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A REVIEW ON EBOLA VIRUS

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ABSTRACT

Ebola virus disease, caused by the filovirus Ebolavirus, leads to viral hemorrhagic fever and is fatal in many cases. Outbreaks of Ebola in sub-Saharan Africa have resulted in fatality rates of up to 90%. The 2014 outbreak in West Africa is the largest epidemic to date. The virus enters the human chain through close contact with infected primates and other animals and can be passed human to human through contact with the bodily fluids of infected persons. Currently, neither a vaccine nor an effective antiviral treatment is available for use in humans. Preventive strategies and supportive therapy are the only options available for high-risk individuals and infected patients.

1. INTRODUCTION

Zoonotic diseases are increasingly affecting human health. Causative agents include viruses, bacteria, parasites and fungi. In recent years, zoonotic diseases originated in wildlife such as birds, swine and bats, have hit several countries causing infection and mortalities to large numbers of human individuals. Viruses are responsible for the most lethal and widespread zoonotic outbreaks in human populations. Examples of these epidemics are those of influenza A virus, serotype H5N1, originated in China in 2003. This epidemic affected 15 countries with 650 cases and a mortality rate of 60%. In 2011, five countries: Bangladesh, Cambodia, China, Indonesia and Egypt, reported 62 cases of human infections of which 34 died. An outbreak of the influenza virus serotype H1N1 “swine flu” was first reported in Mexico in early 2009 and soon after it spread worldwide. An estimate of the global mortalities caused by this outbreak is 201200 deaths by respiratory failure (range 105700-395600) and 83 300 deaths by cardiovascular arrest (46 000-179 900). Most of the people who died (80%) were younger than 65 years and most of them (51%) from Asia and Africa. Another epidemic occurred in 2003.

When the severe acute respiratory syndrome (SARS) was first reported in Asia. The agent is a coronavirus. This pathogen spread to more than 24 countries in North and South America, Europe and Asia before the global outbreak was contained. The World Health Organization estimated that during the 2003 outbreak, a total of 8 098 people worldwide became sick with SARS and 774 died. A recent outbreak caused by another coronavirus has been responsible for a respiratory syndrome in the Middle East. It is called Middle East Respiratory syndrome (MERS)-CoV. This disease originated in Saudi Arabia in 2012 and it has spread to virtually all the Arabic Peninsula, and it has reached countries in Europe, Asia, Northern Africa, as well as the United States. Until mid-2013, 90 cases of MERS-CoV have been reported with 50% mortality rate. The most recent and expanded outbreak of a lethal viral disease has occurred since early 2014 in West African countries (Guinea,Liberia, Sierra Leone, Nigeria). This epidemic further expanded to Senegal and Mali. Later this year, another outbreak independent from that of West Africa occurred in the Democratic Republic of Congo. The pathogen responsible for these two outbreaks is the Ebola virus. Until October 1st, 2014, 3 431 out of 7470 infectedpersons have died (46% mortality rate). Most infected people are ocated in Guinea, Liberia and Sierra Leone, whereas the outbreaks in Senegal and Nigeria seem to be contained. The Ebola outbreak from The Democratic Republic of Congo has recorded 70 cases and 43 deaths (61%) by October 1st, 2014. The concern that this epidemic may extend.Infected people maytravel abroad. The first confirmed case of Ebolavirus infection in the United States was announced on September 30th, and became the first Ebola casualty in America. Also, foreign personnel doing humanitarian work in Africa have become infected with the virus.

2. MORPHOLOGY AND ULTRASCTUCTURE

The two Americans were cured whereas the two Spanish priests died. Another person travelling from Liberia to the United States was infected with the Ebola virus and died. Because of breaches in safety protocols, health workers in contact with this patient became exposed to infectionand at least two nurses have tested positive to Ebola infection. The two American physicians and other patients in the United States, Germany, Spain and Norway have been treated with experimental drugs against the infection. In the case of the two American medics, the experimental treatment was successful. Although such results against Ebola infection in humans is encouraging, still no effective or safe treatment exist for Ebola virus infection. A number of different treatments have been experimentally tested in animal models, including non-human primates. Some results have shown great rates of virus inhibition and reduction of clinical signs. Yet, large numbers of persons are at risk of Ebola infection not only in Africa, but also in Asia, Europe and America. Because of the sanitary importance of this pathogen and the High mortality rates in infected people, the aim of this paper is to present data on the features of the Ebola virus, the history of disease outbreaks in Africa and the tools that are being developed in order caused a lethal infection in humans and is weak pathogenic virus in experimentally infected nonhuman primates compared with Zaire ebolavirus. Three Ebolavirus species (Zaire, Sudan and Bundibugyo) are the main responsible for the Ebola outbreaks in Africa. The 2014 Ebola outbreak from West Africa is caused by a Zaire ebolavirus species with a mortality rate of 47%. Since Ebolavirus is a highly contagious and lethal pathogen, it is classified as a biosafety level 4 pathogen based on its high mortality rate, ease to transmission among persons, with potential infectivity by aerosol and lacking of treatment such as vaccines or chemotherapy. Maximum containment is required for all laboratory work with infectious material.

3. ECOLOGY OF EBOLA VIRUS

Ebola Virus Disease (EVD) is a rare and deadly zoonotic disease most commonly affecting people and nonhuman primates (monkeys, gorillas, and chimpanzees). It is caused by an infection with one of five known Ebola virus species, four of which can cause disease in people:

Ebola virus (Zaire ebolavirus)

Sudan virus (Sudan ebolavirus)

Taï Forest virus

Bundibugyo virus (Bundibugyo ebolavirus)

Reston virus (Reston ebolavirus), known to cause disease in nonhuman primates and pigs, but not in people,

Ebola virus was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of Congo. Since then, the virus has been infecting people from time to time, leading to outbreaks in several African countries. Scientists do not know where Ebola virus comes from. However, based on the nature of similar viruses, they believe the virus is animal-borne, with bats being the most likely source. The bats carrying the virus can transmit it to other animals, like apes, monkeys, duikers and humans.

Ebola virus spreads to people through direct contact with bodily fluids of a person who is sick with or has died from EVD. This can occur when a person touches the infected body fluids (or objects that are contaminated with them), and the virus gets in through broken skin or mucous membranes in the eyes, nose, or mouth. The virus can also spread to people through direct contact with the blood, body fluids and tissues of infected fruit bats or primates. People can get the virus through sexual contact as well.

Marburg and Ebola viruses emerged approximately three decades ago, but the reservoir(s) of these zoonotic pathogens and the routes of primary transmission to human and nonhuman primates remains a mystery. Recent outbreaks have been associated with multiple introductions into the population, indicating the circulation of distinct strains that have evolved in reservoir species that occupy different ecological niches. Identification of the viral reservoir(s) is a research priority, with a high impact on public health and prevention.

Since Ebola virus was first identified more than 30 years ago, tremendous progress has been made in understanding the molecular biology and pathogenesis of this virus. However, the means by which Ebola virus is maintained and transmitted in nature remains unclear despite dedicated efforts to answer these questions. Recent work has provided new evidence that fruit bats might have a role as a reservoir species, but it is not clear whether other species are also involved or how transmission to humans or apes takes place. Two opposing hypotheses for Ebola emergence have surfaced; one of long-term local persistence in a cryptic and infrequently contacted reservoir, versus another of a more recent introduction of the virus and directional spread through susceptible populations. Nevertheless, with the increasing frequency of human filovirus outbreaks and the tremendous impact of infection on the already threatened great ape populations, there is an urgent need to better understand the ecology of Ebola virus in nature.

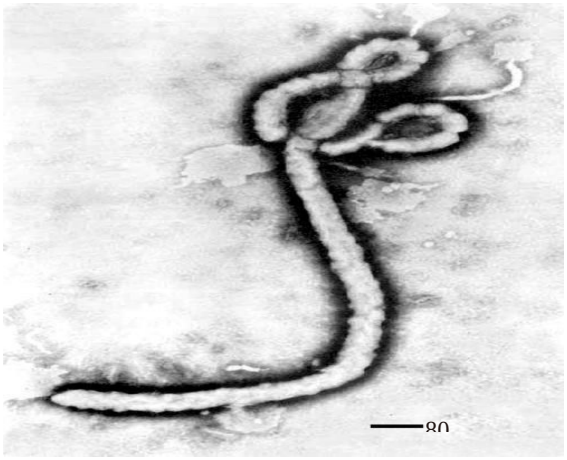
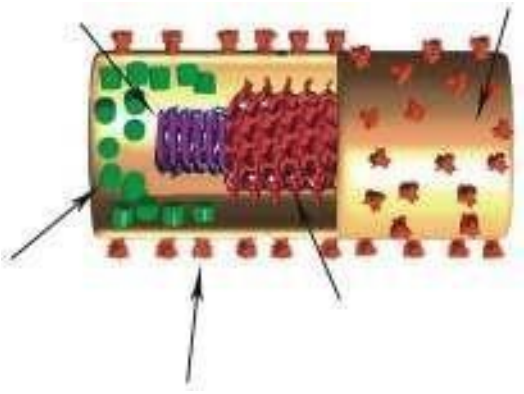


Figure 1. Transmission Electron Microscope View of an Ebolavirus Virion.

The nucleocapsid consists of units of the nucleoprotein (NP) associated to the genomic RNA. The inner nucleocapsid is formed by large subunits linked with vertical contacts, which contains a complex of RNA and NP. The NPRNA complex works as the template for genome replication. Further, the outer nucleocapsid contains NP subunits linked by an outer horizontal layer. This layer consists of a ring of bridges between adjacent large subunits. These bridges are composed of twolobes, one bigger than the other. Experimental results showedthat recombinant nucleocapsid-like structures expressed VP24 and VP35. Each of these two proteins independently associates with NP, but all three proteins are required to be together to produce 50 nm diameter helical nucleocapsid-like structures. The ribonucleoprotein complex is formed by NP, VP30 (transcriptionfactor), VP35 (polymerase cofactor) and the RNA- dependent RNA polymerase.

RNA-NP-Polymerasecompled (innernucleocapsid). **Envelope**



VP40

VP30,VP35,VP24
Bridges(outer nuleocapsid)

Fig-2 Virion Structure of The Ebola Virus

4. Virology

He genome of Ebola virus is 18,959 nucleotides in length and 80nanometers (nm) in width containing only seven Open Reading Frames (ORFs). Despite limited encoding capacity, this virus expandsits gene functions by forming more proteins and assigning more functions to each of them. Nine proteins have been known to be translated, including nucleoprotein (NP), the polymerase cofactor viralprotein (VP35), the major matrix protein (VP40), glycoprotein (GP),soluble glycoprotein (sGP), small soluble glycoprotein (ssGP),transcription activator (VP30), the minor matrix protein (VP24), and viral RNA- dependent RNA polymerase (L). He GP, a surface protein nserted into the viral membrane, functions during virus entry into the host cells by binding to its receptor and fusion with cell membrane[16].Viral genes including 3'- UTR (un translated regions)-NP-VP35-VP40-GP-VP30-VP24-L-5'-UTR, that are transcribed by the vira lRNA dependent RNA Polymerase present in the virion. He single strand of RNA is covered by helically arranged viral nucleo proteins NPand VP30, which are linked by matrix proteins VP24 and VP40 to the lipid bilayer that coats the virion. Viral protein 35 (VP35)is a multi functional dsRNA binding proteinthat plays important roles in viral replication, innate immune evasion,and pathogenesis. He multifunctional nature of these proteins also presents opportunities to develop counter measures that target distinct functional regions.He EBOV matrix protein is VP40, which is also found localized under the lipid envelope of the virus where it bridges the viral lipid envelope and nucleocapsid. He VP40 a peripheral protein that mediates the plasma membrane binding and budding of the virus prior to egress. He Ebola virus structural glycoprotein is responsible for the virus' ability tobind to and infect targeted cells. He viral RNA polymerase encoded bythe L gene, partially uncoated the nucleocapsid and transcribes the genes into positive-strand mRNAs, which are then translated into structural and non structural proteins.

5. PATHOGENESIS

He path physiology of Ebola is not yet fully understood, however,most studies report that the incubation period varies depending on the type of exposure (i.e., six days for percutaneous and ten days for contact exposure). He WHO Ebola response team's findLngs have documented that the mean incubation period was 11.4 days, which did not vary by country. Following viral transmission most all data on the pathogenesis of Ebola virus disease have been obtained from laboratory experiments employing mice, guinea pigs, and nonhuman primates. However, case reports and largescale observational studies of patients in the 2014-2015 West Africa outbreaks are providing urgently needed data on the pathogenesis of the disease in humans (Figure2).

Phase I can be characterized as the transfer of EBOV from ananimal carrying the virus to a human, usually via small cutaneous lesions. Similar principles apply in human-to-human transmission during Ebola outbreaks. Phase II can be characterized as the early sympto matic stage - usually between days four and ten - where symptoms of a viral illness appear and gradually progress toward more advanced manifestations of the disease. Finally, Phase III represents theadvanced Ebola virus disease, with hemorrhagic manifestations, impaired immunity, and end-organ failure. Adapted from Journal of global

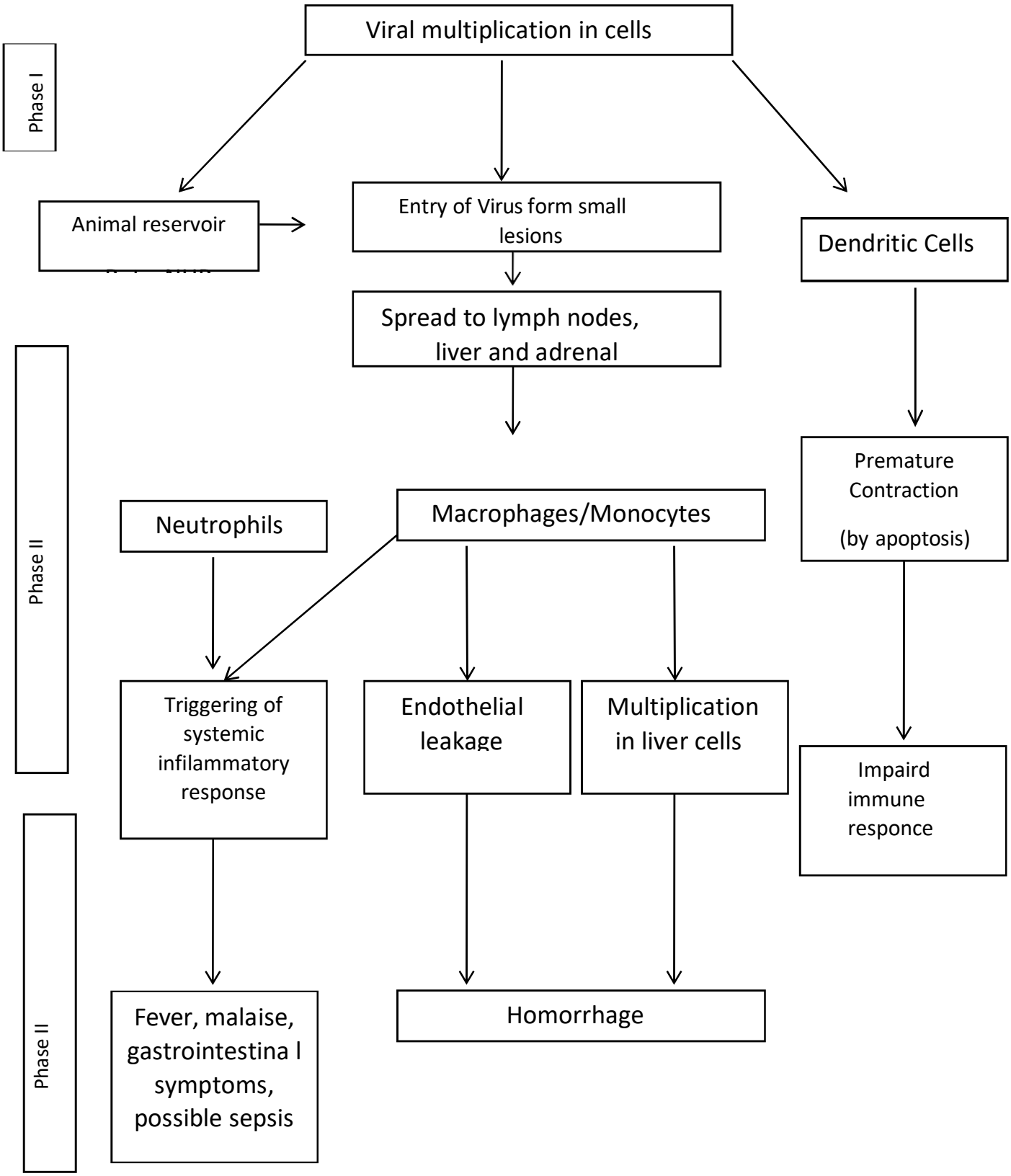


Fig.3.Diagram Demonstrate The Pathogenesis of Ebola Virus Infection.

6. MODE OF TRANSMISSION

Epidemics of Ebola virus disease are generally through to begin when an individual becomes infected through contact with the meat or body fluids of an infected animal. Once the patient becomes ill or dies, the virus then spreads to others who come into direct contact with the infected individual's blood, skin or other body fluids. Studies inlaboratory primates have found that animals can be infected with Ebola virus through droplet inoculation of virus into the animal mouth or eyes suggesting that human infection can result from the inadvertent transfer of virus to these sites from contaminated hands.Person-to-person transmission occurs through direct contact with blood, body fluLds, or skin of patients with Ebola virus disease, including those who have died from the infection. Kissing the body is also common. Hese practices can be extremely dangerous because Ebola victims are oien most contagious just aier death, when the viral load in their blood is at its highest [10,24]. According to the WHO, the most infectious body fluids are blood,feces, and vomit. Infectious virus has also been detected in urine, semen, saliva, and breast milk. Ebola virus can also be spread through direct contact with the skin of patient, but the risk of developing infection from this type of exposure is lower than from bexposure to body fluids .A number of studies examining airborne transmission broadly concluded that transmission from pigs to primates could happen without direct contact, because pigs with EVD get very high Ebola virus concentrations in their lungs, and not their blood stream.Herefore pigs with EVD can spread the disease through droplets in the air or on the ground when they sneeze or cough. By contrast, humans and other primates accumulate the virus throughout their body and specifically in their blood, but not very much in their lungs.Human infection with Ebola virus can occur through contact with wild animals such as hunting, butchering, and preparing meat from infected animals.

6.1 Clinical Presentation and Diagnosis:

1) Clinical Presentation:

He incubation period and duration of the disease course of Ebola virus disease varies between 2-21 days with an average of 4-10 days.Symptoms Symptoms usually begin with a sudden flu-lLke symptoms like quickly on-coming fever, mayopathy, and headache, which are soo followed by bloody vomit and diarrhea, nausea and vomiting, anorexia conjunctivitis, rashes on the body. Some days later, typically begins five to seven days aier the first symptoms victims can begin to bleed through the eyes, nose, or mouth. A hemorrhagic rash can develop on the entire body, which also bleeds. Muscle pain and swelling of the pharynx also occur in most victims. He most common signs and symptoms reported from West Africa during the current outbreak from symptom-onset to the time the case was detected include: fever (87%), fatigue (76%), vomiting (68%), diarrhea (66%), and loss of appetite (65%). Unexplained bleeding has been reported from only 18% of patients, most oien blood in the stool (about 6%) (Figure 4).

Fig. 4: Bleeding of blood from throughout the body characteristics symptoms of Ebola virus.

2) Diagnosis & Differential Diagnosis:

When Ebola virus disease is suspected in person, his or her travel and work history, along with an exposure to wildlife, are important factors to consider with respect to further diagnostic.

3) Specific Laboratory Testing:

Possible laboratory indicators of Ebola virus disease include a low platelet count; an initially decreased white blood cell count followed by an increased white blood cell count; elevated levels of the liver enzymes alanine-aminotransferase (ALT) and aspartate aminotransferase (AST); and abnormalities in blood clotting oien consistent with disseminated intravascular coagulation (DIC) such as a prolonged prothrombin time, partial thromboplastin time, and bleeding time.

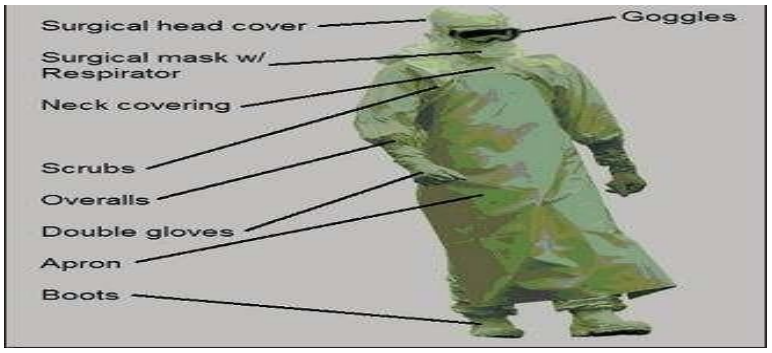
4) Non-Laboratory Testing :

He diagnosis of EVD is confirmed by isolating the virus, 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) are methods best used in early stages of the disease and also for detecting the virus in human remains. Detecting antibodies against the virus is most reliable in later stages of the disease and in those who recover. IgM antibodies are detectable two days aier symptom on set antibodies can be detected 6 to18 days aier symptom onset.

7. PREVENTION AND TREATMENT

1) 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 quickly if signs and symptoms develop. During the 2014 Boutbreak, 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 ℃ 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.

2) 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.

3) Environmental infection control:

If a patient with suspected orconfirmed Ebola virus disease is being cared for in a healthcare setting,specLfic precautions should be taken to reduce the potential risk of virus transmission through contact with contaminated surfaces. He 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 aier the last known exposure; the development of fever and/or other clinical manifestations suggestive of Ebola virus disease should be reported immediately.

4) Breast Feeding & Infant Care:

Ebola virus can be transmitted by close contact of an infected mother with her children. Hus, 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.

5) Precautions During The Convalescent Period:

Patients recovering from Ebola virus disease may continue to have virus present in certain body fluLds (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.

6) Pregnancy :

He 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 usedwhen 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.

7) Vaccines:

Due to the pathogencity of the virus, no conventional vaccines consisting of inactivated/killed virus, or made from an attenuated viralstrain, are being developed for Ebola because of the risk of incomplete inactivation of the virus or of reversion to a fully active form. Instead, these vaccines are based on relatively new approaches that have been made possible with the advancement of molecular biology and recombinant genetic technologies introduced during the last 10-20 years. several candidate vaccines are in various phases and a safe and effective vaccine is hoped for by the end of 2015.Currently, two vaccine candidates are entering trials in humans[39,40].He first is cAd3- ZEBOV developed by GlaxoSmithKline and tested by the US National Institute of Allergy and Infectious Diseases(NIAID). He second is the rVSV tested by the New Link Genetics.Corporation aier being licensed from the Public Health Agency of Canada. Both vaccines demonstrated promising rates of in abnonhuman primates, but the translation of these results to human subjects has not yet been accomplished

8. TREATMENT

1) Approach to therapy:

Here are no approved treatments available for EVD. Clinical management should focus on supportive care of complications, such ashypovolemia, electrolyte abnormalities, hematologic abnormalities, refractory shock, hypoxia, hemorrhage, septic shock, multi-organfailure. He mainstay of treatment for Ebola virus disease involves supportive care to maintain adequate cardiovascular function whilet he 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. He efficacy of these agents is unclear and is an active area of investigation. In addition, the availability of these drugs is limited.

2) Antiviral:

Antivirals have emerged since the mid 1980s with the need to treat deadly viral infections such as HIV. Since then, severalmolecules with antiviral activity have been developed and assayed in vitro and in vivo. In Ebolavirus infection, various antiviral strategies have been tested. Some approaches include inhibitors of a cellularenzyme, S-adenosyl-L-homocysteine (SAH) hydrolase, which is involved in 5’ cap methylation of viral messenger RNA, inducing the intracellular accumulation of SAH and triggering feedback inhibition of methylation. These type of compoundshave broad-spectrum antiviral activity attributed to decreased methylation of the 5’ cap of viral messenger RNA, resulting in inefficient translation. The molecule 3- deazaneplanocinA (3-DNP) is one of such SAH inhibitors and has showed a potent antiviral effect against Ebolavirus infection in a mouse model. Upon treatment, 3-DNP induces an excess of IFN-α production in the tissues of infected animals but not in uninfected ones. A direct relationship between IFN serum concentration and the number of infected cells was observed, indicating that IFNinduction by 3-DNP requires presence of virus within cells. Under experimental conditions, 3-DNP given for a week three times daily after an Ebolavirus challenge, prevented infected mice from disease and death.

Treatment approaches against Ebolavirus infection

Treatment	Types	Example	Modelevaluated
Antibodies	Passivetransfer	Whole-blood/serumfromsurvivingpatients	Rodents nhp & Humans
	Neutralozingmnoclonal	Z mapp	NH Pandhumans
Vaccines	Viralvectorvaccines(live-attenuatedvirus	Replicationcompetentvaccines(vesicularstomatitis virusexpressing GP)	Rodenstand NHP

		Humanparainfluenza 3 virusexpressing ebola gp	Rodents
		Kunjinreplication vlps	Rodents
		DNA-Recombinant ebola gp adenovirus	Rodents
Inhibitorsfft		Recombinantadenovirusexpression np gp	RodentsrodentssandNHP
Modulatorsofcoagulation		Recombinathumanadenovirustypes5expression GP	
Antivirals		Recombinantvesicukarstomatitisviruseex pressiON GP	NHPEb Rodents RodentssandNHP
		Ebola GP human G1FC	
		Againstseveresepsis	NHP
		Inhibitoro TF-FV IAcomplex	NHP
		inhibits5’capmethylationofviralmesswngER RNA	Rodents
		Not Described	Rodents
		Syntheticadenosineanalog	RodentssandNHP

			Invitroanhumans
		Bolck translationnofviral rna inhibiting vral replication rodents nhp	
		Bolck translationnofviral rna inhibiting vral replication rodents nhp	

These vaccines intend to induce a more robust activation of both innate (humoral) and adaptive (cellular) immune responses, maximizing vaccine efficacy. Examples of vaccines include a DNA-prime and adeno virus boost. This strategy required six months to induce protective immunity. A single dose of recombinant adenovirus expressing NP and GP protected non-human primates against a lethal dose (1 500 LD of Ebola at 28 d after vaccination. An adeno virus sero ype 5 expressing the Zaire ebolavirus GP protected mice against an adapted Zaire ebolavirus. This recombinant virus protected guinea pigs against a lethal guinea pig-adapted Ebola virus challenge when delivered by intramuscular or intranasal routes. Animals with pre-existing immunity to adenovirus had lower survival. A recombinant human adenovirus type 5 viral vector expressing full or truncated Ebolavirus GP forms was tested in the interferon α/β receptor knock-out mouse model. The recombinant vaccine induced strong protection and antibody response in this mouse model and animals intranasally inoculated with the recombinant virus vaccine showed 40%-100% survival upon a lethal intraperitoneal challenge. Another approach used recombinant VSV encoding the Ebola GP surface protein. This vaccine showed protection efficacy in 50% of non-human primates challenged with Zaire ebola virus when administered soon after challenge (30 min). A new generation of inactivated Ebola virus vaccine has been recently done by deleting the VP35 gene, essential for virus replication . Recombinant vaccines based on human para influenza virus protected.

Guinea pigs from Ebola infection after a single intranasal inoculation. A new live-attenuated Ebolavirus vaccine using a chimeric human parainfluenza virus type 3 expressing Ebola virub GP as the only transmembrane envelope protein, induced a strong immune response against GP. A single dose protected animals against a lethal intraperitoneal challenge with a guinea pig adapted Ebolavirus. Live attenuated viruses are better than replication-deficient vaccines in terms of production scale and induction of strong innate and adaptive (humoral and cellular) immune responses, though the safety concerns on this type of vaccines may limit its application in humans. A vaccine candidate using Ebolavirus VLPs have been synthesized in mammalian or insect cell expression systemsThe VLPs were generated by coexpression of the viral proteins VP40, NP and GP[or baculovirus pseudotyped with the Ebolavirus proteins GP or VP40. TheseVLPs have successfully protected mice, guinea pigs and nonhuman bprimates. Another VLP-producing approachis to use a replicon- recombinant kunjin virus, expressing VLPs with full length Ebolavirus GP or a mutated GP. These replicon VLPs induced dose-dependent protection in guinea pigs against a lethal challenge of an adapted Ebolavirus strain.

An Ebolavirus GP-human IgG1 Fc fusion protein was expressed in mammalian cells. The fusion protein was cleaved with enter okinase and purified. Mice immunized with the fusion protein GP-Fc developed T-cell immunity against Ebolavirus GP and neutralizing antibodies against an engineered, replication competent VSV recombinant virus containing Ebolavirus GP. Also, mice vaccinated with the GP-Fc were protected against a lethal Ebolavirus challenge. Cross protection among different Ebola species in experimental n contrast, administration of siRNA-SNALP complex 1 h after the Ebola challenge showed a complete protection against viremia and mortality.

Other experiments showed that one (EK1) of the four siRNAs alone could completely protect animals from Ebola infection. The same siRNA approach against Ebolavirus was assayed in a non-human primate model.. mg/kg per dose, bolus intravenous infusion) at 30 min, and on 1, 3, and 5 d after an Ebola challenge. Another set of macaques (n=4) were treated with the same molecule pool at 30 min, and on 1, 2, 3, 4, 5, and 6 d after an Ebola challenge. Protection against Ebola challenge was observed in 2 out of 3 (66%) and 7 out of 7 (100%) monkeys in the first and second experiments, respectively. These results indicate the efficacy of siRNA-SNALPs as a post-exposure treatment against Ebola infection, with potential application in humans. A similar siRNA approach is already in the pipeline. A phase I clinical trial has started. The experimental treatment is termed TKM- Ebola and is based on the EK1-4 molecules.

9. CONCLUSION

The Ebola virus is one of the most contagious and deadly zoonotic viruses to infect humans in the last four decades. This virus produces a terrible illness called Ebola hemorrhagic fever, which is fatal in 50% of cases. Only African countries have experienced outbreaks that resulted in significant deaths. The present Ebolavirus outbreak is continuing progressing, and it is estimated that by the end of 2014, up to 5,000 people might be infected every week unless appropriate containment and treatment methods are implemented. The World Health Organization has set a goal of containing the spread by following three rules: 70% safe burials, 70% proper isolation and treatment for sick people, and they must all be followed.Further more, the World Health Organization has advised that a number of treatments be evaluated in the worst-affected areas. Whole blood transfusions from surviving patients are one of them. The goal of this study is to use passive serum transfer as a first-line therapy. Other efforts should be made to examine several successful experimental medicines in fast-track clinical trials, such as Canadian-developed recombinant VSV-GP vaccines, siRNA-SNALPs, and tiny broad-spectrum antiviral compounds. The current Ebola virus pandemic plainly necessitates a quick response from the scientific community in order to develop a safe and effective vaccine against a re-emergent disease that has been largely overlooked in the past.

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