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Ebola – The Deadliest Viral Infection

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ABSTRACT

Ebola is the life threatening viral infection which was first time occurred in 1976 in the remote villages of central & west Africa. Ebolainfections occurred due to some native animals like fruit bats of family, “pteridopodidae” after that it come back by modifying itself with a new terrible face in 2014. As it is native host is animal, it is transmitted by direct contact with bodily fluids of infected animal or human beings. EVD (Ebola Virus Disease) shows very dangerous symptoms like bleeding from open orifices, kidney & liver damage, joint muscle pain and decreased level of WBCs. Because of bleeding it also called as Ebola Hemorrhagic Virus. As there is no any effective curative measures at present the individual should follow preventive measures to stay away from it. Infected patient can be treated by enhancing their immune system. Allopathic, Ayurvedic & Homeopathy systems of medicines are trying at their best to find out the medicine to combat the EVD. The object of this article is to throw a focus on this deadliest disease and to inspire our medicinal systems for developing an appropriate medicine & vaccine.

Keywords: EVD, Epidemic, Viral infection, Endemic, Pathogen.

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INTRODUCTION

Ebola virus disease (EVD) is a severe, often fatal illness in humans. EVD outbreaks have a case fatality rate of up to 90%. Ebola first appeared in 1976 in two simultaneous outbreaks, in Nzara, Sudan, and in Yambuku, Democratic Republic of Congo. The latter was in a village situated near the Ebola River, from which the disease takes its name. There are different species of the Ebola virus. Of these, the Reston Ebola virus was first discovered in laboratories in Reston, Virginia; however, it is of public health concern in the Asia-Pacific region because, although very rare, it is a newly emerging disease in animals and humans.

Geographical distribution EVD outbreaks occur primarily in remote villages in Central and West Africa, near tropical rainforests. The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. Human contact with infected fruit bats or monkeys/apes and the consumption of their raw meat leads to wild-life-to-human transmission of the virus. Human-to-human transmission is through direct or close contact with infected patients, and particularly through contact with blood and body fluids of an infected patient. Currently there is no vaccine or specific treatment for Ebola virus disease¹⁻⁴.

Virus:

Name : Ebola virus

Family : Filoviridae (Filovirus)

Order: Mononegavirales

Species: There are 5 species as follows,

- Bundibugyo Ebola virus (BDBV)
- Zaire Ebola virus (EBOV)
- Ebola virus disease
- Sudan Ebola virus (SUDV)
- Reston Ebola virus (RESTV).

Four of the five subtypes occur in an animal host native to Africa. BDBV, EBOV, and SUDV have been associated with large EVD outbreaks in Africa, whereas RESTV and TAFV have not. Pathogenicity varies among Ebola viruses, from EBOV, which is highly lethal in humans, to RESTV, which causes disease in pigs and macaques but asymptotically infects humans.

Reservoir Fruit bats of the Pteropodidae family are considered to be the natural host of the Ebola virus. 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. A recent study suggests

that bats might be a reservoir for Ebola virus in Bangladesh (Figure 1). The study found antibodies against Zaire and Reston Ebola viruses circulating in 3.5% of the 276 bats scientists screened in Bangladesh⁵⁻⁷.

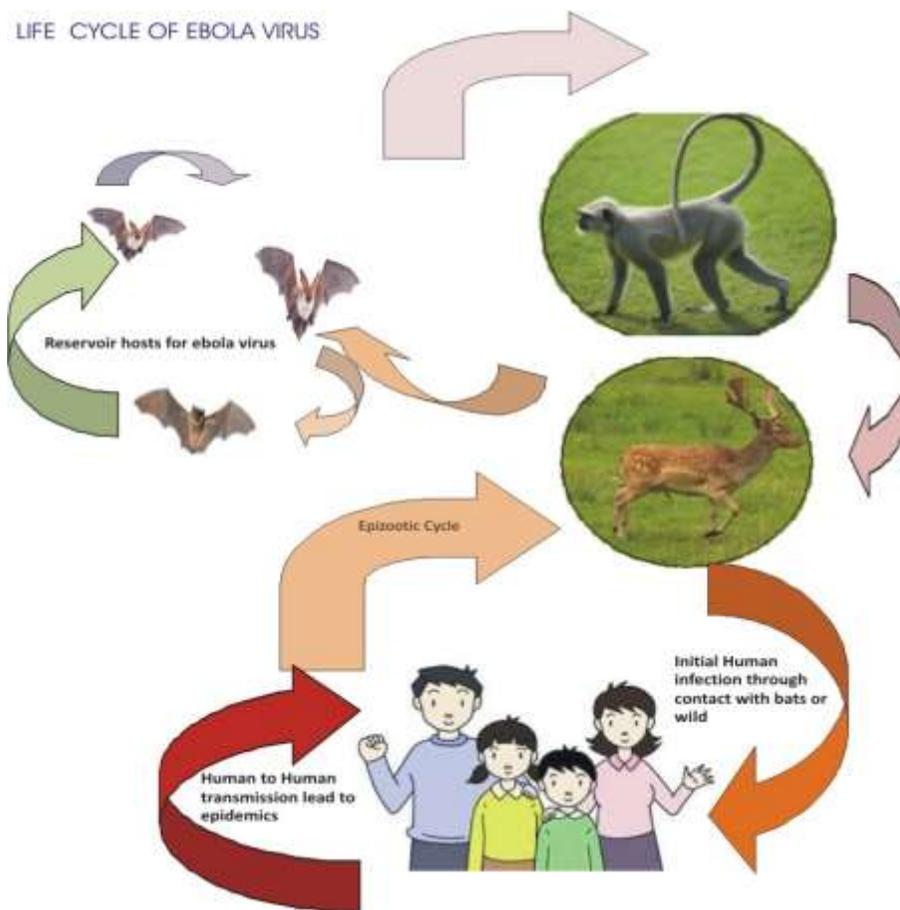


Figure 1: Life Cycle of Ebola Virus

Infection:

Ebola or Ebola Virus Disease (EVD) is viral infection spreads by coming in direct contact with the skin or bodily fluids of an infected animal like a monkey, chimp and fruit bat. Then it moves from person to other healthy person in the same way and kills up to 90% of people who are infected. Those who care for a sick person like nurses or physician, bury someone who died from the EVD often get infected immediately.

As the virus spreads through the body, it damages the immune system and organs. Ultimately, it causes levels of blood-clotting cells to drop. This leads to severe, uncontrollable bleeding.

The Ebola virus is not spread as easily as common viruses like colds or the flu. It is not spread through the air, or in water or food. There is no evidence that mosquitoes or other insects can spread the Ebola virus⁸.

The Ebola virus is spread through direct contact with

- Blood of infected person.
- Body fluid (like breast milk, saliva, stool, semen, urine, vomit) of a person infected with Ebola virus
- Virus contaminated Objectives (such as needle, syringe,).
- Visiting the places where Ebola outbreak occurred.
- Handling the dead body of Ebola infected person.

Signs & symptoms:

The signs & symptoms of Ebola disease is according to the exposure of individual to the infection causing parameters. There are two types of exposure,

- Primary exposure – This typically involves travel to or work in an Ebola-endemic area
- Secondary exposure – This refers to human-to-human exposure (e.g. medical caregivers, family caregivers, or persons who prepared deceased patients for burial), primate-to-human exposure (e.g. animal care workers who provide care for primates), or persons who collect or prepare bush meat for human consumption

Different Symptoms are seen at each stage of disease that is signs & symptoms are stage specific.

During early stage:

- Fever
- Pharyngitis
- Severe constitutional signs and symptoms
- Maculopapular rash (best seen in white patients)
- Bilateral conjunctival injection

During later stage:

- Expressionless faces
- Bleeding from intravenous (IV) puncture sites and mucous membranes
- Myocarditis and pulmonary edema
- In terminally ill patients, tachypnea, hypotension, anuria, and coma

C. Survivors of Ebola virus disease have developed the following late manifestations:

- Headache
- Fatigue
- Amenorrhea
- Hearing loss
- Tinnitus

- Unilateral orchitis

As the disease proceeds, the person starts feeling certain physiological changes in his body that are as follows,

- Bleeding from the mouth, ears, nose and ears.
- Increased sensitivity to pain on the skin,
- Genital swelling
- Conjunctivitis
- Rashes all over the body,
- And reddening of the roof of the mouth.

Diagnosis

Usually a doctor will be able to diagnose the condition with the symptoms alone, but in order to confirm the diagnosis he/she may prescribe tests like -

CBC (Complete Blood Count):

- Coagulation studies (a test to check for the amount of time a person's blood needs to clot)
- Complete blood count(CBC) with differential, bilirubin, liver enzymes, blood urea nitrogen (BUN), creatinine, pH
- Studies for isolating the virus – Tissue culture (only to be performed in one of a few high-containment laboratories throughout the world), reverse-transcription polymerase chain reaction (RT-PCR) assay
- Serologic testing – Enzyme-linked immunosorbent assay (ELISA) for antigens or for immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies
- Other studies – Immunochemical testing of postmortem skin, electron microscopy
- Liver function test

Demography:

Ebola virus disease was outbreak in West Africa in 1976 & once again it evoked in 2014 with very terrible face. The very large scale spreading of Ebola was found again in West Africa due to consumption of infected meat of fruit bat & via infected native animals in that region⁹. As in West Africa there is larger area under the forests the variety of animals have their native house in these forests. Because of these all suitable geographical factor Ebola virus spread over there with very fast rate. The area affected by EVD in West Africa & the species wise spreading of Ebola in different areas can be easily understood by following graphical data (Figure 2 and 3).

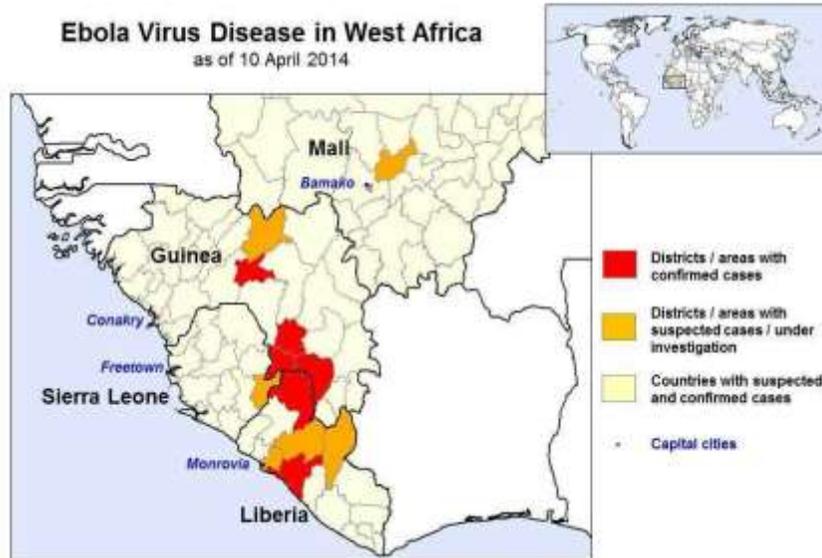


Figure 2: Ebola virus Disease in West Africa (Courtesy WHO data 10/04/2014)

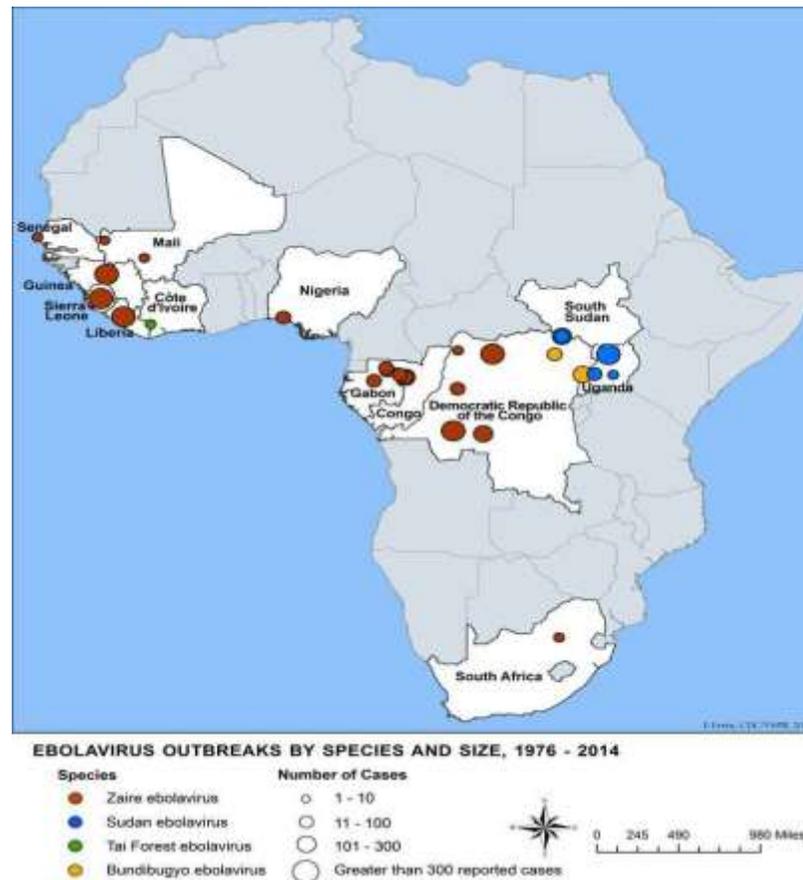


Figure 3: Ebola virus Disease species wise (Courtesy WHO data 10/04/2014)

Common viral infections:

There are various viral infections which are there in the community from ancient period & day by day viruses are modifying themselves & rising their head with new threatening makeup. So as the

human going on finding the cure on existing one the another threatening one stands again him as a challenge. Thus the virus study, incubation period and effect should be clearly & carefully studied. There are different common viral diseases like Malaria, Chicken pox, Dengue, Measles, Pertussis, Influenza, Hepatitis C, HIV, SAR, Tuberculosis etc. But nowadays the EBOLA is one of the dangerous disease standing in front of us with a very cruel face! As compared to other viral diseases EVD is threatening the life as there is no any specific vaccine or medicinal treatment on this.

Bye comparing the common viral diseases & EVD we can get idea about its severity (Figure 4 &5).

 DIRECT CONTACT WITH BODILY FLUIDS	 AIRBORNE	 VECTOR-BORNE (mosquito)
Ebola Hepatitis C HIV	Influenza Measles Pertussis SARS Tuberculosis	Malaria

Figure 4: Transmisson Pathway of Ebola and other infectious diseases

	VACCINE	TREATMENT	CURE
Ebola	NO	NO	NO
Measles		NO	NO
Pertussis			
HIV	NO		NO
Influenza - Seasonal			NO

Figure 5: Treatment measures available for Ebola and other infectious diseases

Risk associated with Ebola infection:

For most people, the risk of being infected with the Ebola virus is extremely low. The risk is increased if you:

- Travel to an area where Ebola virus outbreaks have occurred
- Help take care of someone infected with the Ebola virus
- Have direct contact with the dead body of a person infected with the Ebola virus. An infected body can still spread the virus.

High risk includes:**Any Country:**

Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen¹) from a person with Ebola who has symptoms

Direct contact with a person with Ebola who has symptoms, or the person's body fluids, while not wearing appropriate personal protective equipment (PPE)

Laboratory processing of blood or body fluids from a person with Ebola who has symptoms while not wearing appropriate PPE or without using standard biosafety precautions

Providing direct care to a person showing symptoms of Ebola in a household setting

In countries with widespread transmission or cases in urban settings with uncertain control measures:

Direct contact with a dead body while not wearing appropriate PPE.

Low (but not zero) risk includes any of the following:**In any country:**

- Brief direct contact (such as shaking hands) with a person in the early stages of Ebola, while not wearing appropriate PPE. Early signs can include fever, fatigue, or headache.
- Brief proximity with a person with Ebola who has symptoms (such as being in the same room, but not in close contact) while not wearing appropriate PPE
- Laboratory processing of blood or body fluids from a person with Ebola who has symptoms while wearing appropriate PPE and using standard biosafety precautions
- Traveling on an airplane with a person with Ebola who has symptoms and having had no identified *some* or *high* risk exposures

In countries with widespread transmission, cases in urban settings with uncertain control measures, or former widespread transmission and current, established control measures

- Having been in one of these countries and having had no known exposures

- Direct contact with a person with Ebola who has symptoms, or the person's body fluids, while wearing appropriate PPE
- Being in the patient-care area of an Ebola treatment unit

No identifiable risk includes any of the following:

- Laboratory processing of Ebola-containing specimens in a Biosafety Level for facility
- Any contact with a person who isn't showing symptoms of Ebola, even if the person had potential exposure to Ebola virus
- Contact with a person with Ebola before the person developed symptoms
- Any potential exposure to Ebola virus that occurred more than 21 days previously
- Having been in a country with Ebola cases, but without widespread transmission, cases in urban settings with uncertain control measures, or former widespread transmission and now established control measures, and not having had any other exposures
- Having stayed on or very close to an airplane or ship (for example, to inspect the outside of the ship or plane or to load or unload supplies) during the entire time that the airplane or ship was in a country with widespread transmission or a country with cases in urban

TREATMENT AVAILABLE:

Though there is no any specific vaccine or curative treatment available on EVD, the different medicinal systems have tried different therapies and medicine for the treatment. The different medicinal systems proposed different treatment according to their studies & practices as described below.

Allopathy:

Allopathic, as the most widely used medicinal system, proposed different treatment parameters by studying the viral mechanism, patient's physiology & symptoms shown by the victim. Along with actual drug therapy this system also provides treatment on specific symptoms to provide symptomatic relief to the patient¹⁰⁻¹⁵.

The different drugs & therapies:

- Ant diarrheal & antiemetic for prevention of volume depletion because of vomiting & diarrhea.
- Electrolyte replenisher to balance the decreased electrolyte ions.(given by I.V. or Oral route)
- Antipyretics to decrease the body temperature of patient (such as Acetaminophen)
- Analgesics for reducing the pain in critical conditions.
- Anti-motility agent are given to control the diarrhea & indirectly fluid loss by it.(loperamide)
- Antiepileptic medication to prevent the seizures in critical patients.

- Blood products like packed red blood cells, platelets, fresh frozen plasmatic. Are also administered according to need.
- Total parental nutrition (TPN) is also given to bed ridden hospitalized patients.
- Renal replacement therapy like dialysis is done in critical cases.

So along with these general medicinal therapies the actual drug therapy & their mechanism are as follows:

Actual drug therapy:

- Favipiravir & Brincidifovir –shows anti Ebola virus activity which is checked on cell culture.
- The specific analogues of above two drugs are used because of their specific action as follows,
 - a. Favipiravir (T705, Avigan)– RNA Replication inhibitor
 - b. Brincidifovir (CMX001) – Acyclic nucleotide analogue
 - c. BCX 4430 – Viral RNA polymerase inhibitor.
 - d. TKM Ebola
 - e. ZMapp- design to cultivate at large quantity in tobacco plant

So this is all about Allopathy system & its treatment measures. But none of the antiviral agent has shown 100% result against EVD yet.

Ayurveda:

This system curtails & cures Ebola virus infection by simple & inexpensive way. This therapy consist of a precursor of a vaccine which contains production of autoantibody within the body of infected patient the therapy also called as Auto Urine Therapy (AUT) i.e. the infected person drinking his or her own urine as a medicine¹⁶⁻¹⁷.

Steps involved in AUT:

The first day –

Start drinking all the urine that comes out, no matter what the condition of patient is!If the patient is hesitating to do that then use the Naso-gastric feeding tube to feed the urine to the patientCollect the urine in the clean glass container as soon as it is evacuated from bladder through urethra & immediately feed to patient.Do not change the taste or save to drink later.

The next day –

Feed all the urine that comes out in the morning then at afternoon & before going to bed. Follow the urine therapy with the help of water

The third day –

Drink the urine all morning & after mid afternoon

The fourth day –

Drink the urine all morning and then continue the drinking of urine at morning for 11 more days. So this is the procedure of AUT therapy. The ayurvedic physician claimed that this method is very effective & enhances immune system of patient against the disease.

Cultural differences and presence of metabolic waste products in urine make the method scientifically unacceptable

Homeopathic:

Homeopathy is a system of medicine which works on principle of “*like cures like*” (similia similibus curanter) so homeopathic physicians also tried to cure the EVD by this principle .By this principle they concluded that poison kills poison so they claimed that snake venom is the best remedy for EVD¹⁸.

Homeopathic physician also practiced for the same on laboratory level and found some positive results but they were disapproved by government so they could not invent further medicine or exact treatment.

Snake venom and other remedies used for treatment of EVD are:

Crotalushorridus (rattle snake venom)

- Bothrops (yellow viper venom)
- Lachasis (bushmaster snake)
- Phosphorus
- Mercury.

According to Homeopathic experts so far best probability is crotalushorridus with 397.2 points with confidence rating of 81 points.

Yoga

It does not have any curative treatment for Ebola virus disease but it helps to empower the immune system of the patient as Ebola virus directly attack on immune system of patient¹⁹.

General treatment measures:

- Supportive & caring treatment should be given by the trained physician only.
- Multidisciplinary treatment should be given
- Prevent intravascular fluid volume depletion
- Correct the electrolyte abnormalities by electrolyte replenished.
- Avoid complications of shock (hypovolemic shock)
- The use of non-invasive mechanical ventilation or high-flow oxygen therapy (e.g., Vapotherm)

Global Statistical analysis of infection:

The Ebola outbreak in West Africa was first reported in March 2014, and rapidly became the deadliest occurrence of the disease since its discovery in 1976. In fact, the epidemic killed five times more than all other known Ebola outbreaks combined²⁰⁻²².

More than 21 months on from the first confirmed case recorded on 23 March 2014, 11,315 people have been reported as having died from the disease in six countries; Liberia, Guinea, Sierra Leone, Nigeria, the US and Mali. The total number of reported cases is about 28,637.

But on 13 January, 2016, the World Health Organization declared the last of the countries affected, Liberia, to be Ebola-free.

Death records as per WHO:

According to World Health Organization 11,315 Deaths were confirmed and suspected up to 13 January 2016.

This Includes one in the US and six in Mali.

Total analytical data of death occurred by EVD in year 2014 to 2016 in different places in West Africa.

- 4,809 Liberia
- 3,955 Sierra Leone
- 2,536 Guinea
- 8 Nigeria

Ebola in India:

As per Indian statistical information is considered there are no evidence of Ebola virus disease patient in India. The Indian government has taken lot of efforts to stay away from EVD. The persons residing in Africa were not allowed to enter country without their medical examination²³⁻²⁴.

Preventive measures:

- Avoid visiting to Ebola outbreak places & area under danger zone
- The healthcare worker who comes in contact with EVD patients must use the Personal Protecting Equipment (PPE)
- Repeated trainings of healthcare workers for maintaining precautions during handling of victims & use of PPE should be taken.
- The sterilized PPE should be used & must be decontaminated after each use.
- Avoid eating animal meat like fruit bat etc.

- Avoid direct contact with bodily fluids of the Ebola infected person.
- The persons involving in burial process must protect himself from the dead body of EVD patient.
- Avoid sexual contact even after recovery of disease & if done then use the protections.
- The breast feeding mothers should stop that & stay away from her infant if she found to be positive towards the test.
- The pregnant women have to take higher precaution as it affects the fetus directly.
- Follow the proper body hygiene programs for prevention of disease.



Figure 6: Preventive measures for Ebola diseases

Role of WHO in prevention and control of EVD

WHO along with one of the U.S. organization called as Centers for Disease Control & Prevention (CDC) plays an important role in the prevention & control of Ebola. CDC & WHO prepared & published so many guidelines & prevention programs to control the spreading of the EBOLA. The different programs & guidelines under this are as follows (Figure 6),

Infection Control Precaution Program:

CDC& WHO provides guidelines regarding measures needed to manage suspected or confirmed patient with Ebola virus. The guidelines include,

- Regarding isolation of hospitalized patients.
- Regarding proper hand hygiene programs
- Standard contact & droplet precaution program

Regarding use of PPE:

CDC & WHO provides detail guidelines regarding the use of PPE. The healthcare worker must follow these guidelines regarding PPE who are in direct contact with suspected or confirmed patients. The guidelines are as follows,

- The proper 'Donning' (careful placement) & 'Doffing' (removal) procedures of PPE.
- Updates of additional infection control resources & general overview of infection updated on its own website which helps to physician.

Environmental Infection Control:

CDC& WHO provides guidelines for environment infection control which consist of following program,

- Medical waste management program.
- Environment infection control in hospitals, healthcare setting & laboratories.

Monitoring & travel restriction:

CDC & WHO provides guidelines for restriction on Travel & Transport of asymptomatic person who have been exposed to Ebola virus. The guideline for this is,

- Document on Travel & Transport risk assessment.

Regarding Breastfeeding & Infant Care:

CDC & WHO suggest that mother under investigation or with confirmed EVD avoid close contact (breast feeding to child) with her infants

Sexual Transmission Prevention:

CDC & WHO suggested that Ebola survivor refrains from sexual activities or if done then protective measures must be used.

WHO stated that the semen of infected male is said to testing after 3 months of onset of disease & tested by Reverse-Transcriptase polymerase chain reaction (RT-PCR). If the test comes negative for two subsequent testing then the person can be resumed his sexual activities.

Vaccines & treatment given by WHO:

During the Ebola outbreak in 2014 in West Africa, in September 2014 WHO identified only two candidate vaccines as the best to cure the EBOLA & these two vaccines are used for saving the life of that peoples. That the two vaccines are as follows,

- virus vesicular stomatitis (VSV)- vector encoding Ebola surface GP

- chimpanzee-adenovirus type 3 vaccine (ChAd3)- encoding Ebola virus GP

So these two vaccines were used to save the life of people recommended by WHO.

WHO continues to track the evolving infectious disease situation, sound the alarm when needed, share expertise, and mount the kind of response needed to protect populations from the consequences of epidemics, whatever and wherever might be their origin.

- Epidemic intelligence - systematic event detection
- Event verification
- Information management and dissemination
- Real time alert
- Coordinated rapid outbreak response

International Health Regulations (IHR) – Operational aspects:

The International Health Regulations (2005) or "IHR (2005)" have been in force since 15 June 2007. The purpose and scope of the IHR (2005) are to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade. The IHR (2005) provide a framework for WHO epidemic alert and rapid response activities already being implemented in collaboration with countries to control international outbreaks and to strengthen international public health security.

The IHR (2005) introduce new operational concepts including:

- Specific procedures for disease surveillance, notification and reporting of public health events and risks to WHO by countries
- Requests by WHO for verification of public health events occurring within countries
- Rapid collaborative risk assessment with and assistance to countries
- Determinations as to whether an event constitutes a public health emergency of international concern
- Coordination of international response

Comprehensive event management for international outbreak alert and response:

Epidemiological data and operational information about outbreaks is dynamic and changes rapidly. WHO has developed a comprehensive “event management system” to manage critical information about outbreaks and ensure accurate and timely communications between key international public health professionals, including WHO Regional Offices, Country Offices, collaborating centers and partners in the Global Outbreak Alert and Response Network.

Features of the event management system include:

- Comprehensive databases on epidemic intelligence, verification status, laboratory investigation and operational information.
- Tracking and recording outbreak history, critical decisions, important actions by WHO and partners and key documents.
- Management of logistic support and specialized response equipment, materials and supplies.
- Integrated database on the skills, experience and availability of international experts for response teams. S
- Profiling of technical institutions in the Global Outbreak Alert and Response Network concentrating on readiness and capacity to support international outbreak response.
- Standardized information products for Member States, public health officials, media and the public.
- Communications with the Global Outbreak Alert and Response Network to enhance operational readiness.

The WHO event management system generates a dynamic picture of Alert and Response Operations and provides information for action in a systematic way to enable both WHO and the Global Outbreak Alert and Response Network to prepare better, respond faster, and manage resources more effectively. The WHO event management system is being further strengthened to support alert and response operational aspects of the revised International Health Regulations.

Responding to intentional use of biological agents:

WHO's global alert and response activities and the Outbreak Alert and Response Network represent a major pillar of global health security aimed at the detection, verification and containment of epidemics. In the event of the intentional release of a biological agent these activities would be vital to effective international containment efforts.

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