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"Review on Ebola Virus

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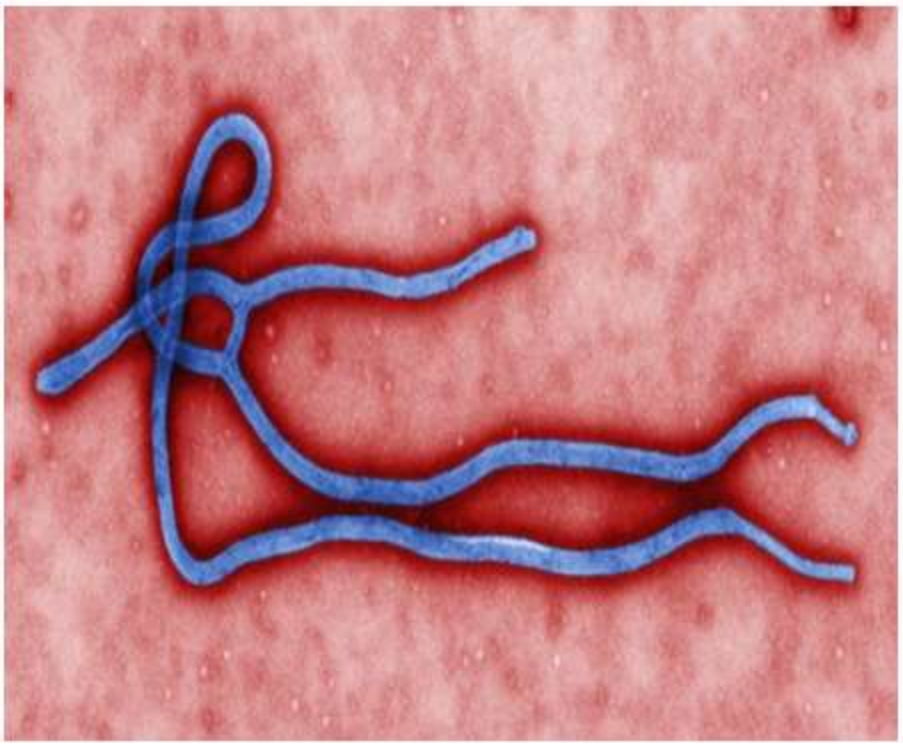
ABSTRACT: Within less than a year after its epidemic started (in December 2013) in Guinea, Ebola virus (EBOV), a member of the filoviridae, has spread over a number of West-African countries (Guinea, Sierra Leone and Liberia) and gained allures that have been unprecedented except by human immunodeficiency virus (HIV). Although EBOV is highly contagious and transmitted by direct contact with body fluids, it could be counteracted by the adequate chemoprophylactic and -therapeutic interventions: vaccines, antibodies, siRNAs (small interfering RNAs), interferons and chemical substances, i.e. neplanocin A derivatives (i.e. 3-deazaneplanocin A), BCX4430, favipiravir (T-705), endoplasmic reticulum (ER) α-glucosidase inhibitors and a variety of compounds that have been found to inhibit EBOV infection blocking viral entry or by a mode of action that still has to be resolved. Much has to be learned from the mechanism of action of the compounds active against VSV (vesicular stomatitis virus), a virus belonging to the rhabdoviridae, that in its mode of replication could be exemplary for the replication of filoviridae.

I. INTRODUCTION:--

Ebola Virus:-



Ebola virus was first discovered in 1976 near the Ebola River in what is now the

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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 or nonhuman primates (chimpanzees, apes, monkeys, etc.) being the most likely source.

Infected animals carrying the virus can transmit it to other animals, like apes, monkeys, duikers and humans.The virus spreads to people initially through direct contact with the bloodbody fluids and tissues of animals.

Ebola virus then spreads to other people through direct contactwith body fluids of a person who is sick with or has died from EVD .This can occur when a person touches these 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. People can get the virus through sexual contact with someone who is sick with EVD, and also after recovery from EVD. The virus can persist in certain body fluids, like semen, after recovery from the illness.

A virus that causes severe bleeding, organ failure and can lead to death.Humans may spread the virus to other humans through contact with bodily fluids such as blood.

EBOV is subdivided into 5 Species:

1. Zaire (EBOV-Z),
2. Sudan (EBOV-S),
3. Reston (EBOV-R),
4. Tai Forest (EBOV-TF),
5. Bundibugyo (EBOV-B)

Ebola disease is a severe, often fatal illness in humans

• The virus is transmitted to people from wild animals and then spreads in the human population through human-to-human transmission.

• The average Ebola case fatality rate is around 50%.Early supportive care with rehydration, symptomatic treatment improves survival.

• Five species of Ebola virus have been identified. Among them, Bundibugyo ebolavirus, Zaïre ebolavirus, and Sudan ebolavirus have been associated with large outbreaks in Africa.A virus that causes severe bleeding, organ failure and can lead to death.Humans may spread the virus to other humans through contact with bodily fluids such as blood.

History of Ebola Virus

Ebola virus disease (EVD) is a severe disease caused by Ebola virus, a member of the filovirus family, which occurs in humans and other primates. The disease emerged in 1976 in almost simultaneous outbreaks in the Democratic Republic of the Congo (DRC) and Sudan (now South Sudan).

Between 1979 and 1994 no cases or outbreaks were detected, however since that time outbreaks have been recognised with increasing frequency .

The largest outbreak to date took place in West Africa between March 2014 and June 2016, affecting primarily Guinea, Liberia and Sierra Leone. Over 28,000 cases were recorded.

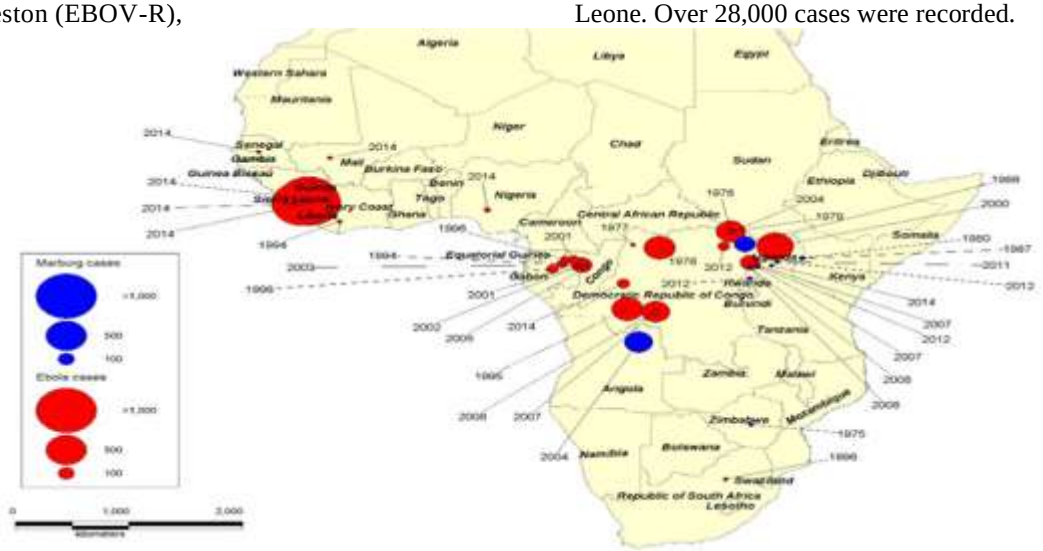

Fig: EBOLA OVERVIEW HISTORY & TRASMISSION

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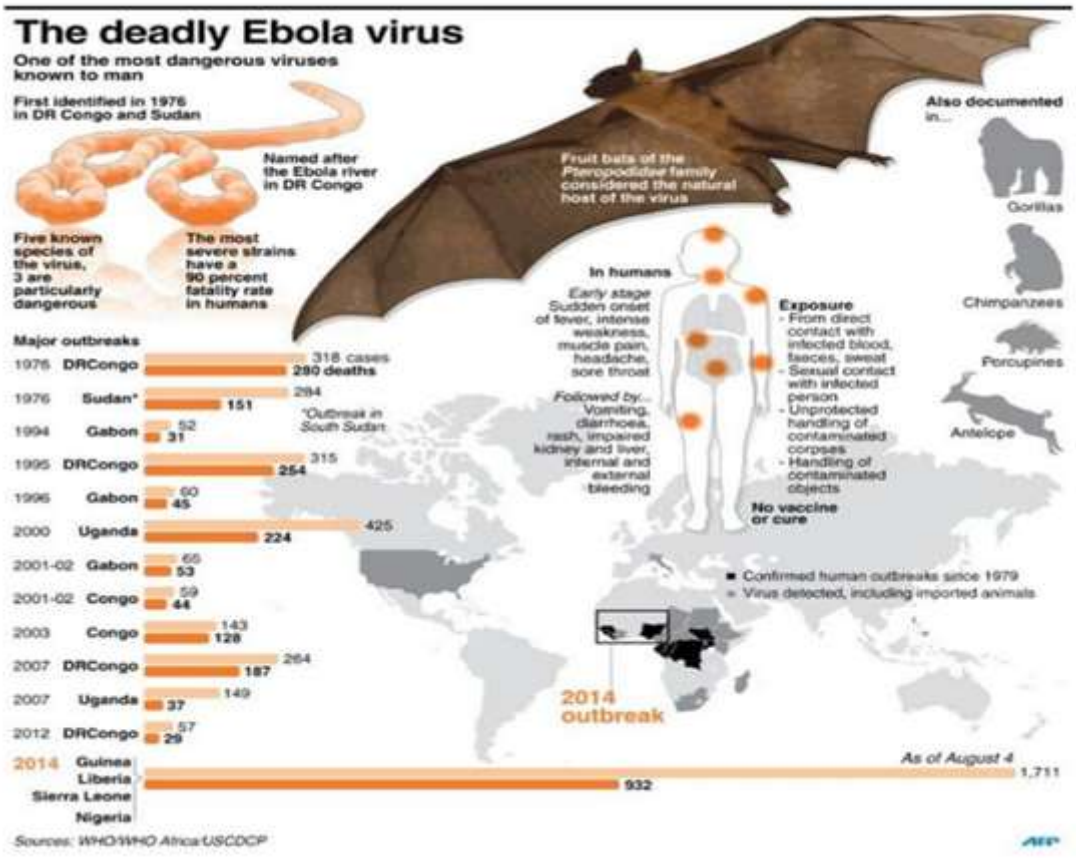
The most recent EVD outbreakhas been ongoing in the Democratic Republic of Congo (Equateur Province) since June 2020. As of 9 August 2020, there had been 79 confirmed and probable cases.
There are 6 species of Ebola virus, 4 of which have caused disease in humans:

- Zaïre ebolavirus (EBOV)
- Sudan ebolavirus (SUDV)
- Tai Forest (TAFV) (formerly known as Ebola Ivory Coast)
- Bundibugyo ebolavirus (BDBV)



Reston Ebolavirus (RESTV), has caused severe illness in non-human primates but not in humans. RESTV was first detected in October 1989 in Reston, Virginia (USA) in a colony of monkeys imported from the Philippines, and has subsequently caused outbreaks in non-human primates in Pennsylvania (Philadelphia), Texas (Alice) and Italy (Sienna). Several research workers became infected with the virus during these outbreaks, but did not become ill.

Investigations traced the source of all outbreaks caused by RESTV to one export facility in the Philippines, but how the facility was contaminated was not determined. In December 2008, RESTV was found in sick pigs in the Philippines. A number of workers developed antibodies but none had had any symptoms.

A 6th species of ebolavirus was discovered in bats in Sierra Leone in 2018, and named Bombali ebolavirus. It is not yet known if this species is pathogenic for humans.

In Africa between 1976 and 2014, outbreaks of EVD primarily occurred in remote villages close to tropical rainforests in Central and West Africa. Most confirmed cases were reported from the Democratic Republic of the Congo (DRC, formerly Zaire), Sudan, Gabon, Uganda, and the Republic of Congo.In 2014, Ebola outbreaks occurred for the first time in West Africa (Guinea, Liberia and Sierra Leone), and in these countries there was intense transmission in urban areas.

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Associated with this extensive outbreak, Ebola cases were imported into Italy, Nigeria, Mali, Senegal, Spain, the UK and the USA.

In India 2014, Kerala also faced a threat of Ebola virus transmission as many people coming from infected areas in African subcontinent visited India. What are symptoms of Ebola virus infection? Person infected with Ebola virus has similar symptoms than that of malaria, typhoid fever or meningitis.

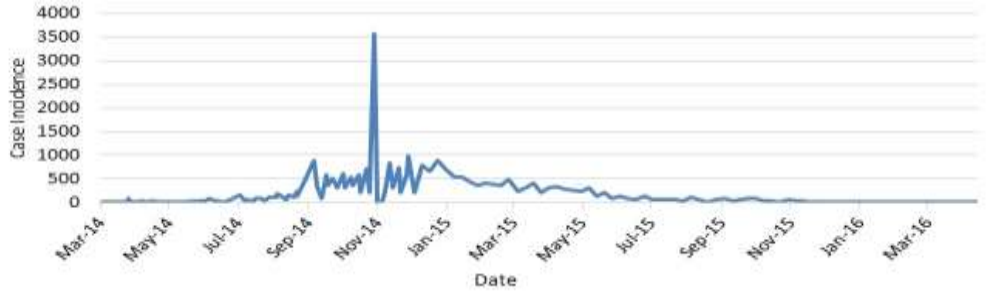
II. EBOLA OUTBREAK:

On March 23, 2014, the World Health Organization (WHO) reported the first cases of EVD in West Africa in what would become the largest Ebola virus epidemic in history. Over two years, a total of 28,616 cases of EVD and 11,310 deaths were reported in Guinea, Liberia, and Sierra Leone. An additional 36 cases and 15 deaths occurred when the outbreak spread outside these three countries.

The following graphs demonstrate the incidence of newly suspected, probable, and confirmed cases over the duration of the epidemic in Guinea, Liberia, and Sierra Leone, the countries most impacted by the epidemic, both in the aggregate and separated by country.

The Frequency of New Cases in Guinea, Liberia, and Sierra Leone during the Ebola Outbreak from March 25, 2014 to April 13, 2016
Epi Graph-1: The Frequency of New Cases in Guinea, Liberia, and Sierra Leone during the Ebola Outbreak from March 25, 2014 to April 13, 2016
ResizeView Larger

Graph 1: Case Incidence in Guinea, Liberia, and Sierra Leone.



This graph shows the frequency of newly reported cases in Guinea, Liberia, and Sierra Leone provided in WHO Situation Reports beginning on March 25, 2014, through the last situation report on June 10, 2016. The numbers are a total of suspected, probable, and confirmed cases.

Countries with Widespread Transmission and other Countries Affected During the Epidemic

Country	Total Cases (Suspected, Probable, Confirmed)	Laboratory Confirmed Cases	Total Deaths
Countries with Widespread Transmission			
Guinea	3,814	3,358	2,544
Liberia	10,678	3,163	4,810
Sierra Leone	14,124	8,706	3,956
Affected Countries			
Italy	1	1	0
Mali	8	7	6
Nigeria	20	19	8
Senegal	1	1	0
Spain	1	1	0
United Kingdom	1	1	0
United States	4*	4	1
Total	28,652	15,261	11,325

Graph 1: Case Incidence in Guinea, Liberia, and Sierra Leone.

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This graph shows the frequency of newly reported cases in Guinea, Liberia, and Sierra Leone provided in WHO Situation Reports beginning on March 25, 2014, through the last situation report on June 10, 2016. The numbers are a total of suspected, probable, and confirmed cases.

Table 1: Case Incidence in Guinea, Liberia, and Sierra Leone.

Date	Number of Cases per Month
3/31/2014	120
4/30/2014	114
5/28/2014	75
6/24/2014	290
7/31/2014	723
8/28/2014	1730
9/26/2014	3501
10/31/2014	6987
11/28/2014	3559
12/31/2014	3272
1/28/2015	1886
2/25/2015	1637
3/31/2015	1484
4/29/2015	1120
5/31/2015	847
6/30/2015	395
7/31/2015	300
8/31/2015	225
9/29/2015	323
10/30/2015	159
11/30/2015	54
12/30/2015	0
1/27/2016	2
2/17/2016	0
3/30/2016	7
4/13/2016	6

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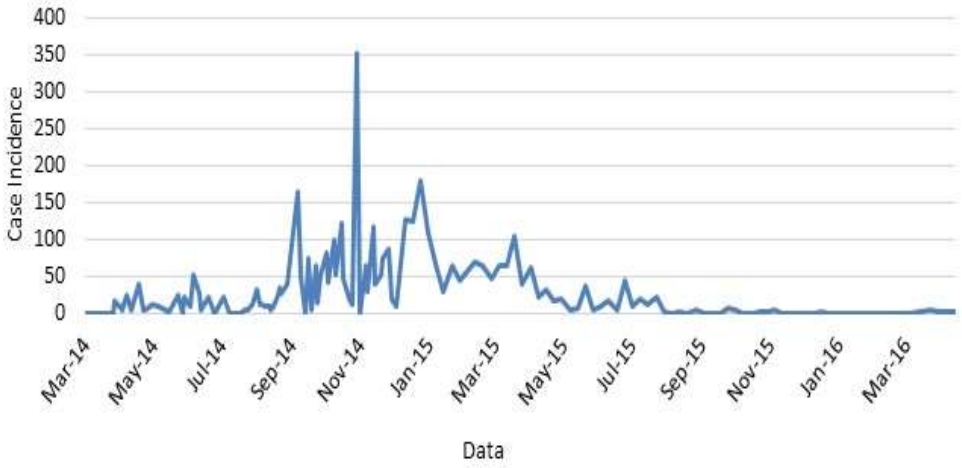
The Frequency of New Cases in Guinea during the Ebola Outbreak from March 25, 2014 to April 13, 2016



The Frequency of New Cases in Guinea during the Ebola Outbreak from March 25, 2014 to April 13, 2016

III. EBOLA EPIDEMIOLOGY:-

EVD, also simply known as Ebola, is a severe disease of humans and nonhuman primates caused by infection with a virus of the family Filoviridae, genus Ebolavirus. Of the five identified species of Ebolavirus,four have been responsible for disease in humans.The name Ebola comes from a river in the Democratic Republic of the Congo where the first Ebola virusdisease (EVD) outbreak occurred, in 1976. Since then, there have been a series of outbreaks. With the exception of the last one, all previous outbreaks occurred in tropical region of Central Africa.

The one with the highest mortality rate dates back to 2003 and took place in the Democratic Republic of Congo, where itkilled almost 90 percent of the infected personsThe largest is currently raging in West Africa, with 15,145cases and 5,420 deaths as of November 16th 2014, which is much more than the sum of the victims in all previous outbreaks.This is the first outbreak of EVD in West Africa and the 25th outbreak globally since the disease was first discovered. Officially reported figures are generally believed to be gross under-estimations of themagnitude of this outbreak since, according to WHO's recently published roadmap, the actual number of cases may be 2 to 4 fold higher than currently reported, and it is estimated that the aggregate count could exceed 20,000 cases over the course of the outbreak.

The outbreak started in Guinea in December 2013 but was only detected in March 2014. Since then, it spread in Liberia and Sierra Leone. In July an infected traveller brought the disease in Nigeria and, by the end of August, a single case was reported in Senegal (a 21-year-old male who recently arrived from Guinea).On October 20th WHO declared Nigeria free of EVD, since no virus transmission had been recorded for 42 days, due to the prompt containment of the disease.

No local transmission of EVD was reported in Senegal, therefore the country is currently not among the list of affected countries as far as November 5th. At the same time, another EVD outbreak started in the Democratic Republic of the Congo. According to viruses identification and sequencing, it is not related to the West Africa one.

This outbreak is unprecedented in size, in geographical distribution, and in affecting densely populated urban areas, even if it is not as lethal as some of the previous ones. The most affected rural area is the cross-border area of Gueckedou (Guinea),Lofa (Liberia) and Kenema and Kailahun (Sierra Leone), but transmission in the capital cities is of particular concern, owing to their population density and the repercussions for travel and trade.

As a result, this last epidemic was declared an international public health emergency (Public Health Event of International Concern, PHEIC) by the World Health Organization (WHO**)** on August 8th 2014**.**

Surveillance and Bio-monitoring:

The recent Ebola virus outbreak in West Africa occurred in five countries: Guinea, Liberia,

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Nigeria, Senegal and Sierra Leone. A total of 11,296 cases, including confirmed and probable cases were reported .Although the Ebola virus outbreak was initially restricted to West Africa, in July of 2014, two American health care workers in West Africa were diagnosed with Ebola and then transported to a hospital in the United States of America (USA) for treatment. Later in the same year, a person who recently traveled to an Ebola-infected country was diagnosed with the virus in Texas .

Through proper surveillance, the USA, West African countries, and non-infected countries can: examine the effectiveness of current control and preventive health measures, keep track of changes of the infectious agent (Ebola virus), support health planning and designate appropriate resources within the healthcare system, identify high risk populations as well as areas needing targeted interventions, and also provide a record of disease activity for future reference .

The 2013-2014 EVD outbreaks mimicked the Ebola outbreak of Zaire in 1976. The causative organism of both was Zaire Ebola virus and they began in rural forest communities. Those infected with EVD reported to hospitals with symptoms resembling those of malaria, typhoid, Lassa fever and/or influenza.Healthcare professionals were unprepared to handle the virus and some even came in contact with infected patient's bodily fluids, further exacerbating the outbreak. To stop the spread of the EVD in Zaire, the government quarantined the people, commercial planes and boats were not allowed in the country, and citizens were not permitted to leave their villages.

The remains of the deceased were properly disposed of by cremation or placed in metal caskets according to the guidelines enforced by the Center for Disease Control and Prevention (CDC) for postmortem preparations.

Surveillance teams led by trained healthcare professionals visited the 550 villages. Teams wore protective gear and brought first-aid kits, thermometers, antimalarials, antibiotics and antipyretics. Patients displaying symptoms of a fever were given medication and advised to stay isolated from others.The most recent Ebola virus outbreak was treated similarly to the outbreak of 1976. Priorities included the identification of infected patients and surveillance and care of those patients and their close contacts.

New York City (NYC) is a common entry point for travelers from West Africa; thus, safety precautions were implemented to prevent an outbreak of Ebola virus in the United States.

This involved screening checkpoints set-up at various international airports around the world, including, but not limited to, the United States: Atlanta Hartsfield-Jackson International Airport, Newark Liberty International Airport, WashingtonDulles International Airport, Chicago-O'Hare International Airport, and New York JFK..

The NYC Department of Health and Mental Hygiene (DOHMH) worked closely with local hospitals and physicians, nongovernmental organizations, community groups, and city, state and federal agencies to control the current situation and reduce the outbreak from spreading.

Clinicians were required to call DOHMH immediately after identifying any patient that met the CDC case definition for a person under investigation (PUI): a person who traveled to an Ebola-affected area within 21 days of onset of symptoms i.e. fever over 38.6°C (101.5°F), severe headache, muscle pain, vomiting, diarrhea, abdominal pain or unexplained bleeding. Also, obtaining a full travel history from febrile patients is needed to further avoid an Ebola outbreak.

Etiology and Pathophysiology

The pathophysiology or functional changes that accompany the single-stranded RNA Ebola virus is not fully understood; however, part of its pathogenesis

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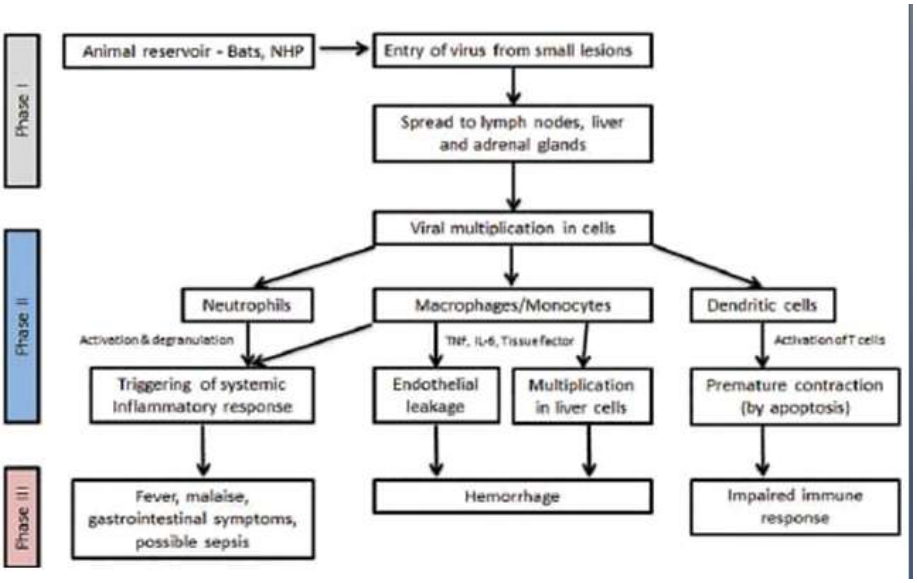

Fig:- DEMONSTRATING THE PATHOGENESIS OF EBOLA VIRUS INFECTION

Studies have suggested that the virus enters the host through mucosal surfaces, breaks and abrasions in the skin, or by parenteral introduction; though recent reports suggest that it is by direct contact with infected patients or cadavers. The organism has a broad cell tropism, which can infect a wide range of cell types. Studies in nonhuman primates have shown that fibroblasts, monocytes, dendritic cells, hepatocytes, macrophages, endothelial cells, adrenal cortical cells, as well as other cell types, have supportive features for the virus to replicate .

The Ebola genome codes for four virion structural proteins: VP30, VP35, nucleoprotein, and a polymerase protein.In addition, there is also VP40, glycoprotein and VP24 which is a three membrane associated protein within the virus.

The surface glycoprotein is encoded in two frames: an open reading frame identified as OPF I and II. Open reading frame I encodes for a small, soluble, nonstructural secretory glycoprotein (SGP) that is readily detected in the serum of the infected hosts. This secretory glycoprotein binds to neutrophil CD16b, which is exclusively expressed by human neutrophils and binds IgG in immune complexes .In other words, sGP is responsible for inhibiting early neutrophil activation and may also be responsible for the profound lymphopenia (a condition of having an abnormally low level of lymphocytes in the blood), a unique feature and characteristic of the Ebola infectThus, studies suggest that sGP plays a pivotal role in the ability of the virus to prevent an early and effective host immune response. In conjunction, there are other transmembrane glycoproteins, respectively referred to as GP1 and GP2 delta-peptide.

These glycoproteins may also be incorporated into the Ebola virion. The exact mechanism is not fully understood; however, it is thought that these transmembrane glycoproteins are responsible for binding to endothelial cells of an unknown cell receptor but not to neutrophils. Therefore, the Ebola virus is known to invade, replicate in, and destroy endothelial cells.

Destruction of endothelial surfaces is associated with disseminated intravascular coagulation (DIC) and this may contribute to the hemorrhagic manifestations that are seen with late-stage Ebola infections.Clinical infection is associated with rapid and extensive viral replication in all tissues and accompanied by widespread and severe focal necrosis. The characterization of filovirus pathogenesis and a thorough understanding of the cellular mechanism are relevant to demonstrate the effectiveness of new biological products for control and prevention of the disease.

The flow chart depicts the pathogenesis of Ebola virus infection. The mode of infection can be divided into three phases. Phase I is characterized as the transfer of the virus from an animal carrying the virus to a human, usually via small cutaneous lesions and subsequently, human-to-human transmission.

Phase II is denoted as the early symptomatic stage. The early symptomatic stage typically occurs between days four and ten and is the stage of infection where symptoms of viral

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illness appear and progressively move toward more advanced manifestations of the disease.Phase III is representative of the advanced disease, with hemorrhagic manifestations, impaired immunity, and end-organ failure.

IV. TRANSMISSION

1. Transmission: Bats and animals

Just how Ebola actually gets from animalsor the environment and into human's isunclear.The virus probably "resides" in bats.From there it may occasionally infecthumans that directly handle or eat bats.Ebola may infect an intermediatespecies, such as monkeys or gorillas(non-human primates), that eatcontaminated partially-eaten fruit thatbats drop.Humans may find the dead "intermediate" animal and then eat its meat.

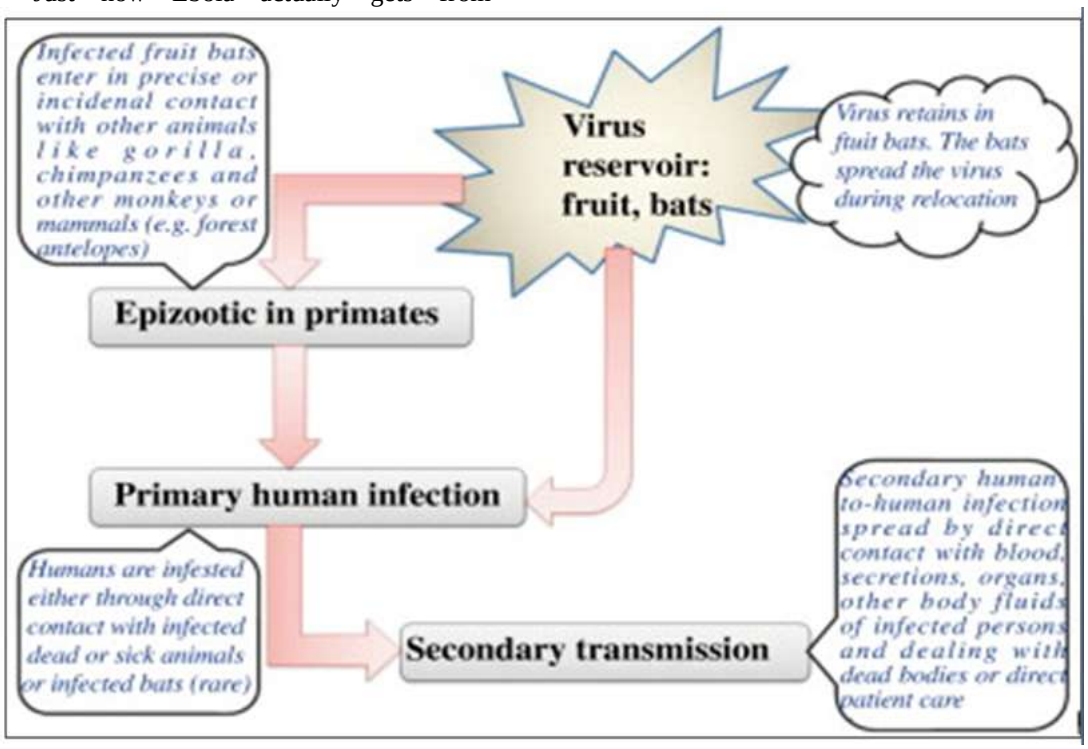

FIG:-MODES OF TRANSMISSION OF EBOLA VIRUS INFECTION

For example:-

Before Tai National Forest outbreak (1994), the chimpanzee population in the area decreased by half.Before and during Gabon outbreak (2001), 64 dead gorillas, chimpanzees, and antelope were discovered.

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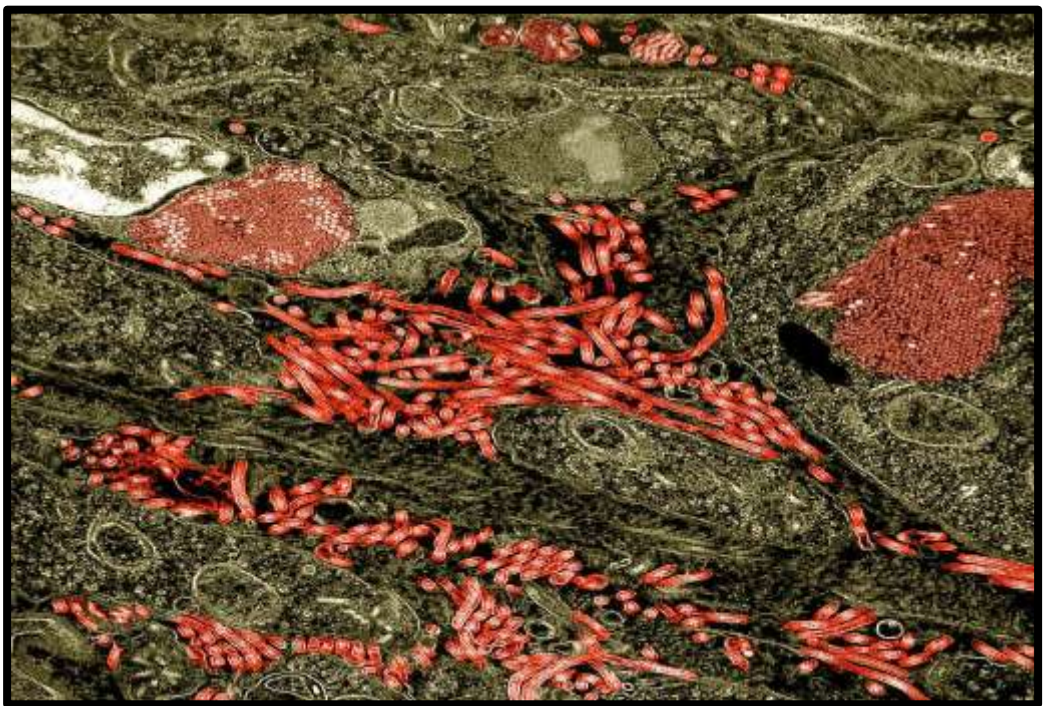

FIG: EBOLA VIRUS INFECTS REPRODUCTIVE ORAGANS IN MONKEY

2. Transmission: Outbreaks in humans

Ebola virus is contained in the blood and body fluids of infected people (vomit,diarrhea, urine, nasal secretions, sweat, ejaculate).The more symptomatic a person is, the greater the risk of catching the virus from their body fluids. In addition, it is possible to become infected by touching contaminated objects. The germs get onto the toucher's hands, and then may accidentally be transferred into the nose, mouth or eyes, or enter the blood stream via cuts on the hands.

Early Surveillance

Outbreaks in nonhuman primates and antelope often precede, or happen at the same time as, human cases of Ebola Virus Disease (EVD) in the same or nearby areas.

For example:

Before Taï National Forest outbreak (1994), the chimpanzee population in the area decreased by half.Before and during Gabon outbreak (2001), 64 dead gorillas, chimpanzees, and antelope were discovered.

Cases of EVD in people typically emerge following the handling and butchering of these infected animals. Once the virus spreads to people, it can spread quickly from person to person within families and other close contacts, as well as in healthcare settings. Rapid identification of cases is critical to prevent large-scale epidemics.

1. Detection and Response

Prompt identification of cases, contact tracing, and monitoring of high-risk individuals are essential to stopping Ebola virus from spreading.

2. Early Detection

Early recognition of EVD is critical for infection control. However, because early symptoms are not specific to EVD, it can be hard to distinguish it from other illnesses, including malaria, leptospirosis, influenza (flu), yellow fever, dengue and other viruses spread by insects, or viral or bacterial infections of the intestines, like typhoid fever.EVD should be considered when clinical illness is combined with an epidemiologic risk factor, like direct contact with a suspected or confirmed case or travel to an Ebola-affected area.

3. Contact Tracing

Once a case of EVD is identified, everyone who has come in direct contact with the sick patient is found. This is called contact tracing. Contacts are watched for signs of illness for 21 days from the last day they came in contact with the Ebola patient. If the contact develops a fever or other EVD symptoms, they are immediately isolated, tested, and provided care. Then the cycle starts again until all of the new contacts are found and watched for 21 days. The World Health

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Organization (WHO) declares an Ebola outbreak over after 42 days (or two incubation periods) have passed without any newly reported infections.

V. CLINICAL INFORMATION :

Ebola is one of the world's most virulent and lethal diseases. It provokes haemorrhagic fever and may leadto liver and kidney failures, with internal and external bleeding. Death may occur in 7-16 (with an average of 8-9) days after the appearance of the first symptoms and is caused by multiple organ dysfunction syndrome. Mortality rate ranges between 25 and 90 percent, according to virus characteristics, patient'scomorbidities, individual immune response, timing and intensity of medical support.

EVD main symptoms are:
• Fever
• Severe headache
• Muscle pain
• Diarrhoea
• Vomiting
• Abdominal (stomach) pain

Risk assessment

1. Exposure in the community

Since the Ebola virus is transmitted through contact with patients' body fluids and infected animals (bats and nonhuman primates, as far as it is known), groups most at risk of being infected are those more in contact with patients:
• Family and friends of infected people
• Healthcare workers
• People who attend to corpses (e.g. in ritual funerals).

So far, no evidence of age-related sensitivity to the disease has been found. However, as of August, 55 to 60 percent of the victims across Guinea, Liberia, and Sierra Leone were women, 75 percent if considering Liberia alone.

In 2007, a WHO report highlighted the issue of gender role by claiming that "differences in exposure between males and females have been shown to be important factors in transmission of Ebola haemorrhagic fever."This is due to the fact that, in these countries, women are usually the primary caregivers for the sick, whilst males rarely do that.The risk of infection for residents and visitors to the affected countries through exposure in the communityis considered low if people adhere to the recommended precautions.People visiting friends and relatives in the affected countries tend to have more frequent and closer contacts in the community, and they are more likely than other visitors to participate in burial ceremonies, an activity known to be associated with transmission of the Ebola virus.
Residents and visitors to the affected areas run a high risk of exposure to EVD in healthcare facilities.

2. Exposure in healthcare settings

The risk of being exposed to the Ebola virus is higher for healthcare workers or volunteers. They are potentially exposed not only through direct contact with cases but also through contaminated hospital materials, medical waste and diagnostic samples.

Transmission to healthcare workers may occur after close contact with EVD patients in settings where infection control measures were either not in place or not strictly adhered to.

The high number of infected healthcare workers indicates that infection control measures have not been successfully implemented. Anyway, the infection risk is not limited to hospitals that provide care to known EVD cases because infectious cases may initially seek medical attention at any healthcare provider. Furthermore, the risk of exposure in healthcare settings also exists in areas that have not yet reported cases because it is suspected that not all cases of EVD are being detected and reported.

VI. SIGNS AND SYMPTOMS :

Symptoms of EVD may appear 2 to 21 days after exposure to the virus, but the average is 8 to 10 days. A person infected with
Ebola virus is not contagious until symptoms appear. Signs and
symptoms of EVD

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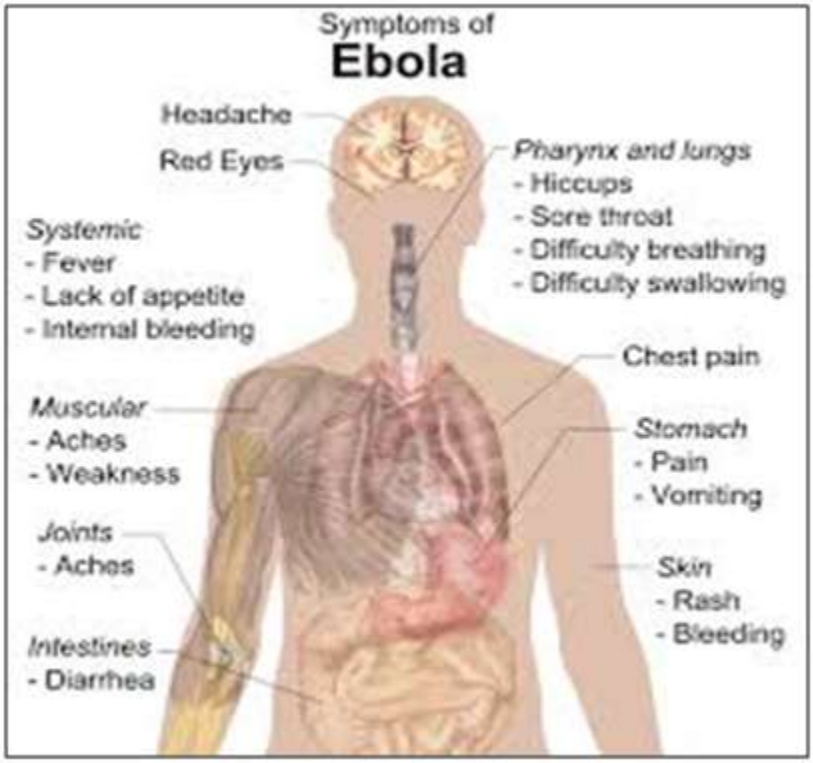

FIG: SIGN AND SYMPTOMS

Include:
• Fever
• Severe headache
• Fatigue
• Muscle pain
• Weakness
• Diarrhea
• Vomiting

Fig:Stomach Pain

• Stomach pain
• Unexplained bleeding or bruising

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Diagnosis:

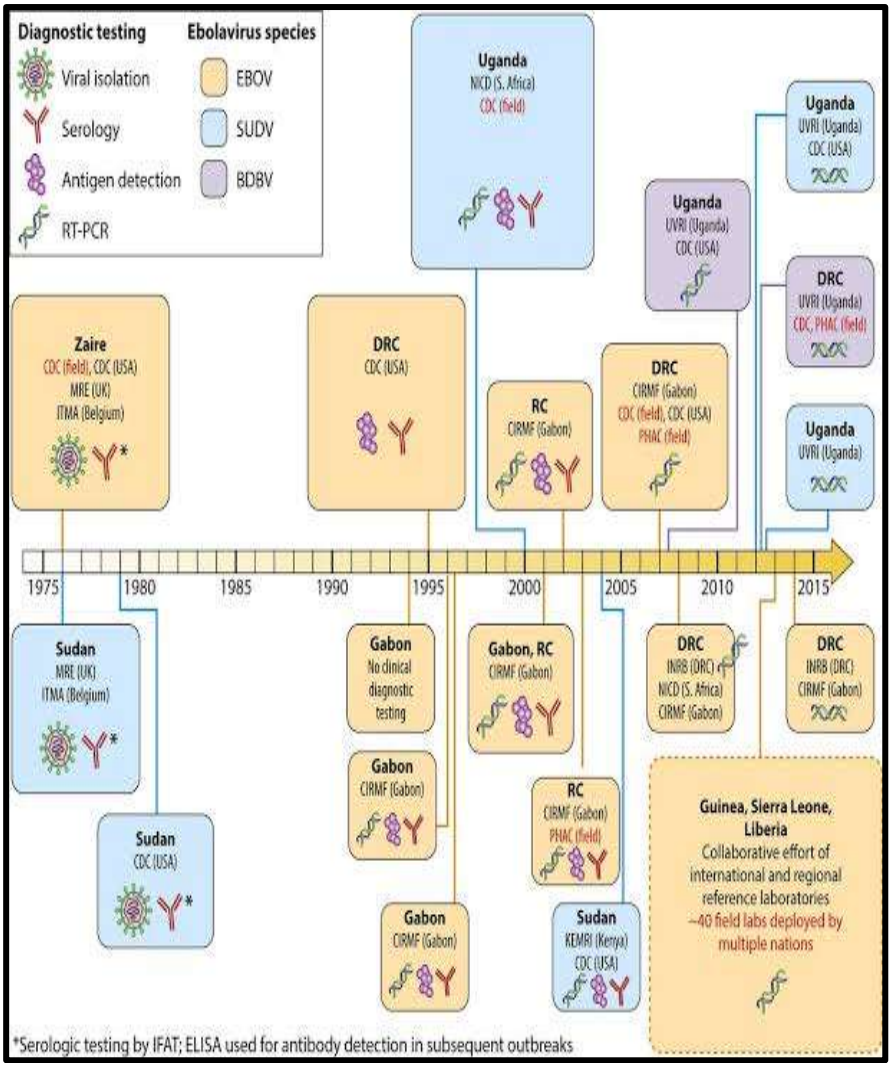

Fig:- DIAGNOSIS OF EBOLA VIRUS DISEASE: PAST, PRESENT, AND FUTURE

Early symptoms of EVD such as fever, headache, and weakness are not specific to Ebola virus infection and are seen in patients with more common diseases, like malaria and typhoid fever. To determine whether Ebola virus infection is a possible diagnosis, there must be a combination of
1) Symptoms suggestive of EVD AND
2) A possible exposure to the virus within 21 days before onset of symptoms.

If a person has early symptoms of EVD and there is reason to believe the virus should be considered, the patient should be isolated and public health professionals notified. Samples from the patient should be collected and tested to confirm infection.

Ebola virus can be detected in blood after onset of symptoms. It may take up to three days after symptoms start for the virus to reach detectable levels.

Treatment:

Symptoms of EVD are treated as they appear. When used early, basic interventions can significantly improve the chances of survival. These include:

- Providing fluids and electrolytes (body salts) through infusion into the vein (intravenously).
- Offering oxygen therapy to maintain oxygen status.
- Using medication to support blood pressure, reduce vomiting and diarrhea and to manage fever and pain.

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• Treating other infections if they occur.Recovery from EVD depends on supportive care and the patient's immune response. People who recover from EVD develop

Antibodies that can last for 10 years. It is not known if people who recover are immune for life or if they can become infected with a different species of Ebola virus. Some survivors may have long-term complications such as joint and vision problems.

There is currently no antiviral drug licensed by the U.S. Food and Drug Administration (FDA) to treat EVD in people. Drugs that are being developed to treat Ebola virus infection work by stopping the virus from making copyofitself.

Ebola Vaccine:

The U.S. Food and Drug Administration (FDA) approved the Ebola vaccine rVSV-ZEBOV (called Ervebo™) on December 19, 2019. This is the first FDA-approved vaccine for Ebola.

This vaccine is given as a single dose vaccine and has been found to be safe and protective against Zaire ebolavirus, which has caused the largest and most deadly Ebola outbreaks to dateOn February 26, 2020, the Advisory Committee on Immunization Practices (ACIP) recommended pre-exposure prophylaxis vaccination with rVSV-ZEBOV for adults ≥ 18 years of age in the U.S. population who are at potential occupational risk of exposure to Zaire ebolavirus. This recommendation includes adults who are

Responding or planning to respond to an outbreak of EVD;

Laboratorians or other staff working at biosafety-level 4 facilities that work with live Ebola virus in the United States.A two-dose vaccine regimen of a different vaccine that was also designed to protect against the Zaire ebolavirus species of Ebola was used under a research protocol in 2019 during an Ebola outbreak in the Democratic Republic of the Congo. The two doses of this vaccine use two different vaccine components (Ad26.ZEBOV and MVA-BN-Filo) and the regimen requires an initial dose and a "booster" dose 56 days later.

Fig: Ebola Vaccine

Prevention and controls:

When living in or traveling to a region affected by the Ebola virus, there are ways to protect yourself and prevent the spread of the virus. Practicing good hand hygiene is an effective method of preventing the spread of dangerous germs, like the Ebola

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Proper hand hygiene means washing hands often with soap and water or an alcohol-based hand sanitizer.While in an area affected by Ebola virus, you should AVOID:

• Contact with blood and body fluids (such as urine, feces, saliva, sweat, vomit, breast milk, semen, and vaginal fluids).

• Items that may have come in contact with an infected person's blood or body fluids (such as clothes, bedding, needles, and medical equipment).

• Funeral or burial rituals that require handling the body of someone who died from EVD.

• Contact with bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals (bushmeat) or meat from an unknown source.

• Contact with semen from a man who had EVD until you know the virus is gone from the semen.After returning from an area affected by Ebola virus, monitor your health for 21 days and seek medical care immediately if
you develop symptoms of EVD.

There is currently no vaccine licensed by the FDA to protect people from Ebola virus. However, an experimental vaccine, proven highly protective against the virus in trials, is currently approved for use during an outbreak while awaiting FDA approval.

Healthcare workers who may be exposed to people with EVD should:

• Wear appropriate personal protective equipment (PPE).

• Practice proper infection control and sterilization measures.

• Avoid direct contact with the bodies of people who have died from EVD.

Ebola virus disease (EVD) is a very rare disease caused by infection with Zaire ebolavirus, one of four types of the virus that is known to cause illness in people. It is believed to occur naturally in specific animal populations that live in multiple sub-Saharan African countries. In the areas of sub-Saharan Africa where EVD is most common, Ebola virus is believed to spread at low rates among certain animal populations. Occasionally people become sick with Ebola after coming into contact with infected animals, which can then lead to Ebola outbreaks being spread person-to-person. It has been brought to the United States on a small

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number of occasions by people who were infected in other countries; in one case, a patient with Ebola went on to spread the virus to two nurses who cared for him. To date, there have only been four cases of EVD diagnosed in the US.

When living in or traveling to a region where Ebola virus is potentially present, there are a number of ways to protect yourself and prevent the spread of EVD.

Avoid contact with blood and body fluids (such as urine, feces, saliva, sweat, vomit, breast milk, amniotic fluid, semen, and vaginal fluids) of people who are sick.Avoid contact with semen from a man who has recovered from EVD, until testing shows that the virus is gone from his semen.
Avoid contact with items that may have come in contact with an infected person's blood or body fluids (such as clothes, bedding, needles, and medical equipment).
Avoid funeral or burial practices that involve touching the body of someone who died from EVD or suspect EVD.

Avoid contact with bats, forest antelopes, and nonhuman primates (such as monkeys and chimpanzees) blood, fluids, or raw meat prepared from these or unknown animals (bushmeat).These same prevention methods should be used when living in or traveling to an area experiencing an Ebola outbreak. After returning from an area experiencing an Ebola outbreak, people should monitor their health for 21 days and seek medical care immediately if they develop symptoms of EVD.

Affected areas:

Due to the virus features, identifying the infected persons, isolating them and treating them in proper facilities can break the chain of human-to-human transmission, thus stopping further spread of the diseasein affected areas. The principle strategies to achieve the above are to:

• instruct community leaders about the disease, ways of transmission and how to protect against infection, and to engage them in communicating this information to community members
• Quickly identify and isolate suspected EVD cases for laboratory diagnosis confirmation and supportive treatment
• identify all contacts of each EVD case, actively monitor their health for the maximum incubation period of 21 days, and isolate, diagnose and treat all contacts who develop symptoms
• Minimise the risk of transmission in healthcare settings through the consistent and appropriate use of personal protective equipment (PPE) and handling of hospital waste
• ensure safe removals and burials of deceased EVD cases
• raise public awareness and promote adherence to protective behaviour.

More specifically, in order to prevent infection in communities, visitors and residents in EVD-affected areas,the following precautions are recommended to:

• avoid contact with symptomatic patients and their bodily fluids
• avoid contact with corpses and/or bodily fluids from deceased patients
• avoid contact with wild animals (including primates, monkeys, forest antelopes, rodents and bats), both alive and dead, and consumption of bush meat

Pathophysiology:

The pathophysiology or functional changes that accompany the single-stranded RNA Ebola virus is not fully understood; however, part of its pathogenesis has been elucidated. Studies have suggested that the virus enters the host through mucosal surfaces, breaks and abrasions in the skin, or by parenteral introduction; though recent reports suggest that it is by direct contact with infected patients or cadavers.

The organism has a broad cell tropism, which can infect a wide range of cell types. Studies in nonhuman primates have shown that fibroblasts, monocytes, dendritic cells, hepatocytes, macrophages, endothelial cells, adrenal cortical cells, as well as other cell types, have supportive features for the virus to replicate.

The Ebola genome codes for four virion structural proteins: VP30, VP35, nucleoprotein, and a polymerase protein. In addition, there is also VP40, glycoprotein and VP24 which is a three membrane associated protein within the virus. The surface glycoprotein is encoded in two frames: an open reading frame identified as OPF I and II. Open reading frame I encodes for a small, soluble, nonstructural secretory glycoprotein (sGP) that is readily detected in the serum of the infected hosts. This secretory glycoprotein binds to neutrophil CD16b, which is exclusively expressed by human neutrophils and binds IgG in immune complexes.

In other words, sGP is responsible for inhibiting early neutrophil activation and may also be responsible for the profound lymphopenia (a condition of having an abnormally low level of lymphocytes in the blood), a unique feature and

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characteristic of the Ebola infection. Thus, studies suggest that sGP plays a pivotal role in the ability of the virus to prevent an early and effective host immune response. In conjunction, there are other transmembrane glycoproteins, respectively referred to as GP1 and GP2 delta-peptide. These glycoproteins may also be incorporated into the Ebola virion.

The exact mechanism is not fully understood; however, it is thought that these transmembrane glycoproteins are responsible for binding to endothelial cells of an unknown cell receptor but not to neutrophils. Therefore, the Ebola virus is known to invade, replicate in, and destroy endothelial cells. Destruction of endothelial surfaces is associated with disseminated intravascular coagulation (DIC) and this may contribute to the hemorrhagic manifestations that are seen with late-stage Ebola infections. Clinical infection is associated with rapid and extensive viral replication in all tissues and accompanied by widespread and severe focal necrosis.

The characterization of filovirus pathogenesis and a thorough understanding of the cellular mechanism are relevant to demonstrate the effectiveness of new biological products for control and prevention of the disease. The flow chart depicts the pathogenesis of Ebola virus infection. The mode of infection can be divided into three phases. Phase I is characterized as the transfer of the virus from an animal carrying the virus to a human, usually via small cutaneous lesions and subsequently.

Human-to-human transmission. Phase II is denoted as the early symptomatic stage. The early symptomatic stage typically occurs between days four and ten and is the stage of infection where symptoms of viral illness appear and progressively move toward more advanced manifestations of the disease.

Phase III is representative of the advanced disease, with hemorrhagic manifestations, impaired immunity, and end-organ failure.

VII. DRUG USE IN EBOLA VIRUS

- **Antiviral Drugs**

There is currently no antiviral drug licensed by the U.S. Food and Drug Administration (FDA) to treat EVD in people.During the 2018 eastern Democratic Republic of the Congo outbreak, four investigational treatments were initially available to treat patients with confirmed Ebola. For two of those treatments, called regeneron (REGN-EB3) and mAb114, overall survival was much higher. These two antiviral drugs currently remain in use for patients with confirmed Ebola.Drugs that are being developed to treat EVD work by stopping the virus from making copies of itself.

Favipiravir (T-705)

I have amply discussed previously the potential of favipiravir for its broad-spectrum activity, that it shares with ribavirin, against a wide variety of both (−)RNA viruses [i.e. influenza (it has been approved in Japan for the treatment of influenza A virus infections), arena, bunya) and (+)RNA viruses (i.e. flavi, picorna, noro]. Hence, it is not surprising that it is also active against the filoviridae, in casu EBOV Structurally, favipiravir is closely related to ribavirin with which it shares a carboxamide (C–(O)–NH2) moiety. Perhaps, favipiravir could be considered as a more specific antiviral version of ribavirin; they are both targeted at the viral RNA polymerase, although ribavirin is principally targeted at the IMP dehydrogenase .

To be converted to its active metabolite, acting at the viral RNA polymerase, favipiravir should first be converted to its phosphoribosyl derivative and subsequently to the triphosphate before it could interact as a RNA polymerase inhibitor, principally in direct competition with GTP

It should be mentioned that VSV would serve as an adequate surrogate virus to judge the potential of favipiravir in the treatment of EBOV infections. An in vivo animal model for VSV infection in newborn mice has been described many years ago

Mechanism of action

The mechanism of action of favipiravir is novel compared to existing influenza antivirals that primarily prevent entry and exit of the virus from cells. The active favipiravir-RTP selectively inhibits RNA polymerase and prevents replication of the viral genome. There are several hypotheses as to how favipiravir-RTP interacts with RNA dependent RNA polymerase (RdRp). Some studies have shown that when favipiravir-RTP is incorporated into a nascent RNA strand, it prevents RNA strand elongation and viral proliferation. Studies have also found that the presence of purine analogs can reduce favipiravir's antiviral activity, suggesting competition between favipiravir-RTP and purine nucleosides for RdRp binding.

Although favipiravir was originally developed to treat influenza, the RdRp catalytic

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domain (favipiravir's primary target), is expected to be similar for other RNA viruses. This conserved RdRp catalytic domain contributes to favipiravir's broad-spectrum coverage.

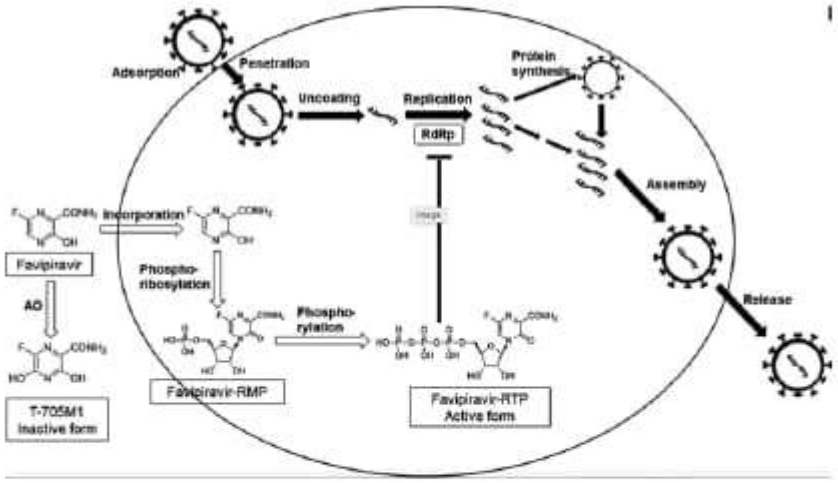

Figure 1: Mechanism of action of favipiravir (T-705) against the virus. Favipiravir is incorporated into cells and converted to favipiravir ibofuranosyl-5′-triphosphate (favipiravir-RTP) by host cells. The triphosphate form, favipiravir-RTP, inhibits the activity of RNA dependent RNA polymerase (RdRp) of RNA viruses. AO: Aldehyde Oxidase; RMP: Ribosyl Monophosphate.

VIII. CONCLUSION:-

Ebola response has yielded dramatic results. The number of people diagnosed with the virus has dropped markedly. Liberia was declared Ebola free on 9 May 2015. This progress is the result of remarkable contributions by numerous actors who have implemented their assistance in a flexible yet strategic manner. But, in April 2015, 30 people are still contracting.

Ebola every week, and we still don't know the causes of all new infections. The outbreak is not over and the response efforts must be sustained until we get to zero cases throughout the region and are able to stay at zero for several months.

At the time of writing, this outcome is not a foregone conclusion. The effects of Ebola go well beyond the thousands of lives lost to the disease. With increased unemployment and food insecurity, reduction of an already scarce health workforce and disruption to essential services such as primary healthcare and education, early recovery must be pursued alongside a meticulous and vigilant response. Services must be kept safe and implemented within a context of thorough and effective surveillance.

Health systems have been stretched to their limits by the outbreak, with a negative effect on maternity wards and reproductive health services as well as other non-Ebola services. Some health facilities closed all together, others were restricted to Ebola patients or offered very limited services. Birth registration and child vaccinations declined and many more services were affected.Many schools were closed with some being converted into ETUs, leaving approximately five million children out of school since the middle of 2014. This year, schools gradually reopened in the three most affected countries but some parents still fear sending their children to study, believing for instance that a child who survived Ebola can still infect others. On the road to recovery, overcoming stigma will be a decisive factor in rebuilding societies.

Survivors face rejection from their families andneighbors. Some have lost their job or their house. Many survivors have themselves been active in combating stigma but more work will be needed to ensure that Ebola survivors are not seen with fear.

The number of people falling below the

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poverty line is expected to increase by about 7.5% in Guinea, 14% in Sierra Leone and 17.5% in Liberia, compared with projections before the Ebola outbreak.40 At the end of last year, some 520,000 people were food insecure due to Ebola, and an estimated 1,235,000 people in the three most affected countries needed immediate assistance to protect their livelihoods and prevent malnutrition at the beginning of this year.

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