International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 2, Issue 2, pp: (187-201), Month: October 2014 - March 2015, Available at: www.researchpublish.com

Modern Era's Most Acute Health Crisis Outbreak of Viral Disease Ebola - a Survey

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Abstract: **Several countries in western Africa are currently contending with the world's deadliest Ebola outbreak. Recently World Health Organisation has declared the Ebola virus is spreading exponentially across Liberia as patients fill taxis in a fruitless search for medical cares. "When patients are turned away at Ebola treatment centers, they have no choice but to return to their communities and homes, where they inevitably infect others, perpetuating constantly higher flare-ups in the number of cases." Healthcare workers are being especially hard hit there. "Some 152 health care workers have been infected and 79 have died," WHO said. When the outbreak began, Liberia had only one doctor to treat nearly 100,000 people in a total population of 4.4 million people. Every infection or death of a doctor or nurse depletes response capacity significantly."In developed countries that hit a bit closer over the past week, three hospitals in New York City have isolated and tested patients suspected of potential Ebola infection.Though condition is not same elsewhere men are looking solitary as no licensed vaccine for EVD yet is available. Several vaccines are being tested, but none are available for clinical use. No specific treatment is available. Only measures are, severely ill patients require intensive supportive care, patients are frequently dehydrated and require oral rehydration with solutions containing electrolytes or intravenous fluids. In the absence of effective treatment and a human vaccine, raising awareness of the risk factors for Ebola infection and the protective measures individuals can take is the only way to reduce human infection and death. Considering the gravity of situation here auther has taken an attempt to highlight the situation so that doctor, resaercher come forward to explore their afforts for savinghomusepience from an epidamic. Here attempt also to aware People to come forward with preventive measures; as from history author believes social men is the first to invent ways to combat odds for its existence.**

1. INTRODUCTION

The disease Ebola typically occurs in outbreaks in tropical regions of Sub-Saharan Africa.[1] Between 1976, when it was first identified, and 2013, fewer than 1,000 people per year have been infected.[1,2] The largest outbreak to date is the ongoing 2014 West Africa Ebola outbreak, which is affecting Guinea, Sierra Leone, Liberia and Nigeria[3,4].As of August 2014 it likely also affecting Nigeria.[5] As of July 2014 more than 1320 cases have been identified.[3] As of July 2014 more than 1320 cases have been identified.[3]

The death toll so far in the outbreak, first reported in Guinea in March, has reached 4,447. The WHO has repeatedly said Ebola cases are under reported in three hardest-hit countries, and that understanding the scale and pace of the outbreak is crucial to stoping it. 'We just for the numbers reported.' The WHO multiplies the numbers from Guinea by 1.5, from Sierra Lione by 2 and from Liberia by 2.5 to get a more accurate picture.According to WHO West Africa could see up to 10,000 new Ebola cases a week within two months and confirmed that the death rate in the current outbreak is now 70 percent.According to the WHO the present outbreak is the 'most severe, acute healrh emergency in modern times.

As of 30 August 2007, 103 people, 100 adults and three children, were infected by a suspected hemorrhagic fever outbreak in the village of Kampungu, Democratic Republic of the Congo. The outbreak started after the funerals of two village chiefs, and 217 people in four villages fell ill. Having information the World Health Organization sent a team to take blood samples for analysis and confirmed that many of the cases were the result of *Ebolavirus*.[6,7]The Congo's last major Ebola epidemic killed 245 people in 1995 in Kikwit, about 320 km from the source of the August 2007 outbreak.[8] The Uganda Ministry of Health confirmed an outbreak of Ebola in the Bundibugyo District on 30 November 2007. After confirmation of samples tested by the United States National Reference Laboratories and the Centers for Disease Control,

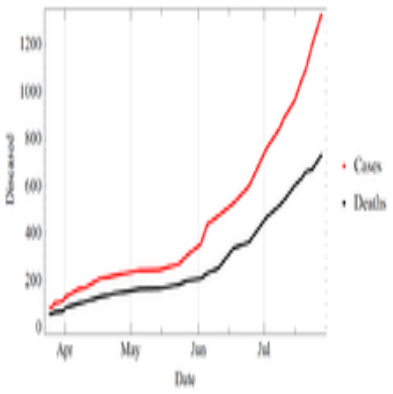
the World Health Organization confirmed the presence of a new species of *Ebolavirus*, which was tentatively named Bundibugyo.[9] The epidemic came to an official end on 20 February 2008. While it lasted, 149 cases of this new strain were reported, and 37 of those led to deaths.

An International Symposium to explore the environment and filovirus, cell system and filovirus interaction, and filovirus treatment and prevention was held at Centre CulturelFrançais, Libreville, Gabon, during March 2008.[10] The virus appeared in southern Kasai Occidental on 27 November 2008,[11] and blood and stool samples were sent to laboratories in Gabon and South Africa for identification.

On 25 December 2008, it was reported that the Ebola virus had killed 9 and infected 21 people in the Western Kasai province of the Democratic Republic of Congo.[12] On 29 December, Doctors Without Borders reported 11 deaths in the same area, stating that a further 24 cases were being treated. In January 2009, Angola closed down part of its border with the Democratic Republic of Congo to prevent the spread of the outbreak.[13]In May 2011, a 12-year-old girl in Uganda died from Ebola (Sudan subspecies). No further cases were recorded.[14]In July 2012, the Ugandan Health Ministry confirmed 13 deaths due to an outbreak of the Ebola-Sudan variant[15] in the Kibaale District.[16] On 28 July, it was reported that 14 out of 20 (70% mortality rate) had died in Kibaale.[17] On 30 July health official in KibaaleDistrictreported the Ebola outbreak had spread from one remote village to several villages.[18]

The World Health Organization's (WHO) global and alert response network reported on August 3 that the suspected case count had risen to 53, including 16 deaths. Of these cases, five were confirmed by UVRI as Ebola cases. On 8 August, the Ugandan Ministry of Health recorded 23 probable and confirmed cases, including 16 deaths. Ten cases were confirmed by the Uganda Virus Research Institute as Ebola. 185 people who came into contact with probable and confirmed Ebola cases were followed during the incubation period of 21 days.[19]

On 17 August, the Ministry of Health of the Democratic Republic of the Congo reported an outbreak of the Ebola-Bundibugyovariant[20] in the eastern region.[21] By 21 August, the WHOreported a total of 15 cases and 10 fatalities.[22] No evidence suggested that this outbreak was connected to the Ugandan outbreak.[23] By 13 September 2012, the WHO revealed that the virus had claimed 32 lives and that the probable cause of the outbreak was tainted bush meat hunted by local villagers around the towns of Isiro and Viadana.[24]



In March 2014, an outbreak of the Ebola virus occurred in the Western African nation of Guinea.[25] This was the first Ebola virus outbreak registered in the region.[25] As of April 10, 157 suspected and confirmed cases and 101 deaths had been reported in Guinea, 22 suspected cases in Liberia including 14 deaths, 8 suspected cases in Sierra Leone including 6 deaths, and 1 suspected case in Mali.[26,27] By late June 2014 the death toll had reached 390 with over 600 cases reported.[28] By 23 July 2014, the World Health Organization had reported 1201 confirmed cases including 672 deaths since the epidemic began in March.[29] On 31 July 2014, WHO reports the death toll has reached 826 from 1440 cases[30].

Increase over time in the cases and Emory University Hospital was the first US hospital to care for people exposed to Ebola.[31] Two American medical providers were exposed while treating infected patients in Liberia. Arrangements were made for them to be transported to Emory via speciality aircraft. Emory Hospital has a specially built isolation unit set up in collaboration with the CDC to treat people exposed to certain serious infectious diseases.[32,33,34]

Top UN officials have warned that the Ebola outbreak in West Africa "will get worse before it gets better" as they called for international action to deal with the crisis, saying misinformation about the disease will only exacerbate an already fragile situation. During a high-level briefing here on the world body's response to the unprecedented outbreak UN Deputy Secretary-General Jan Eliasson said, "The fear factor plays a strong role in the crisis. I encourage the Member States and businesses and individuals as well, to take decisions based on scientific evidence, not on fear." The latest number of Ebola virus disease (EVD) cases in affected countries Guinea, Liberia, Nigeria, and Sierra Leone, stands at 3,069, with over 1,552 deaths, making this the largest Ebola outbreak ever recorded. An unprecedented number of healthcare workers have also been infected and died due to the outbreak. The current Ebola outbreak was the largest, most severe and complex ever seen in the 40-year history of the disease – said World Health Organization director-general

Margaret Chan. International medical agency MedecinssansFrontieres said, the world was "losing the battle" to contain Ebola as the United Nations warned of severe food shortages in the hardest-hit countries. "Every day we have to turn sick people away because we are too full", said Stefan Liljegren, MSF's coordinator at the ELWA Three Ebola unit in Monrovia. The closure of border crossings, as well as reduced trade at seaports, is strangling supply and sending prices soaring, the FAO said. The outbreak of Ebola, transmitted through contact with infected bodily fluids, has sparked alarm throughout west Africa but also further afield, with international flights being halted. The WHO has appealed for the reversal of flight cancellations and virologists said Tuesday travel restrictions could worsen the epidemic, limiting medical and food supplies and keeping out much-needed doctors. "If we impose an aerial quarantine on these countries, we undermine their fight against the epidemic: the rotation of foreign medical staff and distribution of supplies, already inadequate, will become even more difficult," said Sylvain Baize, head of the Pasteur Institute's viral haemorrhagic fever centre in Lyon, France. Meanwhile Michael Kinzer of the US-based Centers for Disease Control and Prevention (CDC) likened closing borders to "closing your eyes". "It makes more sense for countries to spend their money and energy on preparing their health systems to recognise an Ebola case and respond correctly... so that the virus does not spread," he said. Scientistsoredited that there is a 75% chance the virus could be imported to France by ctober 24 and there was a 50% chance it could hit Britain by that day.If this thing continues to rage on in West Africa and indeed gets even worse, as some people have been predicting, then it is only a matter of time before one of these Ebola cases ends up a plane to Europe.

2. SCIENTIFIC STUDY OF EBOLA VIRUS

Zaire ebolavirus is pronounced /zɑːˈɪər iːˈboʊləvaɪərəs/ (*zah-**EER** ee-**BOH**-lə-vy-rəs*). Strictly speaking, the pronunciation of "Ebola virus"should be distinct from that of the genus-level taxonomic designation "ebolavirus/Ebolavirus/ebolavirus". ***Ebola virus*** (**EBOV**), formerly designated ***Zaire ebolavirus***, is the sole member of the *Zaire ebolavirus* species, which is included into the genus *Ebolavirus*, family*Filoviridae*, order *Mononegavirales*, the most dangerous of the five known viruses within the genus *Ebolavirus*.[35] Four of the five known ebolaviruses cause a severe and often fatal hemorrhagic fever in humans and other mammals, known as Ebola virus disease(**EVD**) or **Ebola hemorrhagic fever** (**EHF**) is the human disease. Symptoms typically start two days to three weeks after contracting the virus, with a fever, sore throat, muscle pains, and headaches. Typically nausea, vomiting, and diarrheafollow, along with decreased functioning of the liver and kidneys. At this point, some people begin to have bleeding problems.[35,36]

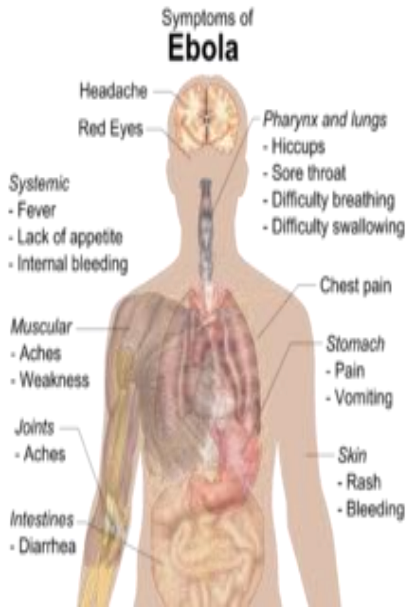
The virus may be acquired upon contact with blood or bodily fluids of an infected animal (commonly monkeys or fruit bats).[35] It is not naturally transmitted through the air.[36] Fruit bats are believed to carry and spread the virus without being affected. Once human infection occurs, the disease may spread between people as well. Male survivors may be able to transmit the disease via semen for nearly two months. In order to make the diagnosis, typically other diseases with similar symptoms such as malaria, cholera and other viral hemorrhagic fevers are first excluded. Blood samples may then be tested for viral antibodies, viral RNA, or the virus itself to confirm the diagnosis.[35]

Ebola virus (abbreviated EBOV) was first described in 1976. The virus and its species were both originally named for Zaire (now the Democratic Republic of Congo), the country where it was first described.[35] The village Zaire situated near the Ebola River, from which the disease takes its name and was at first suspected to be a new "strain" of the closely related Marburg virus;[37][38] the name of the virus (but not its species) was changed to Zaire ebolavirus in the year 2002 andwas renamed to "Ebola virus" in the year 2010 to avoid confusion. The species is a virological taxon species included in the genus *Ebolavirus*, family*Filoviridae* (whose members are called Filovirus[2]), order *Mononegavirales*.[35] The Zaire ebolavirus species is also the type species for *ebolavirus*. Its natural reservoir is believed to be bats, particularly fruit bats, and it is primarily transmitted between humans and from animals to humans, through body fluids.

An International Symposium to explore the environment and filovirus, cell system and filovirus interaction, and filovirus treatment and prevention was held at Centre CulturelFrançais, Libreville, Gabon, during March 2008.[39] On 12 March 2009, an unidentified 45-year-old scientist from Germany accidentally pricked her finger with a needle used to inject Ebola into lab mice. She was given an experimental vaccine never before used on humans. Since the peak period for an outbreak during the 21-day Ebola incubation period had passed as of 2 April 2009, she had been declared healthy and safe. It remains unclear whether or not she was ever actually infected with the virus.[39]

Till date there is no specific treatment for the Ebola virus disease; efforts to help persons who are infected include giving either oral rehydration therapy or intravenous fluids.[40] The disease has high mortality rate: often killing between 50%

and 90% of those infected with the virus.[41,3] Though Ebola virus disease was first identified in Sudan and the Democratic Republic of the Congo the disease typically occurs in outbreaks in tropical regions of Sub-Saharan Africa.[41] Between 1976, when it was first identified, through 2013, fewer than 1,000 people per year have been infected.[41,1] The largest outbreak to date is the ongoing 2014 West Africa Ebola outbreak, which is affecting Guinea, Sierra Leone, Liberia and likely Nigeria.[2,5] As of July 2014 more than 1320 cases have been identified.[5] Efforts are ongoing to develop a vaccine; however, none yet exists.[41]



2.1 Signs and symptoms:

Ebola usually begin suddenly with an flu-like stage characterized by fatigue, fever, headaches, intense weakness, muscle pain and joint, muscle, and abdominal pain.[42,43,44] Vomiting, diarrhea rash, impaired kidney and liver function, and in some cases, both internal and external bleedingand loss of appetite are also common.[44] Less common symptoms include the following: sore throat, chest pain, hiccups, shortness of breath and trouble swallowing.[44] The average time between contracting the infection and the start of symptoms is 8 to 10 days, but can occur between 2 and 21 days.[44] Skin manifestations may include a maculopapular rash (in about 50% of cases).[39] Early symptoms of EVD may be similar to those of malaria, dengue fever, or other tropical fevers, before the disease progresses to the bleeding phase.[43]Ebola virus was isolated from semen 61 days after onset of illness in a man who was infected in a laboratory. Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes. People are infectious as long as their blood and secretions contain the virus.

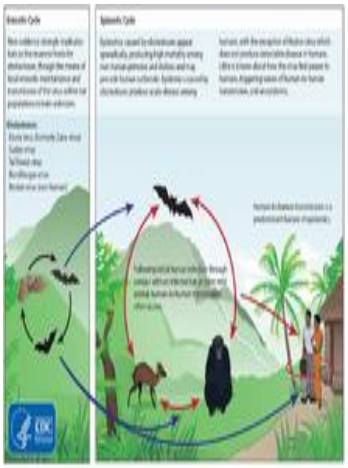
The incubation period, that is, the time interval from infection with the virus to onset of symptoms, is 2 to 21 days.

2.1.1 Bleeding:

Ebola causes bleeding and in the bleeding phase internal and subcutaneous bleeding may present itself through reddening of the eyes and bloody vomit.[43] Some time bleeding into the skin createpetechiae, purpura, ecchymoses, and hematomas.

In all people infected some symptoms of circulatory system involvement, including impaired blood clotting[39] are seen. Bleeding from puncture sites andmucous membranes (e.g. gastrointestinal tract, nose, vagina and gums) is reported in 40–50% of cases.[45] Bleeding known to occur with Ebola virus disease include vomiting blood, coughing it up or blood in the stool. Heavy bleeding is rare and is usually confined to the gastrointestinal tract.[45,46] In general, the development of bleeding symptoms often indicates a worse prognosis and this blood loss can result in death.[47]

2.2 Cause:



Ebola virus disease (EVD) is caused by four of five viruses classified in the genus *Ebolavirus*, family *Filoviridae*, order *Mononegavirales*. These four viruses are Bundibugyovirus (BDBV), Ebola virus (EBOV), Sudan virus (SUDV), Taï Forest virus (TAFV). The fifth virus, Reston virus (RESTV), is not thought to be disease-causing in humans. During an outbreak those at highest risk are health care workers and close contacts of those with the infection.[48]

2.2.1 Natural host of Ebola virus: In Africa, fruit bats, particularly species of the genera *Hypsignathus*monstrosus, *Epomopsfranqueti* and *Myonycteris*

Life cycles of the Ebolavirus*torquata*, are considered possible natural hostsfor Ebola virus. A milder strain of Ebola has been discovered in monkeys and pigs in the Philippines. As a result, the geographic distribution of Ebolaviruses may overlap with the range of the fruit bats.

2.2.2 Ebola virus in animals:

Although non-human primates have been a source of infection for humans, they are not thought to be the reservoir but rather an accidental host like human beings. Since 1994, Ebola outbreaks from the EBOV andTAFV species have been observed in chimpanzees and gorillas.

RESTV has caused severe EVD outbreaks in macaque monkeys (Macacafascicularis) farmed in Philippines and detected in monkeys imported into the USA in 1989, 1990 and 1996, and in monkeys imported to Italy from Philippines in 1992.

Since 2008, RESTV viruses have been detected during several outbreaks of a deadly disease in pigs in People's Republic of China and Philippines. Asymptomatic infection in pigs has been reported and experimental inoculations have shown that RESTV cannot cause disease in pigs.

2.3 Transmission:

It is not entirely clear how Ebola is spread.[49] EVD is believed to occur after an ebola virus is transmitted to an initial human by contact with an infected animal's bodily fluids. Human-to-human transmission can occur via direct contact with blood or bodily fluids from an infected person (includingembalming of an infected dead person) or by contact with contaminated medical equipment, particularly needles and syringes.[50] Butchering or eating infected animals can spread the viruses. Scientists who have operated on infected animals as part of their research have also contracted the virus. Semen is infectious in survivors for up to 50 days. Transmission through oral exposure and through conjunctiva exposure is likely[51] and has been confirmed in non-human primates.[52] The potential for widespread EVD infections is considered low as the disease is only spread by direct contact with the secretions from someone who is showing signs of infection.[53] The quick onset of symptoms makes it easier to identify sick individuals and limits a person's ability to spread the disease by traveling. Because dead bodies are still infectious, some doctors disposed of them in a safe manner, despite local traditional burial rituals.[53] Tourists in certain African caves and some underground mine workers have been infected with the Marburg virus, possibly through contact with the feces or urine of infected bats.

Infected people typically don't become contagious until they develop symptoms. Family members are often infected as they care for sick relatives or prepare the dead for burial.

Medical workers who do not wear appropriate protective clothing may also contract the disease.[54] In the past, hospital-acquired transmission has occurred in African hospitals due to the reuse of needles and lack of universal precautions.[36] Medical personnel can be infected if they don't use protective gear, such as surgical masks and gloves. Some of the worst Ebola epidemics have occurred because contaminated injection equipment wasn't sterilized between uses.

There's no evidence that Ebola virus or Marburg virus can be spread via insect bites.

EVD is not naturally transmitted through the air.[1] They are, however, infectious as breathable 0.8–1.2 micrometre laboratory generated droplets;[55] because of this potential route of infection, these viruses have been classified as Category A biological weapons.[56] Recently the virus has been shown to travel without contact from pigs to non-human primates.[57]

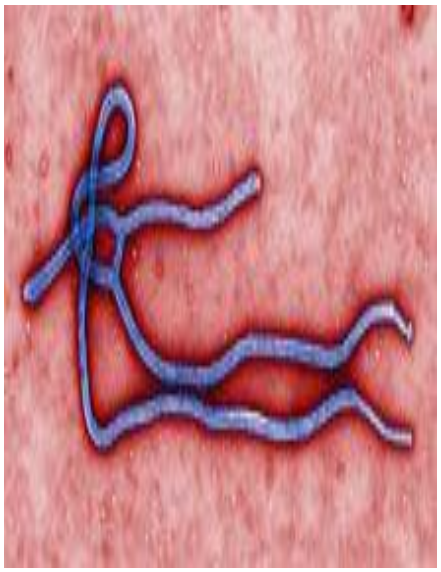
Bats drop partially eaten fruits and pulp, then land mammals such as gorillas and duikers feed on these fallen fruits. This chain of events forms a possible indirect means of transmission from the natural host to animal populations, which have led to research towards viral shedding in the saliva of bats. Fruit production, animal behavior, and other factors vary at different times and places that may trigger outbreaks among animal populations.[58]

Human consumption of equatorial animals in Africa in the form of bushmeat has been linked to the transmission of diseases to people, including Ebola.[59]Bats are considered the most likely natural reservoir of the Ebola virus; plants, arthropods, and birds have also been considered.[60] Bats were known to reside in the cotton factory in which the first cases for the 1976 and 1979 outbreaks were employed, and they have also been implicated in Marburg virus infections in 1975 and 1980.[61] Of 24 plant species and 19 vertebrate species experimentally inoculated with EBOV, only bats became infected.[62] The absence of clinical signs in these bats is characteristic of a reservoir species. In a 2002–2003 survey of 1,030 animals including 679 bats from Gabon and the Republic of the Congo, 13 fruit bats were found to contain EBOV RNA fragments.[63] As of 2005, three types offruit bats e.g. *Hypsignathusmonstrosus*, *Epomopsfranqueti*, and *Myonycteristorquata* have been identified as being in contact with EBOV. They are now suspected to represent the EBOV reservoir hosts.[64][65] Antibodies against Ebola Zaire and Reston viruses have been found in fruit bats inBangladesh, thus identifying potential virus hosts and signs of the filoviruses in Asia.[66]Between 1976 and 1998, in

30,000 mammals, birds, reptiles, amphibians, and arthropods sampled from outbreak regions, no *ebolavirus* was detected apart from some genetic traces found in six rodents (*Mussetulosus* and *Praomys*) and one shrew (*Sylvisorexollula*) collected from the Central African Republic[61,67]. Traces of EBOV were detected in the carcasses of gorillas and chimpanzees during outbreaks in 2001 and 2003, which later became the source of human infections. However, the high lethality from infection in these species makes them unlikely as a natural reservoir.[61]

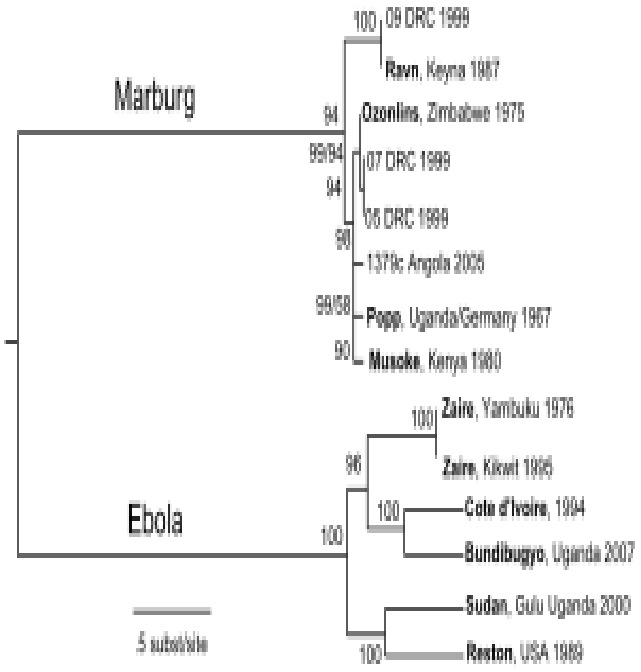
Transmission between natural reservoir and humans is rare, and outbreaks are usually traceable to a single case where an individual has handled the carcass of gorilla, chimpanzee, or duiker.[41] Fruit bats are also eaten by people in parts of West Africa where they are smoked, grilled or made into a spicy soup.[65,37]

2.4 Virology:



Like all mononegaviruses, ebolavirions contain linear nonsegmented, single-strand, non –infectious RNA genomes of negative polarity that possesses inverse-complementary 3' and 5' termini, do not possess a 5' cap, are not polyadenylated, and are not covalently linked to a protein.[38] Ebolavirus genomes are approximately 19 kilobase pairs long and contain seven genes in the order 3'-UTR-*NP-VP35-VP40-GP-VP30-VP24-L*-5'-UTR[68]Electron micrograph of an Ebola virus virionThe genomes of the five (BDBV, EBOV, RESTV,SUDV and TAFV) differ in sequence and the number and location of gene overlaps.

2.4.1Structure: Like all filoviruses, ebolavirions are filamentous particles that may appear in the shape of a shepherd's crook or in the shape of a "U" or a "6", and they may be coiled, toroid, or branched.[68] In general, ebolavirions are 80 nm in width, but vary somewhat in length. Generally the median particle length of ebolaviruses ranges from 974 to 1,086 nm (in contrast to marburgvirions, whose median particle length was measured at 795–828 nm), but particles as long as 14,000 nm have been detected in tissue culture.[40]



Thegenera *Ebolavirus* and *Marburgvirus* were originally classified as the species of the now-obsolete *Filovirus* genus. the "-like Phylogenetic tree comparing the Ebolavirus and Marburgvirus "viruses" to "virus" resulting in today's "viruses" to "-virus" resulting in today's *Ebolavirus* and *Marburgvirus*.[69] Rates of genetic change are 100 times slower than influenza A in humans, but on the same magnitude as those of hepatitis B.Extrapolating backwards using these rates indicates that Ebolavirus and Marburgvirus diverged several thousand Years ago.[70]

Phylogenetic tree comparing the Ebolavirus and Marburgvirus.EBOV carries a negative-sense RNA genome in Numbers indicate percent confidence of branches.virions that are cylindrical/tubular, generally approx.800 nm in diameter, and having a virally encoded glycoprotein (GP) projecting as 7-10 nm long (sometimes up to 1000 nm long) spikes from its lipid bilayer surface, contain viral envelope, matrix and nucleocapsid components. The outer viral envelope of the virion is derived by budding from domains of host cell membrane into which the GP spikes have been inserted during their biosynthesis. Individual GP molecules appear with spacings of about 10 nm. Viral proteins VP40 and VP24 are located between the envelope and the nucleocapsid (see following), in the *matrix space*.[42] At the center of the virion structure is

the nucleocapsid, which is composed of a series of viral proteins attached to a 18–19 kb linear, negative-sense RNA without 3′-polyadenylation or 5′-capping (see following); the RNA is helically wound and complexed with the NP, VP35, VP30, and L proteins; this helix has a diameter of 80 nm and contains a central channel of 20–30 nm in diameter.

However, Paleovirous of filovirous found in mammals indicate that the family itself is at least tens of millions of years old.[71] Fossilized viruses that are closely related to ebolaviruses have been found in the genome of the Chinese hamster.[72]

2.5 Replication:

The ebolavirus life cycle begins with virion attachment to specific cell-surface receptors, followed by fusion of the virion envelope with cellular membranes and the concomitant release of the virus nucleocapsid into the cytosol. The viral RNA polymerase, encoded by the L gene, partially uncoats the nucleocapsid and transcribes the genes into positive-strand mRNAs, which are then translated into structural and nonstructural proteins. Ebolavirus RNA polymerase (L) binds to a single promoter located at the 3' end of the genome. Transcription mayterminates after a gene or continues to the next gene downstream. This means that genes close to the 3' end of the genome are transcribed in the greatest abundance, whereas those toward the 5' end are least likely to be transcribed. The gene order is, therefore, a simple but effective form of transcriptional regulation. The most abundant protein produced is the nucleoprotein, whose concentration in the cell determines when L switches from gene transcription to genome replication. Replication results in full-length, positive-strand antigenomes that are, in turn, transcribed into negative-strand virus progeny genome copy. Newly synthesized structural proteins and genomes self-assemble and accumulate near the inside of the cell membrane. Virions bud off from the cell, gaining their envelopes from the cellular membrane they bud from. The mature progeny particles then infect other cells to repeat the cycle.[41]

2.5.1 Pathophysiology Ebola virus:

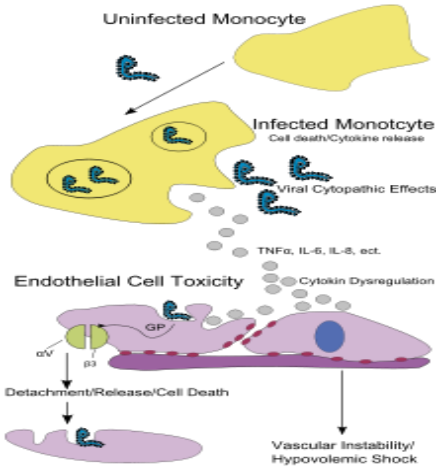
Endothelial cells, mononuclear phagocytes, and hepatocytes are the main targets of Ebolavirusinfection. After infection, a secreted glycoprotein (sGP) known as the Ebola virus glycoprotein (GP) is synthesized. It is already stated Ebola replication overwhelms protein synthesis of infected cells and host immune defenses so the glycoprotein forms a trimeric complex, which binds the virus to the endothelial cells lining the interior surface of blood vessels. The secreted glycoprotein forms a dimeric protein that interferes with the signaling of neutrophils, a type of white blood cell, which allows the virus to evade the immune system by inhibiting early steps of neutrophil activation. Moreover these white blood cells serve as carriers to transport the virus throughout the entire body to places such as the lymph nodes, liver, lungs, and spleen.[73]

The presence of viral particles and cell damage resulting from budding causes the release of cytokines (to be specific, TNF-α, IL-6, IL-8, etc.), which are the signaling molecules for fever and inflammation. The cytopathic effect, from infection in the endothelial cells, results in a loss of vascular integrity. This loss in vascular integrity is furthered with synthesis of GP, which reduces specific integrins responsible for cell adhesion to the inter-cellular structure, and damage to the liver, which leads to coagulopathy.[74]

3. DIAGNOSIS

The medical history, especially travel and work history along with exposure to wildlife are important to suspect the diagnosis of EVD. The 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. Detecting antibodies against the virus is effective late in the disease and in those who recover.[75]

During an outbreak, virus isolation is often not feasible. The most common diagnostic methods are therefore real time PCR and ELISA detection of proteins, which can be performed in field orhospitals. Filovirions can be seen and identified through cell culture by electron microscopy due to their unique filamentous shapes, but electron microscopy cannot tell the difference between the various filoviruses despite there being some length differences.[40]



Pathogenesis schematic

The symptoms of Ebola virus diseaseare similar to those of Marburg virus disease.[76] It can also easily be confused with many other diseases common in Equatorial Africa e.g. viral hemorrhagic fevers, falciparum malaria, typhoidfever, shigellosis, rickettsial diseases viz. typhus, cholera, gram-negative septicemia,borreliosissuch as relapsing fever or EHEC enteritis. Other infectious diseases that should be included in the differential diagnosis include the following: leptospirosis, scrub typhus, plague, Q fever, candidiasis, histoplasmosis, trypanosomiasis, visceral leishmaniasis, hemorrhagic smallpox, measles, and fulminant viral hepatitis.Non-infectious diseases acute promyelocytic leukemia, hemolytic uremic syndrome, snake envenomation, clotting factor deficiencies/platelet disorders, thrombotic thrombocytopenic purpura, hereditary hemorrhagic telangiectasia, Kawasaki disease, and even warfarin poisoning.[78,79,80,81]

4. PREVENTION

All the available information is that it spreads from person to person through contact with bodily fluids from an infected individual. It doesn't seem to spread by being in close proximity, or by casual contact. Prevention predominantly involving behavior changes, proper full body personal protective equipment, and disinfection. So for prevention it is essential to avoid contact with infected individuals' blood, feces, or other bodily fluids.Techniques to avoid infection involve not contacting infected blood or secretions, including from those who are dead.[49] Even sitting next to a person with Ebola is thought not to be enough to transmit the disease, one need contact with body fluids. If effected person sneezes, or bleeds, or a lot of sweat gets on one, then there is risk of transmission because body fluids have transferred from one person to the other, but Ebola is not airborn. So it requires those visibly obvious things to happen for transmission to occur. There's some evidence that there can be sexual transmission of the virus for a substantial period of time after at least some individuals have recovered from infection.

Since Ebola is transmitted through body fluids, all the patient needs is to be in a private room with a door closed. That's enough. Some things, like Tuberculosis, measles, chicken pox, you need to modify the airflow in the room and it's more complicated. For Ebola, it's not so easy to transmit, so it's just a room with a door closed, and everyone who comes and sees them has to take those precautions, but the patient doesn't have to do much.

Prevention involves suspecting and diagnosing the disease early and using standard precautions for all patients in the healthcare setting.[82] Recommended measures when caring for those who are infected include: wearing protective clothing including: masks, gloves, gowns and goggles, equipment sterilization and isolating them.[49] Hand washing is important but can be difficult in areas where there is not even enough water for drinking.[47]

Due to lack of proper equipment and hygienic practices, large-scale epidemics have occured mostly in poor, isolated areas without modern hospitals or well-educated medical staff. Traditional burial rituals, especially those requiring embalming of bodies, should be discouraged or modified.[82] Airline crews who fly to areas of these areas of the world are taught to identify Ebola and are to isolate anyone who has symptoms.[83]

Enforced isolation, Quarantine, is usually effective in decreasing spread.[84][85][86] Governments often quarantine areas where the disease is occurring or those who may be infected.[87][88][89] In the United States the law allows quarantine of those infected with Ebola.[60] The lack of roads and transportation may help slow the disease in Africa. During the 2014 outbreak Liberia closed schools.[61]

Prevention includes decreasing the spread of disease from infected monkeys and pigs to humans. This may be done by checking such animals for infection and killing and properly disposing of the bodies if the disease is discovered. Properly cooking meat and wearing protective clothing when handling meat may also be helpful, as are wearing protective clothing and washing hands when around a person with the disease. Samples of bodily fluids and tissues from people with the disease should be handled with special caution.[35]

Genus Ebolavirus is 1 of 3 members of the *Filoviridae* family (filovirus), along with genus Marburgvirus andgenus Cuevavirus. Genus Ebolavirus comprises 5 distinct species:

i. Bundibugyoebolavirus (BDBV)

ii. Zaire ebolavirus (EBOV)

iii. Reston ebolavirus (RESTV)

iv. Sudan ebolavirus (SUDV)

v. Taï Forest ebolavirus (TAFV)

Reston virus (RESTV), is not thought to be disease-causing in humans. During an outbreak those at highest risk are health care workers and close contacts of those with the infection.[48]

5. TREATMENT

No ebolavirus-specific treatment exists.[90] Treatment is primarily supportive in nature and includes minimizing invasive procedures, balancing fluids andelectrolytes to counter dehydration, administration of anticoagulants early in infection to prevent or control disseminated intravascular coagulation, administration of procoagulants late in infection to control bleeding, maintaining oxygen levels, pain management, and the use of medications to treat bacterial or fungal secondary infections.[91,92,93] Early treatment may increase the chance of survival.[94] A number of experimental treatment are being studied.

As there is no specific treatment for the Ebola virus disease till date; efforts to help persons who are infected include giving either oral rehydration therapy or intravenous fluids.[35] The disease has high mortality rate: often killing between 50% and 90% of those infected with the virus.[35][5] Though Ebola virus disease was first identified in Sudan and the Democratic Republic of the Congo the disease typically occurs in outbreaks in tropical regions of Sub-Saharan Africa.[35] Between 1976, when it was first identified, through 2013, fewer than 1,000 people per year have been infected.[35,2] The largest outbreak to date is the ongoing 2014 West Africa Ebola outbreak, which is affecting Guinea, Sierra Leone, Liberia and likely Nigeria.[3,4] As of July 2014 more than 1320 cases have been identified.[3] Efforts are ongoing to develop a vaccine; however, none yet exists.[35]

Researchers are looking at slides of cultures of cells that make monoclonal antibodies. These are grown in a lab and the researchers are analyzing the products to select the most promising of them.

During an outbreak 1999 in the Democratic Republic of the Congo, seven of eight people who received blood transfusions from individuals who had previously survived the infection survived themselves.[95] However, this potential treatment is considered controversial.[96] Intravenous antibodies appear to be protective in non-human primates who have been exposed to large doses of ebola.[97]

5.1 ZMapp antibody treatment:

In August of 2014 an experimental treatment based on plants was used for the first time in two humans. The treatment drug was referred to as ZMapp, an antibody response related therapy. The initially response appears positive. ZMapp was produced by MAPP Biopharmaceutical Inc. using a three-mousemonoclonal antibody, manufactured in genetically modified tobacco plants (of the genus Nicotiana).[98][99] In the three-mouse drug production process, mice were exposed to three different fragments of the virus strain and antibodies were harvested to create the medicine.[100,101] In 2013, these antibodies, were effective when given within a day of exposure primates other than humans.[102]

5.2Other treatments:

Other promising treatments rely on antisense technology. Both small interfering RNAs (siRNAs) and phosphorodiamidatemorpholino oligomers (PMOs) targeting the Zaire Ebola virus (ZEBOV) RNA polymerase L protein could prevent disease in nonhuman primates.[103][104]

Vaccine:

No vaccine is currently available for humans.[35][105][90] Given the lethal nature of Ebola, and since no approved vaccine or treatment is available, it is classified as a biosafety level 4 agent, as well as a Category A bioterrorism agent by the Centers for Disease Control and Prevention.

The most promising candidates are DNA vaccines[105][106] or vaccines derived from adenoviruses,[64] vesicular stomatitis Indiana virus (VSIV)[107][108][109] or filovirus-like particles (VLPs)[109] because these candidates could protect nonhuman primates from ebolavirus-induced disease. DNA vaccines, adenovirus-based vaccines, and VSIV-based vaccines have entered clinical trials.[110][112][113][114]A vaccine based on attenuated recombinant vesicular stomatitis virus (VSV) vector carrying either the Ebola glycoprotein or the Marburg glycoprotein in 2005 protected nonhuman primates,[115] opening clinical trials in humans.[111] The study by October completed the first human trial, over three months giving three vaccinations safely inducing an immune response. Individuals for a year were followed, and, in 2006, a study testing a faster-acting, single-shot vaccine began; this new study was completed in 2008.[116] Trying the vaccine on a strain of Ebola that more resembles the one that infects humans is the next step.An experimental vaccine made by researchers at Canada's national laboratory in Winnipeg was used in 2009 to pre-emptively treat a German scientist who might have been infected during a lab accident.[117] However, actual EBOV infection could never be demonstrated without a doubt.[118] Experimentally, recombinant vesicular stomatitis Indiana virus (VSIV) expressing the glycoprotein of EBOV or SUDV has been used successfully in nonhuman primate models as post-exposure prophylaxis.[119][120]

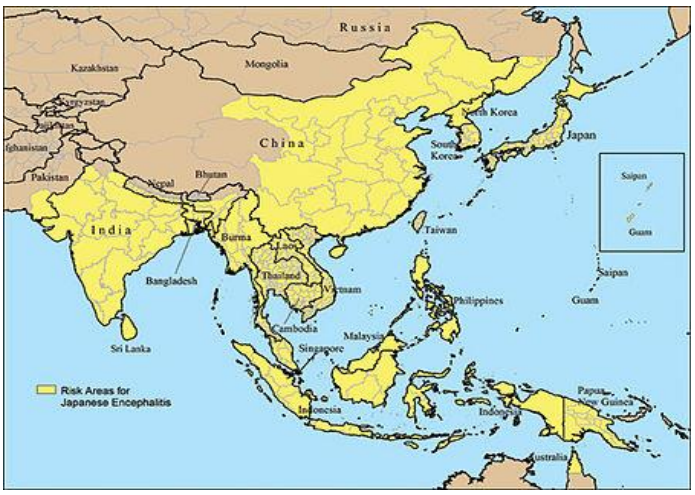
Laboratory:

Ebola viruses are World Health Organization Risk Group 4 pathogens, requiring biosafety level 4-equivalent containment. Laboratory researchers must be properly trained in BSL-4 practices and wear proper personal protective equipment.Eesearcher working in the laboratory with the Ebola virus only while wearing a BSL-4 positive pressure suit to avoid infection.

6. CONCLUSION

The disease has a high mortality rate, often between 50 percent and 90 percent.[3][40] If an infected person survives, recovery may be quick and complete. Prolonged cases are often complicated by the occurrence of long term problems, such as inflammation of the testicles, joint pains, muscle pains, skin peeling, or hair loss. Eye symptoms, such as light sensitivity, excess tearing, iritis, iridocyclitis, choroiditis and blindness have also been described. EBOV and SUDV may be able to persist in the semen of some survivors for up to seven weeks, which could give rise to infections and disease via sexual intercourse.[40]

As mortality rate due to Ebola is high, no ebolavirus-specific treatment exists and treatment is primarily supportive in nature it has the potential to be weaponized for use in biological warfare.[121]



From figure it is clear severe affected area of Japanese Encephalitis. On August 04, 2014 Health Minister the government of India said in LokSabhaAround 700 people have lost their lives due to encephalitis that has hit four states, including Assam and West Bengal, as members demanded that the disease be termed as an epidemic. The disease has claimed 208 lives in West Bengal, 197 in Assam, 159 in Bihar and 123 in Uttar Pradesh so far this year, Health Minister Harsh Vardhan said replying to a calling attention motion. Also it is known that epidamicaligical background of Ebola and Japanese Encephalitis are very close. So, it is high time to be aware of for searching preventive The geographic distribution of Japanese encephalitis (in yellow)measure for saving people of the area thickly populated. It is a challenge to the Scientists, Doctors and social workers to extend their hands for collaborative activities to save human race from the mortal attack of Ebola virus. Particularly for India it is most essential.

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