

AR_{VIEW}

Ebola virus disease with special reference to epidemiology and management

■ CHANDRA SHEKHAR

AUTHOR FOR CORRESPONDENCE :

CHANDRA SHEKHAR
Department of Veterinary Public Health and Epidemiology, College of Veterinary Science and Animal Husbandry, N.D. University of Agriculture and Technology, FAIZABAD (U.P.) INDIA
Email: cshekharvph@gmail.com

Abstract : *Ebola* virus disease (EVD) is a highly fatal viral zoonotic disease. The disease was first reported in Africa in 1976. Since then the disease outbreaks have occurred several times in different years. The disease is mainly found in African countries. The causative agent is *Ebola* virus which belongs to the family *Filoviridae*. The case fatality rate is around 50 per cent but in different outbreaks, it showed variations from 25 per cent to 90 per cent. Monkeys and chimpanzees are important reservoirs of *Ebola* virus. The virus is transmitted to people from wild animals. *Ebola* is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected wild animals such as chimpanzees, gorillas, fruit bats, monkeys etc. *Ebola* then spreads through human-to-human transmission via direct contact with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials contaminated with these fluids. The disease is characterized by fever, headache and myalgia, followed by diarrhoea, vomiting, abdominal symptoms and dehydration. Collapse, neurological manifestations and bleeding particularly in gastrointestinal tract may occur in the last phase of the disease. Community awareness is important in controlling the outbreaks of disease. The disease management involves case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilization. Early supportive care with rehydration, symptomatic treatment improves survival of affected person. No licensed vaccines are available yet, but 2 potential vaccines are undergoing human safety testing. cAd3-ZEBOV is a chimpanzee derived adenovirus vector with an *Ebola* virus gene inserted. rVSV-ZEBOV is an attenuated vesicular stomatitis virus with one of its genes replaced by an *Ebola* virus gene. ZMapp is the best known emerging treatment so far. It is a combination of three humanised monoclonal antibodies targeted at three *Ebola* virus glycoprotein epitopes. Before the current 2014 outbreak, ZMapp had proved protective when given to non-human primates 24-48 hours after infection. TKM-Ebola is another drug consists of a combination of small interfering RNAs that target *Ebola* virus RNA polymerase L, formulated with lipid nanoparticle technology. It has been shown to be protective in non-human primates.

Key words : *Ebola* virus, Epidemiology, Current outbreaks, Transmission, Management

How to cite this paper : Shekhar, Chandra (2015). *Ebola* virus disease with special reference to epidemiology and management. *Vet. Sci. Res. J.*, 6(2) : 103-112.

Paper History : Received : 01.05.2015; Accepted : 28.09.2015

INTRODUCTION

Ebola virus disease (EVD), formerly known as *Ebola* hemorrhagic fever, is a severe, often fatal illness in

humans (Hensley *et al.*, 2010). The *Ebola* virus causes an acute, serious illness which is often fatal if untreated. *Ebola* virus disease (EVD) first appeared in Africa in 1976 in 2 simultaneous outbreaks, one in Nzara, Sudan, and the other in Yambuku, Democratic Republic of Congo. The latter occurred in a village near the *Ebola* river, from which the disease takes its name. All known epidemics have occurred as a result of nosocomial infections with unknown primary infections. Case fatality rate is high in human beings depending on the species of *Ebola* virus and quality of supportive care available (CDC, 2014). The disease is transmitted from wild animals to humans. The infection is also frequently transmitted from human to human.

Etiology:

The disease is caused by *Ebola* virus which belongs to the family *Filoviridae*. The *Filoviridae* includes 3 genera that are *Cueva* virus, *Marburg* virus and *Ebola* virus. There are 5 species that have been identified namely, Zaire, Bundibugyo, Sudan, Reston and Tai Forest (Haenninen, 2001). The first 3, Bundibugyo *Ebola* virus, Zaire *Ebola* virus and Sudan *Ebola* virus have been associated with large outbreaks in Africa. The virus causing the 2014 West African outbreak belongs to the Zaire species. The two important genera of *Filoviridae* are *Ebola* virus and *Marburg* virus. These are enveloped, single-stranded negative-sense RNA virions. Overall the virion is tubular in appearance, with a diameter of 80 nm but varying in length from 800 to several thousand nanometers and may sometimes have branched or ring structure. The surface spikes are 7 nm high. There are seven peptides associated with the virion including nucleoproteins, transcriptase and membrane proteins.

The virus genome consists of a single 19 kb strand of negative sense RNA with seven viral genes that are transcribed by the viral RNA dependent RNA polymerase present in the virion. The single strand of RNA is covered by helically arranged viral nucleoproteins NP and VP30, which are linked by matrix proteins VP24 and VP4 to the lipid bi-layer that coats the virion (Ramanan *et al.*, 2011). There is a minor antigenic overlap between *Ebola* and *Marburg* viruses. Maridi virus was isolated in 1976 which is distinct from *Ebola* virus (Jahrling *et al.*, 2003).

Epidemiology :

The first EVD outbreaks occurred in remote villages in Central Africa, near tropical rainforests, but the most recent outbreak in West Africa has involved major urban as well as rural areas. Human infection carries a high case fatality rate depending on the species of *Ebola* virus and quality of supportive care available (CDC, 2014 and Bah *et al.*, 2014). The average EVD case fatality rate is around 50 per cent. Case fatality rates have varied from 25 per cent to 90 per cent in past outbreaks. There are three distinct subtypes of *Ebola* virus which has been isolated from Africa. The strain Maridi was first time isolated from southern Sudan in 1976. Later on this strain was isolated from Gulu in 1979 and north-west Uganda in 2000. In these outbreaks the fatality rate has ranged from 32.5-65 per cent.

The Zaire subtype of *Ebola* virus originally isolated from a patient in Yambuku. Later on this subtype was reappeared in Kikwit in 1995. This subtype was also isolated from patients in several outbreaks in Gabon in the Democratic Republic of the Congo (formerly Zaire) and more recently from outbreaks in the Republic of Congo. In these outbreaks the fatality rates has ranged from 60-90 per cent. The third subtype Ivory Coast was isolated only in association with an outbreak in chimpanzees in the Tai forest in Ivory Coast (Le Guenno *et al.*, 1999). The fatality rate was high in chimpanzees. The fourth subtype Reston virus has been isolated from cynomolgus monkey in Reston during 1989-1990 and in Italy in 1991. This subtype has also been isolated in Philippines from monkey. It was the first subtype of Filovirus virus from outside of Africa. *Ebola* virus disease occurred in Democratic Republic of the Congo and Gabon in December 2001. Total 32 cases were reported with 72 per cent fatality rate. In these outbreaks the important sources of *Ebola* virus were monkey, chimpanzee and humans. However, the transmission cycle and reservoir of Filovirus have remained unknown. Monkeys were the source of human infection with Reston virus from the Philippines. In Africa, human infection with subtype Zaire and Ivory Coast were associated with fatal disease in chimpanzees. Monkeys are only known sources of Filovirus infection acquired by humans. However, they can hardly be reservoir of this infectious agent because of its high Filovirus pathogenicity in monkeys.

The current outbreak in West Africa, (first cases notified in March 2014), is the largest and most complex *Ebola* outbreak since the *Ebola* virus was first discovered in 1976. There have been more cases and deaths in this outbreak

Table 1 : Known cases and outbreaks of *Ebola* virus disease in reverse chronological order (CDC, 2015)-

Sr. No.	Year	Country	<i>Ebola</i> virus subtype	Reported number of human cases	Reported number (%) of deaths among cases
1.	Mar. 2014- April 2015	Guinea, Liberia, Sierra Leone	Ebola	25890	10717 (41%)
2.	Aug.-Nov. 2014	Democratic Republic of Congo	Ebola	66	49 (74%)
3.	Nov. 2012- Jan. 2013	Uganda	Sudan	6*	3* (50%)
4.	June-Nov. 2012	Democratic Republic of Congo	Bundibugyo	36	13* (36.1%)
5.	June-Oct. 2012	Uganda	Sudan	11*	4* (36.4%)
6.	May 2011	Uganda	Sudan	1	1 (100%)
7.	Dec. 2008- Feb. 2009	Democratic Republic of Congo	Zaire	32	15 (47%)
8.	Nov. 2008	Philippines	Reston	6	0 (0%)
9.	Dec. 2007- Jan. 2008	Uganda	Bundibugyo	149	37 (25%)
10.	2007	Democratic Republic of Congo	Zaire	264	187 (71%)
11.	2004	Russia	Zaire	1	1 (100%)
12.	2004	Sudan (South Sudan)	Sudan	17	7 (41%)
13.	Nov.-Dec. 2003	Republic of the Congo	Zaire	35	29 (83%)
14.	Dec. 2002- April 2003	Republic of the Congo	Zaire	143	128 (89%)
15.	Oct. 2001- Nov. 2002	Republic of the Congo	Zaire	57	43 (75%)
16.	Oct. 2001-March 2002	Gabon	Zaire	65	53 (82%)
17.	2000-2001	Uganda	Sudan	425	224 (53%)
18.	1996	Russia	Zaire	1	1 (100%)
19.	1996	Philippines	Reston	0	0 (0%)
20.	1996	USA	Reston	0	0 (0%)
21.	1996	South Africa	Zaire	2	1 (50%)
22.	Jan. 1996-July 1997	Gabon	Zaire	60	45 (75%)
23.	Jan.-April 1996	Gabon	Zaire	37	21 (57%)
24.	1995	Democratic Republic of Congo	Zaire	315	250 (81%)
25.	1994	Cote d' Ivoire (Ivory Coast)	Tai forest	1	0 (0%)
26.	1994	Gabon	Zaire	52	31 (60%)
27.	1992	Italy	Reston	0	0 (0%)
28.	1990	USA	Reston	4	0 (0%)
29.	1989	USA	Reston	0	0 (0%)
30.	1979	Sudan (South Sudan)	Sudan	34	22 (65%)
31.	1977	Zaire	Zaire	1	1 (100%)
32.	1976	England	Sudan	1	0 (0%)
33.	1976	Sudan (South Sudan)	Sudan	284	151 (53%)
34.	1976	Zaire	Zaire	318	280 (88%)

* Numbers reflect laboratory confirmed cases only

than all others combined. It has also spread between countries starting in Guinea then spreading across land borders to Sierra Leone and Liberia, by air (1 traveller only) to Nigeria, and by land (1 traveller) to Senegal. The most severely affected countries, Guinea, Sierra Leone and Liberia have very weak health systems, lacking human and infrastructural resources, having only recently emerged from long periods of conflict and instability. The *Ebola* outbreak has infected some 25,000 people and killed around 10,000 of them has also reduced vaccination coverage in Guinea, Liberia and Sierra Leone, as health facilities and staff focus on halting the outbreak (WHO, 2015). The details of current outbreaks of *Ebola* virus disease are given in the Table 2.

Transmission :

The virus is thought to be initially acquired by exposure to body fluids or tissue from infected animals, such as bats and non-human primates; however, the natural reservoir and mode of transmission to humans has not been confirmed (Peters and LeDuc, 1999; Feldmann and Geisbert, 2011). The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. It is thought that fruit bats of the Pteropodidae family are natural *Ebola* virus hosts. *Ebola* is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest. *Ebola* then spreads through human-to-human transmission *via* direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids.

Human to human transmission occurs through contact with body fluids from infected patients (Dowell, 1999). In early epidemics, the re-use of non-sterile injections was responsible for many healthcare associated transmissions (WHO, 1978). In a study of viral shedding in various body fluids, *Ebola* virus was isolated from saliva, breast milk, stool, tears, and semen up to 40 days after the onset of illness, (Emond *et al.*, 1977; Rowe *et al.*, 1999 and Bausch *et al.*, 2007). Virus may be found in urine during recovery and the duration of this phenomenon needs further study (Kreuels *et al.*, 2014).

Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD. This has occurred through close contact with patients when infection control precautions are not strictly practiced. Burial ceremonies in which mourners have direct contact with the body of the deceased person can also play a role in the transmission of *Ebola*. People remain infectious as long as their blood and body fluids, including semen and breast milk, contain the virus. Men who have recovered from the disease can still transmit the virus through their semen for up to 7 weeks after recovery from illness.

The epidemics of *Ebola* virus have occurred predominantly at the end of the rainy season. The role of arthropod vectors in transmission of *Ebola* virus has not been found. Disease transmission in cases has been found due to personal contact or contact with blood and accidental inoculation. In the Zaire epidemic during 1976, half of the cases were associated with transmission of this disease due to inoculation with reused needles in the hospital. Disease

Sr. No.	Country	Cases	Deaths
1.	Guinea	3515	2333
2.	Liberia	9862	4408
3.	Sierra Leone	12138	3831
4.	Mali	8	6
5.	Nigeria	20	8
6.	Senegal	1	0
7.	Spain	1	0
8.	UK	1	0
9.	USA	4	1
		Total = 25550	Total = 10587

transmission was also found due to bare hand contacts with deceased during burial rituals in Africa. In Gabon, the disease transmission has also been occurred on several occasions due to consumption of dead chimpanzees as food. This route of transmission has also been reported in recent epidemic in Republic of Congo.

An outbreak of *Ebola* virus hemorrhagic fever occurred during 2000 in Gulu, Uganda. Total 329 cases were reported in which the fatality rate was 32.5 per cent (WHO, 2000). Male patients should be reminded about importance of using condoms to prevent sexual transmission in three months after resolution of infection (Emond *et al.*, 1977 and Rowe *et al.*, 1999). Women should be advised not to breast feed during infection (Bausch *et al.*, 2007).

Clinical manifestations :

The incubation period after infection is usually 5-9 days, with a range of 1-21 days in 95 per cent or more of patients (WHO, 2014) and patients are not considered infectious until they develop symptoms. There are typically three phases of illness, starting with a few days of non-specific fever, headache and myalgia, followed by a gastrointestinal phase in which diarrhoea and vomiting, abdominal symptoms and dehydration are prominent. In the second week, the patient may recover or deteriorate, with a third phase of illness including collapse, neurological manifestations and bleeding, which is often fatal (Chertow *et al.*, 2014). Massive bleeding, typically in the gastrointestinal tract is usually seen only in fatal cases (Kortepeter *et al.*, 2011). Children present with similar symptoms to adults; however, younger children are reported to have more respiratory (such as cough and dyspnoea) and gastrointestinal symptoms, but less bleeding and neurological signs than adults (Mupere *et al.*, 2001 and Peacock *et al.*, 2014).

Other complications include acute kidney injury, hepatitis and pancreatitis (Ramanan *et al.*, 2011). An early antibody response, along with reduced lymphocyte depletion is associated with effective viral clearance and survival (Emond *et al.*, 1977). The development of shock is still not well understood. Many factors may contribute, including bacterial sepsis, possibly through gut translocation of bacteria; a direct effect of the virus; disseminated intravascular coagulation; and haemorrhage (Fletcher *et al.*, 2014). Late manifestations during convalescence are uncommon but include uveitis, orchitis, myelitis, parotitis, pancreatitis, hepatitis, psychosis, hearing loss and tinnitus (Bwaka *et al.*, 1999).

Hemorrhagic diathesis has been found in 75 per cent cases while maculopapular exanthema in 50 per cent cases (Baxter, 2000). Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes. The fatality rate varies according to the pathogenicity caused by different strains of the *Ebola* virus. Reston virus is not pathogenic for humans. Patients who die tend to develop clinical signs early on in the infection, with death, usually attributed to shock and multi-organ failure, typically occurring between days 6 and 16 (median 9 days) from symptom onset (Furuta *et al.*, 2009; Auffermann *et al.*, 2015 and Warren *et al.*, 2014).

Diagnosis:

The specimens of plasma, EDTA-treated blood, urine or liver and spleen of from deceased persons are suitable for detection of *Ebola* virus by following methods :

Microscopic examination :

Electron microscopy is useful for detection of *Ebola* virus.

Serological examination :

Ebola virus can be detected using antigen capture ELISA technique. A serological diagnosis based on IgM capture ELISA is superior to immunofluorescence towards the end of the first week of the disease. ELISA technique is used in epidemiological surveys.

Isolation :

Ebola virus can be isolated using cell culture (Vero cell clone E6).

RT-PCR technique :

There are considerable variations in the sequence of different African strains of *Ebola* virus. A highly conserved

sequence of GP gene was used by Haenninen as the target for the single-tube RT-PCR and nested PCR. RT-PCR has been found useful for the diagnosis in the suspected cases.

Note :

Samples from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions.

Disease management :

The disease management includes both the prevention and control. Community engagement is key to successfully controlling outbreaks of disease. Outbreaks of disease can be controlled by case management, surveillance and contact tracing, a good laboratory service, safe burials, social mobilization etc. There is as yet no licensed treatment proven to neutralize the virus but a range of blood, immunological and drug therapies are under development. Early supportive care with rehydration and symptomatic treatment improve survival. A range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. No licensed vaccines are available yet, but 2 potential vaccines are undergoing human safety testing. However, following measures can be adopted for management of *Ebola* virus disease.

Awareness :

Raising awareness of risk factors for *Ebola* infection and protective measures that individuals can take is an effective way to reduce human transmission.

Prevention of direct contact :

Health-care workers caring for patients with suspected or confirmed *Ebola* virus should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. When in close contact (within 1 meter) of patients with *Ebola* virus, health-care workers should wear face protection (a face shield or a medical mask and goggles), long-sleeved gown, and gloves (sterile gloves for some procedures). It is also important to prevent the virus transmission that may occur due direct contact during cremation of the person died of *Ebola* virus infection.

Reduction of wildlife-to-human transmission :

Reducing the risk of wildlife-to-human transmission from contact with infected fruit bats or monkeys/apes and the consumption of their raw meat. Animals should be handled with gloves and other appropriate protective clothing. Animal products (blood and meat) should be thoroughly cooked before consumption.

Reduction of human-to-human transmission :

Reducing the risk of human-to-human transmission from direct or close contact with people with *Ebola* symptoms, particularly with their body fluids. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.

Careful handling of samples :

Laboratory workers are also at risk. Samples taken from humans and animals for investigation of *Ebola* infection should be handled by trained staff and processed in suitably equipped laboratories. Safe handling of infected persons as well as infected materials is very important to prevent the spread of *Ebola* virus. Special precautions should be taken while handling or subjecting the specimen to centrifugation.

Outbreak containment measures :

These include prompt and safe burial of the dead, identifying people who may have been in contact with someone

infected with *Ebola* virus, monitoring the health of contacts for 21 days, the importance of separating the healthy from the sick to prevent further spread, the importance of good hygiene and maintaining a clean environment.

Biosafety measures :

Experimental work should be performed in biosafety level 4 laboratories. Specimens must be inactivated by fixation or by thermal (56 °C for 30 minutes) or chemical treatment before removing from the isolation ward.

Hygienic measures :

Health-care workers should always take standard precautions when caring for patients, regardless of their presumed diagnosis. These include basic hand hygiene, respiratory hygiene, use of personal protective equipment (to block splashes or other contact with infected materials), safe injection practices and safe burial practices.

Environmental measures :

Wear a full set of personal protective equipment (PPE) and heavy duty/rubber gloves when cleaning the environment and handling infectious waste. Environmental surfaces or objects contaminated with blood, other body fluids, secretions or excretions should be cleaned and disinfected as soon as possible using standard hospital detergents/disinfectants (Hoffman *et al.*, 2011). A 0.5 per cent chlorine solution or a solution containing 5000 ppm available free chlorine has been recommended by WHO (2010). The *Ebola* virus can be eliminated from the environment with heat, alcohol-based products and sodium hypochlorite (bleach) or calcium hypochlorite (bleaching powder) at appropriate concentrations. It is also susceptible to a wide range of commonly used disinfectants, including aldehydes, halogens, peroxides, phenolics and quaternary ammonium compounds.

Waste management :

Waste should be segregated at the point of generation to enable appropriate and safe handling. Ideally, waste should not be stored more than 24 hours before being destroyed. Sharp objects (e.g. needles, syringes, glass articles) and tubing that has been in contact with blood or body fluids should be placed inside puncture resistant waste containers. These should be located as close as practical to the patient care area where the items are used, similarly in laboratories. All solid, non-sharp, infectious waste should be collected using leak-proof waste bags in covered bins.

Vaccination :

Vaccines have been tested in the animals. The best protection has been found with a GP DNA vaccine followed by a booster inoculation of a recombinant GP. There are currently no licensed *Ebola* vaccines but 2 potential candidates are undergoing evaluation (Bishop, 2015 and WHO, 2014). cAd3-ZEBOV is a chimpanzee derived adenovirus vector with an *Ebola* virus gene inserted (Ledgerwood *et al.*, 2014). Trials are under way in the United Kingdom, United States, Switzerland and some African countries. rVSV-ZEBOV is an attenuated vesicular stomatitis virus with one of its genes replaced by an *Ebola* virus gene. Human trials have started in the US.

Treatment :

Contact tracing (family, friends, and work colleagues) is essential. People who have been exposed to *Ebola* virus within the past 21 days and who are asymptomatic need to be monitored for the duration of the incubation period with twice daily temperature readings to ensure rapid recognition of symptoms. If symptoms are detected immediate isolation is essential (CDC, 2014). Healthcare workers suspected of being infected should be isolated and treated in the same way as any other patient until a negative diagnosis is confirmed (WHO, 2014). The patients are symptomatically treated to control hemorrhagic diathesis, shock etc. Traumatic injury should be avoided that may result into extended hemorrhage. Fresh-blood transfusions are recommended to control the hemorrhagic diathesis under African conditions. Exchange transfusion should be strictly avoided.

Experimentally, filoviruses are susceptible to ribavirin and interferon. ZMapp is the best known emerging treatment so far. It is a combination of three humanised monoclonal antibodies targeted at three *Ebola* virus glycoprotein

epitopes and is engineered for expression in tobacco plants (Bishop, 2015 and Goodman, 2014). Before the current 2014 outbreak, ZMapp had proved protective when given to non-human primates 24-48 hours after infection. The drug could rescue non-human primates when treatment was started up to five days after infection (Qiu *et al.*, 2014). Another drug TKM-*Ebola* consists of a combination of small interfering RNAs that target *Ebola* virus RNA polymerase L, formulated with lipid nanoparticle technology. It has been shown to be protective in non-human primates and is effective against *Marburg* virus in guinea pigs and monkeys (Geisbert *et al.*, 2010; Choi and Croyle, 2013 and McCarthy, 2014).

General patient care in any health-care facility :

Strengthen and carefully apply standard precautions (WHO, 2007 and CDC, 2007) when providing care to all patients regardless of the signs and symptoms they present with. This is especially important because the initial manifestations of hemorrhagic fever may be non-specific. Hand hygiene is most important measure. Gloves should be worn for any contact with blood or body fluid. Medical mask and goggles or face shield should be used if there is any potential for splashes of blood or body fluids to the face, and cleaning of contaminated surfaces is paramount.

Direct patient care (for suspected or confirmed patients with haemorrhagic fever) :

Put suspected or confirmed cases in single isolation rooms with an adjoining dedicated toilet or latrine, showers, sink equipped with running water, soap and single-use towels, alcohol-based hand rub dispensers, stocks of personal protective equipment (PPE), stocks of medicines, good ventilation, screened windows etc. Make sure that there is at least 1 metre distance between patient beds. Ensure that clinical and non-clinical personnel are assigned exclusively to hemorrhagic fever patient care areas and that members of staff do not move freely between the hemorrhagic fever isolation areas and other clinical areas during the outbreak. Restrict all non-essential staff from hemorrhagic fever patient care areas. Stopping visitor access to the patient is preferred, but if this is not possible, limit their number to include only those necessary for the patient's well-being and care, such as a child's parent. Do not allow other visitors to enter the isolation rooms/areas and ensure that any visitors wishing to observe the patient do so from an adequate distance (approximately 3 metres). Ensure that all visitors use PPE and perform hand hygiene as recommended by WHO (2009) prior to entry into the isolation room/area. Ensure that all health workers (including aides and cleaners) wear PPE before entering isolation rooms/areas and having contacts with patients and/or the environment. Personal clothing should not be worn for working in the patient areas.

Carefully apply the precautions as recommended by CDC (2009) to avoid any possible unprotected direct contact with blood and body fluids when providing care to any patient with hemorrhagic fever, including suspected cases. Hand hygiene should be performed within the isolation rooms/areas every time it is needed according to the above indications during care to a patient, along with change of gloves. To perform hand hygiene, either use an alcohol-based hand-rub or soap and running water applying the correct technique recommended by WHO (2014). Eye protection (either goggles or face shield) in order to have the mucous membranes of their eyes, mouth and nose should be completely covered by PPE to prevent virus exposure.

Waterproof boots (e.g. rubber/ gum boots) should be worn by all health workers. Before exiting the isolation area, carefully remove and dispose of PPE into waste containers, following standardized procedures (WHO, 2014). Each patient should have exclusively dedicated injection and parenteral medication equipment which should be disposed of at the point of care. Syringes, needles or similar equipment should never be reused. Limit the use of needles and other sharp objects as much as possible. If the use of sharp objects cannot be avoided, ensure the precautions very strictly (WHO, 2010). Limit the use of phlebotomy and laboratory testing to the minimum necessary for essential diagnostic evaluation and patient care (WHO, 2014).

Conclusion :

Ebola virus disease (EVD) causes high mortality in humans. In humans, the disease outbreaks usually occur due to transmission of infection from wild animals. Human to human transmission of infection is also frequent. The disease is highly contagious in nature. Currently there are no licensed drugs for treatment as well as vaccines for

prevention of disease in humans. Therefore, the best strategy is to reduce the transmission of disease. In this regard the public awareness is extremely important in prevention of disease. Outbreaks of disease can be controlled by case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilization. Strict hygienic precautions must be adopted while handling the infected materials or persons. Suspected international travelers must be quarantined until they are proven as disease-free in order to prevent global spread of disease.

LITERATURE CITED

- Auffermann, W.F., Kraft, C.S., Vanairsdale, S., Lyon, G.M. and Tridandapani, S. (2015).** Radiographic imaging for patients with contagious infectious diseases: how to acquire chest radiographs of patients infected with the *Ebola* virus. *AJR Am J Roentgenol.*, **204**(1):44-48.
- Bah, E.I., Lamah, M.C., Fletcher, T., Jacob, S.T., Brett-Major, D.M. and Sall, A.A.(2014).** Clinical presentation of patients with Ebola virus disease in Conakry, Guinea. *N. Engl. J. Med.*, **372** (1): 40-47.
- Bausch, D.G., Towner, J.S., Dowell, S.F., Kaducu, F., Lukwiya, M. and Sanchez, A. (2007).** Assessment of the risk of *Ebola* virus transmission from bodily fluids and fomites. *J. Infect. Dis.*, **196** (2):142-147.
- Baxter, A.G. (2000).** Symptomless infection with *Ebola* virus. *Lancet.*, **355**: 2178-2179.
- Bishop, B.M. (2015).** Potential and emerging treatment options for *Ebola* virus disease. *Ann. Pharmacother.* **49** : 196–206.
- Bwaka, M.A., Bonnet, M.J., Calain, P., Colebunders, R., De Roo, A. and Guimard, Y. (1999).** *Ebola* hemorrhagic fever in Kikwit, Democratic Republic of the Congo: clinical observations in 103 patients. *J Infect Dis.*, **79** (1): 1-7.
- Chertow, D.S., Kleine, C., Edwards, J.K., Scaini, R., Giuliani, R. and Sprecher, A. (2014).** *Ebola* virus disease in West Africa-clinical manifestations and management. *N. Engl. J. Med.*, **371**: 2054-2057.
- Choi, J.H. and Croyle, M.A. (2013).** Emerging targets and novel approaches to *Ebola* virus prophylaxis and treatment. *BioDrugs.*, **27**: 565-583.
- Dowell, S.F., Mukunu, R., Ksiazek, T.G., Khan, A.S., Rollin, P.E. and Peters, C.J. (1999).** Transmission of *Ebola* hemorrhagic fever: a study of risk factors in family members, Kikwit, Democratic Republic of the Congo, 1995. Commission de Lutte contre les Epidémies à Kikwit. *J. Infect. Dis.*, **179** (1): 87-91.
- Emond, R.T., Evans, B., Bowen, E.T. and Lloyd, G. (1977).** A case of *Ebola* virus infection. *BMJ.*, **2**: 541-544.
- Feldmann, H. and Geisbert, T.W. (2011).** *Ebola* haemorrhagic fever. *Lancet.*, **377**: 849-62.
- Fletcher, T., Fowler, R.A. and Beeching, N.J. (2014).** Understanding organ dysfunction in *Ebola* virus disease. *Intensive Care Med.*, **40**: 1936-1939.
- Furuta, Y., Takahashi, K., Shiraki, K., Sakamoto, K., Smee, D.F. and Barnard, D.L (2009).** T-705 (favipiravir) and related compounds: Novel broad-spectrum inhibitors of RNA viral infections. *Antiviral. Res.*, **82**: 95-102.
- Geisbert, T.W., Lee, A.C., Robbins, M., Geisbert, J.B., Honko, A.N. and Sood, V. (2010).** Postexposure protection of non-human primates against a lethal *Ebola* virus challenge with RNA interference: A proof-of-concept study. *Lancet.*, **375**: 1896-1905.
- Goodman, J.L. (2014).** Studying “secret serums”: toward safe, effective *Ebola* treatments. *N. Engl. J. Med.*, **371**: 1086-1089.
- Haenninen, H.M. (2001).** Tai forest *Ebola* Project. Examination of arthropods for presence of Filovirus with the RT-PCR. Inaugural dissertation. Philipps-Universität Marburg, GERMANY
- Hensley, L.E., Wahl-Jensen, V., McCormick, J.B. and Rubins, K.H. (2010).** *Viral hemorrhagic fevers*. In: Cohen J, Powderly W, Opal S, eds. Infectious diseases. 3rd Ed. Mosby., 1231-1237.
- Hoffman, P.N., Bradley, C. and Ayliffe, G.A.J. (2011).** *Health protection agency (Great Britain)*. Disinfection in healthcare. 3rd Ed. Malden, Mass: Blackwell Pub. 2004.
- Jahrling, P.B., Nichol, S.T., Rollin, P.E. and Ksiazek, T.G. (2003).** Filoviruses and Arenaviruses, p.1570-1582. In: Murray, P.R., Baron, E.J., Jorgensen, J.H., Pfaller, M.A. and Tenover, R.H. (Ed.). *Manual of Clinical Microbiology*, 8th Ed., Vol. 2. ASM Press, WASHINGTON, D.C.
- Kortepeter, M.G., Bausch, D.G. and Bray, M. (2011).** Basic clinical and laboratory features of filoviral hemorrhagic fever. *J. Infect. Dis.*, **204** (3): 810-816.
- Kreuels, B., Wichmann, D., Emmerich, P., Schmidt-Chanasit, J., de Heer, G. and Kluge, S. (2014).** A case of severe *Ebola* virus infection complicated by gram-negative septicemia. *N. Engl. J. Med.*, published online 22 Oct.

Ledgerwood, J.E., DeZure, A.D., Stanley, D.A., Novik, L., Enama, M.E. and Berkowitz, N.M. (2014). Chimpanzee adenovirus vector *Ebola* vaccine - preliminary report. *N. Engl. J. Med.*, published online 26 Nov. doi:10.1056/NEJMoa1410863.

Le Guenno, Formenty, B.P. and Boesch. C. (1999). *Ebola* virus outbreak in the Ivory Coast and Liberia, 1994-1995. *Curr. Top. Microbiol. Immunol.*, **235**: 77-84.

McCarthy, M. (2014). US signs contract with ZMapp maker to accelerate development of the *Ebola* drug. *BMJ.*, **349**: 5488.

Mupere, E., Kaducu, O.F. and Yoti, Z. (2001). *Ebola* haemorrhagic fever among hospitalised children and adolescents in northern Uganda: epidemiologic and clinical observations. *Afr. HealthSci.*, **1**: 60-5.

Peacock, G., Uyeki, T.M. and Rasmussen, S.A. (2014). *Ebola* virus disease and children: what paediatric health care professionals need to know? *JAMA Pediatr.*, published online 17 Oct.

Peters, C.J. and LeDuc, J.W. (1999). An introduction to *Ebola*: the virus and the disease. *J. Infect. Dis.*, **179** (1) : 9-16.

Qiu, X., Wong, G., Audet, J., Bello, A., Fernando, L. and Alimonti, J.B. (2014). Reversion of advanced *Ebola* virus disease in nonhuman primates with ZMapp. *Nature.*, **514**: 47-53.

Ramanan, P., Shabman, R.S., Brown, C.S., Amarasinghe, G.K., Basler, C.F. and Leung, D.W. (2011). Filoviral immune evasion mechanisms. *Viruses.*, **3**: 1634-49.

Rowe, A.K., Bertolli, J., Khan, A.S., Mukunu, R., Muyembe-Tamfum, J.J. and Bressler, D. (1999). Clinical, virologic, and immunologic follow-up of convalescent *Ebola* hemorrhagic fever patients and their household contacts, Kikwit, Democratic Republic of the Congo. Commission de Lutte contre les Epidémies à Kikwit. *J. Infect. Dis.*, **179** (1): 28-35.

Warren, T.K., Wells, J., Panchal, R.G., Stuthman, K.S., Garza, N.L. and Van Tongeren, S.A. (2014). Protection against filovirus diseases by a novel broad-spectrum nucleoside analogue BCX4430. *Nature.*, **508**: 402-5.

WHO (1978). Report of an International Commission. *Ebola* haemorrhagic fever in Zaire, 1976. *Bull. World Health Organ.*, **56**: 271-93.

WHO (2000). *Ebola*, Uganda (update). *Wkly. Epidemiol. Rec.*, **75**: 369.

WHO (2014). WHO, Fact sheet N°103, Updated September 2014.

■ WEBLIOGRAPHY

CDC (2007). Guideline for isolation precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Centers for Disease Control and Prevention, Atlanta, GA. Available from: http://www.cdc.gov/HAI/prevent/prevent_pubs.html

CDC (2009). Guidance on personal protective equipment to be used by healthcare workers during management of patients with *Ebola* virus disease in US hospitals. Centers for Disease Control and Prevention, Atlanta, GA. Available from: <http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html>.

CDC (2014). Centers for Disease Control and Prevention. *Ebola fact sheet*. www.cdc.gov/

CDC (2015). Known cases and outbreaks of *Ebola* virus disease in reverse chronological order. Available from www.cdc.gov/vhf/ebola/outbreaks/history/chronology/html.

WHO (2007). Standard precautions in health care AIDE-MEMOIRE. WHO, Geneva, 2007. Available from: <http://www.who.int/csr/resources/publications/standardprecautions/en/>.

WHO (2009). Hand Hygiene Posters. World Health Organization, Geneva, 2009. Available from: http://www.who.int/gpsc/5may/tools/workplace_reminders/en/.

WHO (2010). WHO best practices for injections and related procedures toolkit. WHO Geneva, 2010; Available from: http://www.who.int/injection_safety/toolbox/9789241599252/en/.

WHO (2015). *Ebola* virus disease: Current Situation Report. Available from: <http://www.who.int/ebola/current-situation-report>. Updated up to 8th April 2015.


 ★ ★ ★ ★ ★ of Excellence ★ ★ ★ ★ ★