begin

❖ **Bleeding**

In some cases, internal and external bleeding may occur. This typically begins five to seven days after the first symptoms. Infected people show some decreased blood clotting. Bleeding from mucous membranes or from sites of needle punctures has been reported in 40–50% of cases. This may cause vomiting blood, coughing up of blood, or blood in stool. Bleeding into the skin may create petechial, purpura, ecchymosis or hematomas (esp

ecially around needle injection sites). Bleeding into the whites of the eyes may also occur. Heavy bleeding is uncommon; if it occurs, it is usually in the gastrointestinal tract. The incidence of bleeding into the gastrointestinal tract has decreased since earlier epidemics and is now estimated to be approximately 10% with improved prevention of disseminated intravascular coagulation.

❖ **Recovery and death**

Recovery may begin between seven and 14 days after first symptoms. Death, if it occurs, follows typically six to 16 days from first symptoms and is often due to low blood pressure from fluid loss. In general, bleeding often indicates a worse outcome, and blood loss may result in death. People are often in a coma near the end of life. Those who survive often have ongoing muscular and joint pain, liver inflammation, and decreased hearing, and may have continued tiredness, continued weakness, decreased appetite, and difficulty returning to pre-illness weight. Problems with vision may develop. Survivors develop antibodies against Ebola that last at least 10 years, but it is unclear whether they are immune to additional infections.

Symptoms of Ebola

Early on, Ebola can feel like the flu or other illnesses. Symptoms show up 2 to 21 days after infection and usually include:

- High fever Headache.
- Joint and muscle aches.
- Sore throat.
- Weakness.
- Stomach pain.
- Lack of appetite.

CAUSES[12]

Ebola outbreaks occur when the virus is transmitted first from an infected animal to a human and then between humans. The viral infection is spread from animals to humans through contact with infected wildlife such as fruit bats, chimps, and gorillas. Certain fruit bats are believed to be the natural hosts for the Ebola viruses.

EVD is transmitted from person to person by direct contact (through broken skin and mucous membrane) via bodily fluids or secretions from infected people, such as.

- Blood.
- Breast milk.
- Semen (up to 61 days after infection).
- Sweat.
- Stool.
- Urine.
- Vomit.

Transmission can also occur through contact with objects contaminated with these fluids and the bodies of the deceased with EVD. Since the bodies of the deceased can infect those who handle them, safe burial practices are extremely important in containing outbreaks. The infection can be spread further by cultural burial practices such as ritual washings that bring people into close contact with infected bodies.

PATHOPHYSIOLOGY[33-45]

Like other filo viruses, EBOV replicates very efficiently in many cells, producing large amounts of virus in monocytes, macrophages, dendritic cells and other cells including liver cells, fibroblasts, and adrenal gland cells. Viral replication triggers high levels of inflammatory chemical signals and leads to a septic state.

EBOV is thought to infect humans through contact with mucous membranes or skin breaks. After infection, endothelial cells (cells lining the inside of blood vessels), liver cells, and several types of immune cells such as macrophages, monocytes, and dendritic cells are the main targets of attack. Following infection, immune cells carry the virus to nearby lymph nodes where further reproduction of the virus takes place. From there the virus can enter the bloodstream and lymphatic system and spread throughout the body. Macrophages are the first cells infected with the virus, and this infection results in programmed cell death. Other types of white blood cells, such as lymphocytes, also undergo programmed cell death leading to an abnormally low concentration of lymphocytes in the blood. This contributes to the weakened immune response seen in those infected with EBOV.

Endothelial cells may be infected within three days after exposure to the virus. The breakdown of endothelial cells leading to blood vessel injury can be attributed to EBOV glycoproteins. This damage occurs due to the synthesis of Ebola virus glycoprotein (GP), which reduces the availability of specific integrin's responsible for cell adhesion to the intercellular structure and causes liver damage, leading to improper clotting. The widespread bleeding that occurs in affected people causes swelling and shock due to loss of blood volume. The dysfunctional bleeding and clotting commonly seen in EVD has been attributed to increased activation of the extrinsic pathway of the coagulation cascade due to excessive tissue factor production by macrophages and monocytes.

After infection, a secreted glycoprotein, small soluble glycoprotein (sGP or GP) is synthesized. EBOV replication overwhelms protein synthesis of infected cells and the host immune defenses. The GP forms a trimetric complex, which tethers the virus to the endothelial cells. The sGP forms a diametric protein that interferes with the signaling of neutrophils, another type of white blood cell. This enables the virus to evade the immune system by inhibiting early steps of neutrophil activation.

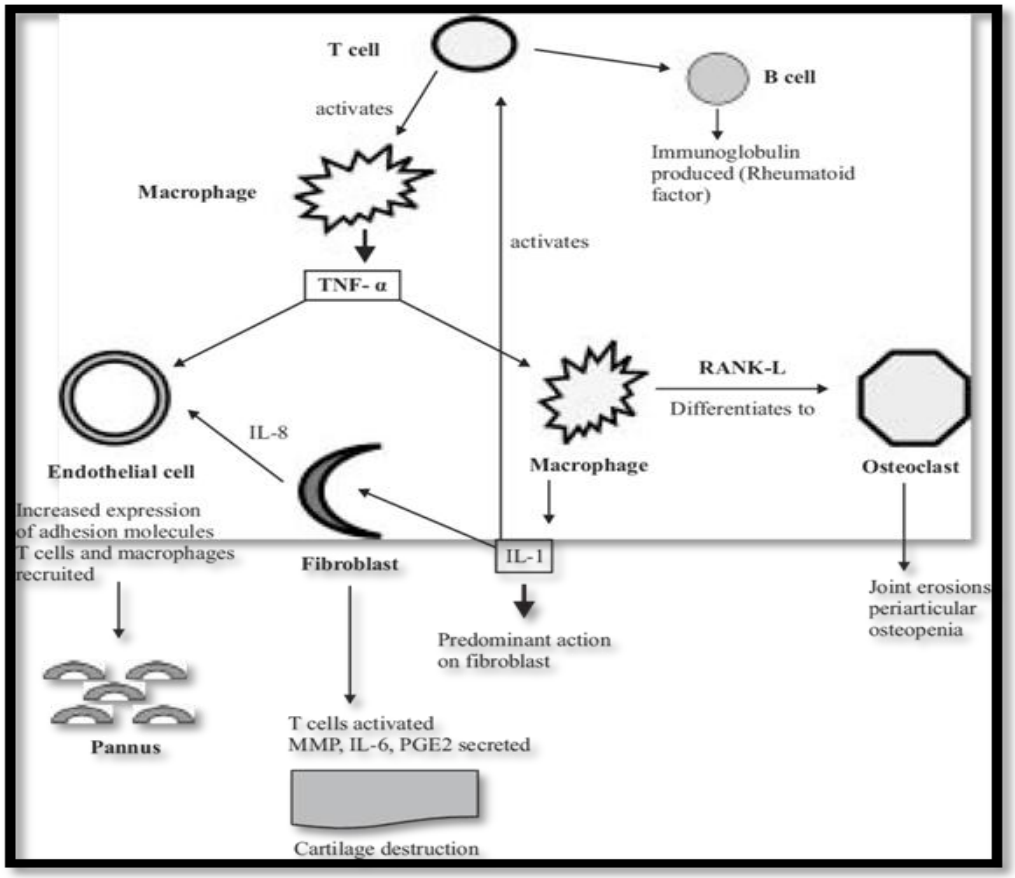

Fig no3: Pathogenesis Schematic

Pathogenesis

The pathogenesis of Ebola is still not well understood because of the difficulty in conducting clinical studies under the conditions of outbreaks. The Ebola virus enters the host through small skin lesions or mucosa. Upon cell entry, the virus replicates in the host cell membranes and the infected cell is destroyed. Analysis of tissues from infected human and non-human primates have demonstrated that viral replication occurs initially in leukocytes, epithelial cells, hepatocytes, spleen, adrenal cortical, and endothelial cells The pathogenesis of Ebola virus can is divided in to two mechanisms, those in which viral infection of host cells results in direct damage to tissues, and those in which tissue injury is brought about indirectly, through interactions between the virus and the host immune systems. The two factors are important for the virus to be able to kill a variety of cells in many different tissues. Antigen presenting cells (APCs) such as macrophages, monocytes and dendritic cells are the first cells to be infected by the virus.

Pathogenesis of Ebola Virus

❖ **Epidemiology**

Ebola virus typically appears in sporadic outbreaks, usually spread within a health-care setting. There is increasing frequency of outbreaks in sub-Saharan Africa of which significant ongoing outbreaks in wild (endangered) non-human primate species (chimpanzees). The important Ebola sources for humans are animal carcasses in the forest. The increasing contact of the human and virus reservoir, combined with its virulence has enhanced EVD epidemics. The virus is zoonotic (animal borne) with four of the five subtypes occurring in an animal host native to Africa except Ebola-Reston subtype, which was isolated from infected cynomolgus monkeys that were imported to the United States and Italy from the Philippines.

❖ **Etiology**

The family Filoviridae consists of three genera, Ebola, Marburg and Cueva virus. Ebola and Marburg viruses are among the most virulent pathogens in humans. In the past, Ebola and Marburg viruses were classified as hemorrhagic fever viruses, based upon their clinical manifestations, which include coagulation defects, bleeding, and shock. However, the term hemorrhagic fever is no longer used to refer to Ebola virus disease since only a small percentage of Ebola patients actually develop significant hemorrhage, and it usually occurs in terminal phase of fatal illness, when the individual is already in shock. Genus Ebola is divided into five identified species, four of which have caused disease in humans. They are Ebola virus (Zaire Ebola virus); Sudan virus (Sudan Ebola virus); Taï Forest virus (Taï Forest Ebola virus, formerly Côte d'Ivoire Ebola virus); and the Bundibugyo virus (Bundibugyo Ebola virus). The fifth, Reston virus (Reston Ebola virus), has caused disease in nonhuman primates but not in humans.

❖ **Morphology**

Viruses in the family Filoviridae are mononega viruses, which mean they have an unsegmented genome with negative polarity. Based on the differences in the genetic make-up, there are two genera in this family: Marburg virus and Ebola virus. Marburg virus has no soluble glycoprotein (sGP) which Ebola do have and may be connected with the regulation of its pathogenicity. There are seven expressed proteins by filo viruses: nucleoprotein (NP), glycoprotein (GP), RNA-dependent RNA polymerase (RdRP), and four structural proteins: viral protein 24 (VP24), viral protein 30 (VP30), viral protein 35 (VP35), and viral protein 40 (VP40). The rib nucleoprotein is derived from the RNA genome, NP, VP30, VP35, and RdRP protein, though Marburg virus is reported to be able replicate in the absence of VP30. The VP35 protein is known to block interferon induction in both Marburg and Ebola viruses.

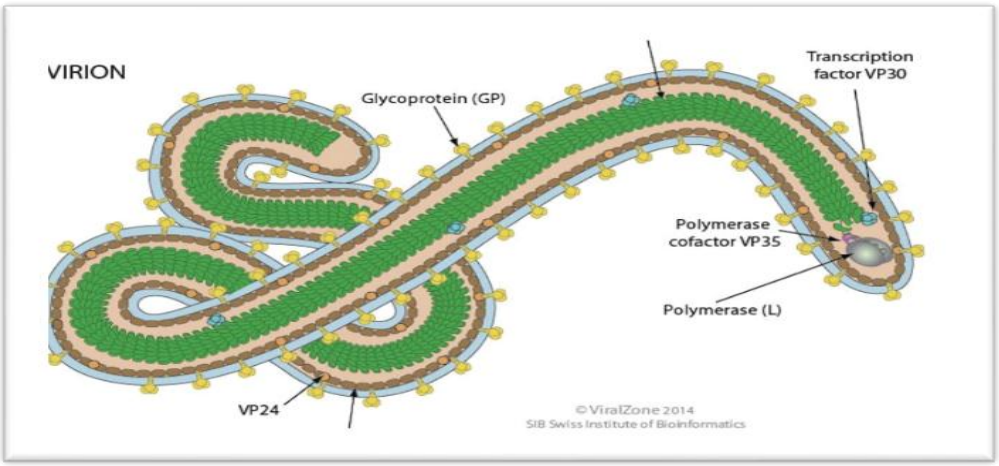

Fig no 4: Structure of Ebola virus and its genome.

❖ **Life Cycle**[50]

The natural reservoir host of Ebola virus remains unknown. However, researchers believe that the virus is animal-borne and bats are most likely reservoir. Molecular studies have demonstrated that bats are natural reservoir host for several recently emerged Ebola viruses .However the role of primates in the natural ecology of Ebola virus is still poorly understood and their role as part of a reservoir complex is unknown. Human disease is frequently linked to contact with infected primate carcasses, though direct contact with other infected hosts is reported .It is not clear whether there is primate to primate transmission. However, it is noticeable that primates, especially great apes, appear to have been severely affected by Ebola (Zaire Ebola virus).

CLINICAL FEATURES[45]

EVD has an incubation period of 2 to 21 days with shorter incubation periods in cases of exposure to contaminated material like needle stick injury. The first symptoms are high‐grade fever, malaise, fatigue, body aches, and sore throat. They are followed by epigastric pain, nausea, vomiting, watery diarrhea leading to intravascular volume depletion, asthenia, headache, conjunctival injection, chest pain, abdominal pain, arthralgia's, myalgia's, hiccups, delirium, shock, hemorrhage including internal (gastrointestinal) and external (gingival bleeding and in stools), secondary infections, mining encephalitis, and persistent neurocognitive abnormalities. Children and pregnant women populations are particularly vulnerable. The survival of neonates born to mothers with EVD has not been reported. Malaria, typhoid fever, shigellosis, leptospirosis, yellow fever, dengue, and other viral hemorrhagic fevers are among the differential diagnoses to consider in EVD‐infected patients. Laboratory findings include lymphocytopenia, thrombocytopenia, and elevated liver enzymes. Prothrombin and partial thromboplastin times are also increased. Confirmation within a few days after symptoms can be obtained with enzyme‐linked immunosorbent assay, polymerase chain reaction assay, and virus isolation. EVD is primarily treated symptomatically. No approved vaccine is currently available for EVD. Supportive care is critical for the patients.

DIAGNOSIS OF EVD[46]

Following laboratory tests are used for the diagnosis of Ebola virus infections:-

ELISA

- Antigen detection tests,
- Serum neutralization test,
- RT-PCR assay,
- Virus isolation by cell culture for appropriate care and management also investigate
- Liver function test,
- Kidney function test,
- Electrolytes,
- Hematocrits,
- Repeated platelet count,
- Hemoglobin,
- WBC

PREVENTION AND TREATMENT[47]

Prevention General Approach: People who care for those infected with Ebola should wear protective clothing

including masks, gloves, gowns and goggles. In 2014, the CDC began recommending that medical personal protective equipment (PPE); in addition, a designated person, appropriately trained in biosafety, should be watching each step of these procedures to ensure they are done correctly. Several concurrent strategies should be employed to prevent the spread of Ebola virus. Strict infection control measures and the proper use of personal protective equipment are essential to prevent transmission to healthcare workers. In addition, individuals who have been exposed to Ebola virus should be monitored, so that they can be identified quickly if signs and symptoms develop. During the 2014 outbreak, kits were put together to help families treat Ebola disease in their homes, which include protective clothing as well as chlorine powder and other cleaning supplies. Education of those who provide care in these techniques, and the provision of such barrier-separation supplies has been a priority of Doctors without Borders. Ebola virus can be eliminated with heat (heating for 30 to 60 minutes at 60 °C or boiling for 5 minutes). To disinfect surfaces, some lipid solvents such as some alcohol-based products, detergents, sodium-hypochlorite (bleach) or calcium hypochlorite (bleaching powder), and other suitable disinfectants may be used at appropriate concentrations. Bus meat, an important source of protein in the diet of some Africans, should be handled and prepared with appropriate protective clothing and thoroughly cooked before consumption. If a person with Ebola disease dies, direct contact with the body should be avoided. Certain burial rituals, which may have included making various direct contacts with a dead body, require reformulation such that they consistently maintain a proper protective barrier between the dead body and the laving. Contact tracing is considering important to contain an outbreak. If any of these contacts comes down with the disease, they should be isolated, tested and treated. Then the process is repeated by tracing the contacts' contacts. Isolation and quarantine: Isolation refers to separating those who are sick from those who are not. Quarantine refers to separating those who may have been exposed to a disease until they either show signs of the disease or are no longer at risk. In the United States, the law allows quarantine of those infected with Ebola virus. During the 2014 Ebola disease outbreak, Liberia closed schools. Environmental infection control: If a patient with suspected or confirmed Ebola virus disease is being cared for in a healthcare setting, specific precautions should be taken to reduce the potential risk of virus transmission through contact with contaminated surfaces. The CDC has provided specific recommendations for environmental infection control in hospitals, general healthcare settings in West Africa, and provides information about restrictions on travel and transport of asymptomatic persons who have been exposed to Ebola virus. Asymptomatic persons who have had a possible exposure at any risk level should be monitored for signs and symptoms of Ebola virus disease. Monitoring should continue for 21 days after the last known exposure; the development of fever and/or other clinical manifestations suggestive of Ebola virus disease should be reported immediately Breastfeeding and infant care: Ebola virus can be transmitted by close contact of an infected mother with her children. Thus, the CDC recommends that mothers with Ebola virus disease avoid close contact with their infants if the infant can receive adequate care and nutrition in other ways. Precautions during the convalescent period: Patients recovering from Ebola virus disease may continue to have virus present in certain body fluids (e.g. urine, semen, vaginal secretions, and breast-milk) even if virus is no longer detectable in the blood. However, the risk of transmission secondary to virus in these sites remains unclear. To prevent sexual transmission of Ebola through semen, the WHO recommends that men abstain from sex (including oral sex) for three months after onset of symptoms, or use condoms if abstinence is not possible. There are currently no recommendations to guide when infected women can resume sexual activity and/or breast feeding. Pregnancy The CDC and the American College of Obstetrics and Gynecology have issued recommendations for the care of pregnant women with Ebola virus disease. Strict infection control precautions must be used when caring for all pregnant patients with Ebola virus disease. Case reports suggest that there is a high risk for fetal death and pregnancy associated hemorrhage. However, there are no data to suggest whether cesarean or vaginal delivery is preferred or when the baby should be delivered.

EBOLA VACCINES[12]

Ebola virus disease (EVD) emerged at unprecedented epidemic levels in West Africa in 2014. Whereas previous EVD outbreaks were contained fairly quickly, this epidemic spread to crowded urban areas where transmissions continued unabated for many months. Retrospective analysis indicates that the first case of the disease may have occurred at the end of 2013. An 18-month-old boy in a small village in Guinea became ill and died in late December, and the disease began to spread. It wasn't until late March 2014 that the disease-causing agent was identified as Ebola virus. Through the fall of 2014, the epidemic was ongoing in Sierra Leone, Guinea, and Liberia. Nigeria and Senegal had small outbreaks related to importations from neighboring countries, but public health authorities there were able to contain spread of the disease. Several cases and deaths were reported from Mali, but spread was limited. In total, by the time the epidemic was over in March 2016, 11,325 confirmed, probable, and suspected deaths occurred. Total EVD cases numbered 28,652. Transmission of the disease was limited to West African countries, with the exception of several transmissions in healthcare settings in Europe and the United States. Two U.S. nurses and one Spanish nurse became ill from contact with patients who acquired the disease in West Africa. The nurse's recovered. Ebola virus disease has no cure, but supportive care in a hospital setting can increase a patient's chance for survival. Additionally, plasma transfusions from convalescent patients and an

experimental antibody preparation have been used to treat certain patients. It is not possible to say at this time whether these treatments have had an effect on the course of the disease in the patients who received them. Ebola virus was first identified in 1976. By the end of that year, two related strains of the virus were known--Ebola Zaire and Ebola Sudan. Three other strains are now known to exist. Vaccine development began in the late 1970s.

Results from a test of inactivated Ebola vaccine in guinea pigs were published in Lancet in 1980. Because EVD outbreaks are rare and have, until 2014, been controlled quickly, commercial vaccine manufacturers have demonstrated little urgency in advancing vaccines through clinical trials. That changed in 2014: several vaccines previously tested only in animals are being fast-tracked into Phase 1 clinical trials.ClinicalTrials.gov, a global registry of trials involving human subjects, lists several Ebola vaccine trials in progress. Ebola Zaire is the strain of the virus that is responsible for the 2014 outbreak; accordingly, all of the vaccine candidates being advanced are designed to prevent that strain. If these vaccines work for Ebola Zaire, it is very likely that the same principles can be applied to the other strains. The two front-running vaccine candidates are a GSK chimpanzee adenovirus vector vaccine (including several versions of it) and a Merck/New Link Genetics recombinant vaccine. Both are being tested in a single Phase 2 trial in Liberia in those at risk for EVD. The trial is being run by NIAID/NIH and began recruiting participants in fall 2015.

The Ebola vaccine licensed by New Link Genetics in Ames, Iowa, was originally developed by the Public Health Agency of Canada, which still holds intellectual property rights for it. The vector for this monovalent Ebola Zaire vaccine is an attenuated vesicular stomatitis virus a virus, like rabies virus, in the Rhabdoviridae family. Vesicular stomatitis virus (VSV) can infect humans though this is a self-limited infection. A safe VSV vaccine for animals has been developed for animal use but it is not currently marketed in the United States.

The version of the GSK Ebola vaccine in the Phase 2 trial is monovalent and offers protection from Ebola Zaire only. This vaccine uses an adenovirus to deliver key Ebola antigens to human cells. Adenoviruses can cause a variety of diseases, but attenuated adenoviruses are safe and have been studied as vaccine vectors. A related bivalent (Ebola Zaire and Ebola Sudan) chimpanzee adenovirus vaccine is being tested in a Phase 1 trial at the NIH Clinical Center.

A vaccine candidate originating from Thomas Jefferson University's Vaccine Center may advance to clinical trials in humans. This vaccine, developed by Jefferson's Matthias Schnell, delivers Ebola antigens with an inactivated rabies virus vector. Versions of the vaccine, which have also delivered Ebola Zaire and Ebola Sudan antigens as well as Marburg virus antigens, have been tested in macaques. Funding from the National Institute of Allergy and Infectious Diseases and the Department of Defense allowed production of a clinical lot of the vaccine for a potential Phase 1 trial. Johnson & Johnson has a prime-boost Ebola vaccine in development. This two-phase strategy starts with direct exposure to DNA (the "prime") followed by offering the same or similar antigen in a virus that does not replicate well in human tissue ("the boost"). This approach has been shown in a variety of settings to yield a robust immune response to the antigen of interest.

The Phase 1 trial starts in January 2015 in the United States and Europe. The first dose of the vaccine uses a DNA vaccine that primes the immune system to make Ebola Zaire and Ebola Sudan surface proteins; the boost vaccine is based on a recombinant adenovirus vector that delivers an Ebola Zaire surface protein. More Phase 2 and 3 vaccine trials are already being planned. In many cases, trial participants will be those at high risk of contracting the disease, such as healthcare workers and family members of people who have EVD.

TREATMENT OF EBOLA[47]

Approach to therapy there are no approved treatments available for EVD. Clinical management should focus on supportive care of complications, such as hypovolemia, electrolyte abnormalities, hematologic abnormalities, refractory shock, hypoxia, hemorrhage, septic shock, multi-organ failure. The mainstay of treatment for Ebola virus disease involves supportive care to maintain adequate cardiovascular function while the immune system mobilizes an adaptive response to eliminate the infection. In addition, several experimental antiviral therapies have been used in patients with Ebola virus disease during the 2014 outbreak in West Africa. The efficacy of these agents is unclear and is an active area of investigation. In addition, the availability of these drugs is limited.

Antiviral therapy There are no approved medications for the treatment of Ebola virus disease or for post-exposure prophylaxis in persons who have been exposed to the virus but have not yet become ill. There is urgent need for evaluation of several experimental therapies that had been developed specifically to treat or prevent Ebola or Marburg virus infection, but have only been tested in laboratory animals. In addition, there is renewed interest in the potential value of convalescent plasma and whole blood transfusions from Ebola survivors. Although experimental treatments for Ebola virus infection are under development, they have not yet been fully tested for safety or effectiveness. Non-clinical and clinical data made available for:

- Three nucleoside polymerase inhibitors: BCX4430, brincidofovir, and favipiravir;
- Two oligonucleotide based products: TKM-100802 and AVI-7537;
- A cocktail of monoclonal antibodies: ZMapp

RISK FACTORS OF EBOLA[48-49]

For most people, the risk of getting Ebola hemorrhagic fever or Marburg hemorrhagic fever is low. The risk increases if you

- **Travel to Africa.** You're at increased risk if you visit or work in areas where Ebola virus or Marburg virus outbreaks have occurred.
- **Conduct animal research.** People are more likely to contract the Ebola or Marburg virus if they conduct animal research with monkeys imported from Africa or the Philippines.
- **Provide medical or personal care.** Family members are often infected as they care for sick relatives. Medical personnel also can be infected if they don't use protective gear, such as surgical masks and gloves.
- **Prepare people for burial.** The bodies of people who have died of Ebola or Marburg hemorrhagic fever are still contagious. Helping prepare these bodies for burial can increase your risk of developing the disease.

CONCLUSIONS

Ebola virus has been a threat to human health due to its dangerous, highly lethal and infectious behavior for which there is no specific remedy available. The spread among humans occurs mainly through the exchange of blood and body secretions. Other noticeable forms of transmission include hospital acquired infection and inadequate hygiene practices. There is an urgent requirement of dissemination of information to community and training programmers for doctors, nurses and other hospital staff. There is an urgent demand for more field studies into the ecology of reservoir species and shedding procedures. The awareness programmers should be organized on large scale to develop the attention about disease for its eradication. It is expected that outcome of research investigations would result in development of easily available and affordable drug for the treatment of this lethal virus.

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