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Ebola Hemorrhagic Fever as Emerging Zoonotic Disease

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Abstract: Ebola hemorrhagic fever (EHF) is a severe, often-fatal, zoonotic viral disease in humans and nonhuman primates (monkeys, gorillas and chimpanzees) that has appeared sporadically since its initial recognition in 1976.Now the disease is emerging that cases are being reported in different regions of the world. The virus is one of two members of a family of RNA viruses called the Filoviridae. There are five identified subtypes of Ebola virus. Four of the five have caused disease in humans: Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast and Ebola-Bundibugyo. The fifth, Ebola-Reston, has caused disease in non-human primates, but not in humans. The disease causes hemorrhagic fever with high mortality rates. Filovirus epidemics have originated from Africa and now spreading to other continents. There is no reported case of the disease in Ethiopia. The virus is classified among the highest priority as bioterrorism agent. Contact with infected people or animal, secretions and sexual intercourse are the major ways of transmission. Symptoms characterizing EHF are unspecific in the first few days of the infection, making the virus even more dangerous. Infection is marked by initial signs of fever, fatigue, exhaustion, muscle aches and dizziness. As the disease progress bleeding under the skin, in internal organs and from the eyes, ears and mouth are seen. Patients with severe progressions of the disease express symptoms of shock, delirium, coma, seizures and nervous system malfunction. The Ebola virus is diagnosed by specific antigens detected in blood specimens, isolation of virus in cell cultures, or detection of IgM and IgG antibodies. ELISA tests are often used to diagnose the viruses. There is no effective treatment for Ebola. Infected patients are treated with general supportive therapy that replenishes intravenous fluids, maintains blood pressure and other bodily functions. There is no vaccine for the disease. Prevention and control is mainly based on appropriate precautions to break ways of transmission.

Key words: Ebola Hemorrhagic Fever · Filovirus · Emerging · Zoonotic

INTRODUCTION

As defined by the World Health Organization, zoonoses are “those diseases and infections which are naturally transmitted between vertebrate animals and man, with or without an arthropod intermediate”. Outbreaks of zoonotic diseases emerge either by apparently new agents or by known microorganisms that appear in areas or species in which the disease was previously unknown. New animal diseases with an unknown host spectrum are also included in this definition [1].

There are about1415 species of infectious organism known to be pathogenic to humans. Out of these, 868 (61%) are zoonotic, that is, they can be transmitted between humans and animals and 175pathogenic species are associated with diseases considered to be 'emerging'. Out of the emerging pathogens, 132 (75%) are zoonotic and overall, zoonotic pathogens are twice more likely to be associated with emerging diseases than non-zoonotic pathogens [2].

Zoonotic diseases represent one of the leading causes of illness and death from infectious disease. Worldwide, zoonotic diseases have a negative impact on commerce, travel and economies. In most developing countries, zoonotic diseases are of major public health significance and contribute to an already overburdened public health system. In industrialized nations, zoonotic diseases are of particular concern for at-risk groups such as the elderly, children, pregnant women and immuno-compromised individuals. The potential use of zoonotic pathogens as bioterrorism agents should be considered as well [1, 3].

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Table 1: Viruses in the family Filoviridae.

Genus or subgenus	Type species	Assumed source (s) of Infection	Geographical Occurrence
Genus Marburg virus	Marburg virus	Vervet monkeys (*Cercopithecus aethiops*)	East Africa
Genus Ebola virus	Ebola virus	Chimpanzees, Gorillas	Equatorial Africa
	Ebola virus Zaire	Chimpanzees (*Pan troglodytes)*	Republic of Congo,Gabon
	Ebola virus Maridi	Unknown	Sudan,Uganda
	Ebola virus Ivory cost	Chimpanzees	West Africa
Subgenus Reston virus	Reston virus	Java cynomolgus monkeys (*Macaca fascicularis)*	Southern Asia

Source: Hartmut *et al*. [10]

The epidemiologic characteristics of the coming decade will be a continuous foreground reprioritizing of diseases because of changes in the frequency and relative1 importance of various inconsistent risk factors and their responses to control. As certain factors become more common, related diseases will occur more frequently. Similarly, changes reducing other factors will in turn result in a lower incidence of other diseases and perhaps a relatively greater dependence on previously minor factors. The importance of viral evolutionary mechanisms and the emergence of new virulence factors encoded by bacteriophages, plasmids and transposons significantly affecting disease incidence is a matter of heated academic argument [4]. Scenarios that have or will increase the incidence of new zoonoses are international travel, increasing proportions and numbers of human and companion animal populations, water contamination, regional, transcontinental and international food industries, emerging specialist farms with exotic species and social engineering and human behavior [4,5].

EHF is an emerging zoonotic viral disease caused by the virus called Ebola virus grouped under the family Filoviridae. In humans, persons with illness caused by Filovirus infection usually have influenza likes symptoms, with subsequent disseminated intravascular coagulopathy (DIC) and often generalized bleeding from body orifices. Pathologically, there is early and sustained infection of the mononuclear phagocyte system. There is no cure or vaccine and treatment is symptomatic. The infections are transmitted by direct contact and all body fluids contain large amounts of the rapidly replicating virus. Nonhuman primates have introduced the virus into human populations, but the animals appear to be amplifiers rather than reservoirs of the disease [5]. Therefore, the objectives of this seminar paper are; to look at the general overview of the disease Ebola Hemorrhagic Fever and to assess the emergence and re-emergence of the disease and its zoonotic importance.

Etiology: Ebola belongs to a family of viruses entitled Filoviridae and is commonly classified under viruses causing viral hemorrhagic fever. The known causes of viral hemorrhagic fever include arena viruses, filoviruses, bunya viruses and flaviviruses. All virions classified as hemorrhagic are enveloped (covered) RNA viruses, whose survivals dependent on an animal reservoir [6].

Four varieties of Ebola virus are known to exist: Ebola Zaire (EBOZ), Ebola Sudan (EBOS), Ebola Reston (EBOR) and Ebola Ivory Coast. Ebola-Reston has caused disease in nonhuman primates, but not in humans [7]. Ebola virus, an elongated filamentous RNA virus can be as long as 0.70nm or longer. The virus was discovered in 1976 and named after the Ebola River in Zaire close to the location of the first cases [8].

Viruses within this family are characterized by enveloped, pleomorphic (filamentous) virions and a genome of single stranded molecule of negative-sense RNA. There are two major groups of filoviruses. Ebola and Marburg are related viruses. Viruses within these groups cause severe fatal disease of humans that are characterized as “hemorrhagic fever” because of the spectacular diseases they cause in affected humans. These viruses infect primates and can be adapted to laboratory animals [9].

Hemorrhagic fever viruses belong to different virus families and are extremely pathogenic although not high contagious. Ebola virus is best known as an agent in hospital-associated disease outbreaks in African hospitals [10]. The virions of the family Filoviridae are threadlike and very long(filo means threadlike).The virus is stable at room temperature and can resist desiccation; inactivated at 60°C for 30 minutes; infectivity greatly reduced or destroyed by UV light and gamma irradiation, lipid solvents, b-propiolactone, formaldehyde, sodium hypochlorite and phenolic disinfectants [11]. Both Marburg and Ebola viruses have several serotypes and all are African viruses, with the exception of Reston Ebola virus, which was traced to the Philippines. The natural histories, reservoirs and epidemiology’s of the viruses are largely unknown [12].

Genome of the Virus: Filoviridae have non-segmented single strand genome which are closely related to the genus Pneumovirus, Marburg virus and Ebola virus each

constitute a separate genus based on difference in their genome organization. Antigenically distant subtype of Ebola virus is Reston virus [.Samples from Sudan and Zaire have revealed the presence of a new virus, morphologically similar to Marburg virus but antigenically different [13].

Viruses in the family Filoviridae are mononegaviruses, which means they have an unsegmented genome with negative polarity. Based on the differences in the genetic make-up, there are two genera in this family: Marburg virus and Ebola virus. Marburg virus has seven gene products. Ebola virus has an additional soluble glycoprotein (sGP) which may be connected with the regulation of its pathogenicity. The 3` and 5` ends of the RNA are conserved and reveal a high degree of complementarity. Both viruses have a nucleocapsid protein gene at the 3` end of the genomic RNA [10]. Filovirus virions are characterized by having one molecule of single stranded; negative sense RNA, as well as their unique "U" shaped structures. The capsomer covered nucleocapsid is helicoid in shape [14].

Emergence of the Disease: An emerging viral disease is one that is newly recognized or newly evolved or that has occurred previously but shows an increase incidence or expansion in geographical, host or vector range. Constant changes in demographic, ecological and anthropogenic factors ensure that new and recurring diseases will continue to emerge, but virological and host determinants also contribute to the emergence of some viral diseases and the emergence of new diseases in particular [15].

The most important factors for emerging zoonotic diseases are the transportation of humans and animals to new areas, increased contact between animals and humans, changes in the environment and husbandry practices, a larger immuno-compromised population, increased recognition of diseases as zoonotic in origin and the discovery of new organisms not previously recognized [5].

There are multiple explanations for the emergence and reemergence of infectious diseases: Climate change, injudicious and widespread use of antimicrobials, bioterrorism (‘weaponization’ of pathogens), mobile human populations, environmental modification, human population encroachment on wilderness (vector populations, concentration of human populations, dispersal of vectors (and pathogens) through trade, transport, migration and immuno-compromised populations [16].

Table 2: Reports of Ebola Hemorrhagic Fever from 1976-2000

Year	Location	Total cases reported	Mortality (%)
1976	Zaire	318	88
1995	Zaire	315	81
1994	Ivory cost	2	0
1994	Gabon	44	64
1996	Gabon	37	57
1996	Gabon	60	75
1976	Maridi	284	53
1979	Maridi	34	65
2000	Uganda	329	32.5
2001	South Sudan	20	25
2003	Uganda	425	53
2007	DRC	249	73.5
2007	Uganda	49	28.6
2008	Uganda	149	24.8
2012	Uganda	24	70.8
2014	Guinea	236	70
2014	Liberia	22	63.6
Total	-	2597	54.4

Source: CDC and WHO report postings

Marburg and Ebola viruses are emerging viruses as they have newly appeared or are rapidly expanding their range with a corresponding increase in cases of disease. In general, there is no way to predict when or where the next important new zoonotic pathogen will emerge or what its ultimate importance might be. A pathogen might emerge as the cause of a geographically limited curiosity, intermittent disease outbreaks, or a new epidemic [3].

Epidemiology: Ebola Hemorrhagic Fever typically appears in sporadic outbreaks, usually spread within a health-care setting (a situation known as amplification). It is likely that sporadic, isolated cases occur as well, but go unrecognized [17].

The disease burden of Ebola in comparison to HIV/Malaria/TB is small.Total number of identified cases are less than 3000. There is increasing frequency of outbreaks in sub-Saharan Africa of which significant ongoing outbreaks in wild (endangered) non-human primate species (chimpanzees) [16].

The exact origin, locations and natural habitat (known as the "natural reservoir") of Ebola virus remain unknown. However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic (animal borne) with four of the five subtypes occurring in an animal host native to Africa. A similar host, most likely in the Philippines, is probably associated with the Ebola-Reston subtype, which was isolated from infected *cynomolgus* monkeys that were imported to the United States and Italy from the Philippines. The virus is not known to be native to other continents, such as North America [17].

Distribution: The known geographic range of primary Filovirus infection is in tropical Africa with the exception of Reston Ebola virus, which occurs in Philippines. The fact that the Ebola virus subtypes that have caused human disease episodes have been different from each other makes it clear that a common source transmission chain extending across sub-Saharan Africa is not the case rather distinct virus subtypes from each site of human disease episodes have been responsible [15].

Confirmed cases of Ebola HF have been reported in the Democratic Republic of the Congo, Gabon, Sudan, the Ivory Coast, Uganda and the Republic of the Congo. EHF typically appears in sporadic outbreaks, usually spread within a health-care setting. It is likely that sporadic, isolated cases occur as well, but go unrecognized [17].

Risk Factors: In a study among the post primary case-1patients, the most important risk factor was direct repeated contact with a sick person's body fluids, as occurs during the provision of care. As expected, the risk was higher when the exposure took place during the late stage of the disease at home. The risk was reduced when the patient stayed in hospitals, probably because of the use of gloves, even before strict barrier nursing was implemented. However, having washed the clothes of a sick person and having participated in the ritual hand washing during the funeral ceremony were significant risk factors [18].

There is a specific risk for healthcare workers, especially if involved in caring for Ebola hemorrhagic fever patients (e.g. volunteers). However, the level of precaution taken in such settings should effectively prevent the transmission of the disease. There is a risk of transmission through unprotected sexual contact with a patient that has recently recovered from the disease [19]. Women are mostly affected by disease because they process the bush-meat for conservation and meal preparation. They also mourn the dead with tendency to physical contact with corpse. Families of those who have been infected are stigmatized and smeared even long after the epidemic outbreak has been declared over [20].

Individuals considered at risk for Ebola hemorrhagic fever include persons with a travel history to sub-Saharan Africa, persons who have recently cared for infected patients and animal workers who have worked with primates infected with African-derived Ebola subtypes. In 2011, Uganda experienced a reemergence of the disease [21].

In the 1995 outbreak in Kikwit, DRC, infection rates were significantly lower in children than in adults. During this outbreak, only 27 (8.6%) of the 315 patients diagnosed with Ebola virus infection were aged 17 years or younger. This apparent sparing of children occurs even though 50% of the population of the DRC is younger than 16 years. Although definitive evidence is lacking, epidemiologic evidence suggests that children are less likely to come into direct contact with ill patients than adults are [17].

Ebola virus infection has no sexual predilection, but men and women differ with respect to the manner in which direct exposure occurs. Men, by the nature of their work exposure in forest and savanna regions, may be at increased risk of acquiring a primary infection from gathering "bush meat" (primate carcasses) for food, as well as an unknown vector or vectors. Evidence from Africa and the Philippines is compatible with bats being a principal vector of Ebola virus. Because women provide much of the direct care for ill family members and are involved in the preparation of the bodies of the deceased, they may be at increased risk of acquiring Ebola virus infection through their participation in these activities. However, men and women who are medical healthcare providers seem to share a high and equal risk of infection [5].

Because most cases of Ebola virus infection have occurred in sub-Saharan Africa, most patients have been black. However, no evidence exists for a specific racial predilection. During outbreaks of EHF, those at highest risk include health care workers and the family and friends of an infected individual. Health care workers in Africa should consult the Infection Control for Viral Hemorrhagic Fevers [6].

Source of Infection: The reservoir of the virus in nature is unknown. In studies conducted in Sudan and DRC the virus couldn't be isolated and antibodies couldn't be detected in more than 1,000 captured animals most of them being mammals [14].Nonhuman primates have introduced the virus into human populations, but the animals appear to be amplifiers rather than reservoirs of the disease.

Recent study suggests bats are reservoir for Ebola virus in Bangladesh. Experimentally infected fruit bats shown to replicate Ebolavirus without developing overt disease. Virus-specific antibody and genome RNA detected predominantly in Egyptian fruit bats (*Rousettus aegyptiacus*) in Gabon, Durba DRC, Kitaka Uganda and Python Cave, Uganda. Multiple virus isolates from Kitaka and Python caves [22].

Mortality: The mortality rate has been very high up to 80% with Marburg virus, 60%with Sudan Ebola virus and 90% with Zaire Ebola virus infections. Convalescence is slow and marked by prostration, weight loss and often by amnesia for the period of acute illness. Death is usually attributed to hypovolemic shock, sometimes accompanied by disseminated hemorrhage. Human infections with Reston Ebola virus have so far been subclinical [15].

Transmission: African-derived filovirus infections are characterized by transmission from an unknown host (possibly bats) to humans or nonhuman primates, presumably via direct contact with body fluids such as saliva or blood or other infected tissues. Evidence in nonhuman primates indicates that Sudan Ebola virus and Zaire Ebola virus may be transmitted by contact with mucous membranes, conjunctiva, pharyngeal and gastrointestinal (GI) surfaces; through small breaks in the skin; and, at least experimentally, by aerosol [23].

Dogs have been shown to acquire asymptomatic Ebola virus infections, possibly by contact with virus-laden droplets of urine, feces, or blood of unknown hosts. Of epidemiologic significance was the observation that sero-prevalence rates in dogs rose in a linear fashion as sampling approached areas of human cases, reaching as high as 31.8%. Thus, an increase in canine sero-prevalence may serve as an indicator of increasing Ebola virus circulation in primary vectors within specific geographical areas [15].

Human infection with African-derived strains has often occurred in caregivers (either family or medical) and in family members who have prepared dead relatives for burial. Late stages of Ebola virus disease are associated with the presence of large numbers of virions in body fluids, tissues and, especially, skin. Individuals who are exposed to patients infected with Ebola without proper barrier protection are at high risk of becoming infected [10].

A report from the DRC identified Ebola virus RNA in 100% of oral secretions from patients who had the viral RNA in their serum. Both serum and oral secretions were tested with reverse-transcriptase polymerase chain reaction (RT-PCR) assay. Thus, oral secretions may be capable of transmitting Ebola virus [18].

The first recorded outbreak occurred in 1976, in Yambuku, DRC, where 316 patients were infected. In the largest recorded urban outbreak to date (DRC, 1995; 318 cases), admission to a hospital greatly amplified the frequency of transmission. The lack of proper barrier protection and the use and reuse of contaminated medical equipment, especially needles and syringes, resulted in rapid nosocomial spread of infection. Only after adequate barrier protection and alteration in burial rituals were implemented was the outbreak contained [17].

Because the natural reservoir of Ebola viruses has not yet been proven, the manner in which the virus first appears in a human at the start of an outbreak is unknown. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal. When an infection does occur in humans, there are several ways in which the virus can be transmitted to others. These include, direct contact with the blood or secretions of an infected person, exposure to objects (such as needles) that have been contaminated with infected secretions [8].

The viruses that cause EHF are often spread through families and friends because they come in close contact with infectious secretions when caring for ill persons. During outbreaks of Ebola HF, the disease can spread quickly within health care settings (such as a clinic or hospital). Exposure to Ebola viruses can occur in health care settings where hospital staffs are not wearing appropriate protective equipment, such as masks, gowns and gloves. Proper cleaning and disposal of instruments, such as needles and syringes, is also important. If instruments are not disposable, they must be sterilized before being used again. Without adequate sterilization of the instruments, virus transmission can continue and amplify an outbreak [6].

Unlike Asian-derived Ebola virus (Reston Ebola virus, traced to a Philippine supplier of primates), African-derived species appear to be spread more often by direct contact than via the respiratory route. However, the Reston species has repeatedly been demonstrated to spread among nonhuman primates and possibly from primates to humans via the respiratory route. Fortunately, although the Reston species has been documented to be capable of infecting in humans, it does not appear to be pathogenic to humans [15].

Pathogenesis: Pathogenesis is the entry, primary replication, spread to target organs and establishment of infection in the target organs whereas virulence can be defined as the degree of pathogenicity of an infectious agent, indicated by case fatality rates and/or its ability to invade and damage tissues of the host. The process by which a pathogen replicates itself in the human host depends on cell-specific and organ-specific receptors, cell and tissue injury and host immunity and other defense factors [1].

Although poorly understood, it has been proposed that several mechanisms may be responsible for the pathophysiologic changes that make Marburg and Ebola infections so devastating. In several studies, necrosis of the parenchymal cells of the liver was correlated with the presence of large numbers of Ebola virions intarget cells. The high AST: ALT ratio combine with normal bilirubin also suggest the importance of extra-hepatic targets of infection. Endothelial cell infection and in-situ deposition of fibrin point to DIC. Increased endothelial permeability leading to extensive visceral effusions, pulmonary interstitial edema and renal tubular dis-function are important components of shock seen in Ebola infected patients. In infected primates, apart from the severe thrombocytopenia, the presence of agonists such as adenosine diphosphate renders the remaining platelets incapable of agglutination. After infection, human and nonhuman primates experience an early period of rapid viral multiplication that, in lethal cases, is associated with an ineffective immunologic response [8].

Acute infection of humans with Ebola, one principal etiologic agent of hemorrhagic fevers, often results in a paradoxical pattern of immune responses: early infection, characterized by an outpouring of inflammatory mediators such as TNF-á, IL-10 and IL-6, late stage infections, which are associated with poor immune responses. The mechanisms underlying these diverse outcomes are poorly understood. In particular, the role played by cells of the innate immune system, such as dendritic cells (DC), is not known [6].

Ebola viruses infect human monocyte-derived DC and impair their function. Monocyte-derived DC exposed to either virus fail to secrete pro-inflammatory cytokines, do not up-regulate co-stimulatory molecules and are poor stimulators of T cells. Ebola virus target DC to impair adaptive immunity [24].

Data from in vitro experiments and animal models suggest that Ebola infect macrophages and endothelial cells early in infection. Infection of these cell types, two principal players of the innate immune system, are believed to act as critical triggers for the rapid and uncontrolled secretion of inflammatory mediators, However, despite the systemic release of inflammatory mediators that occurs following infection with Ebola, severe orfatal diseases are often associated with a generalized suppression of adaptive immunity, as evidenced by the low specific antibody and poor cellular immunity [17].

Although a full understanding of Ebola virus disease must await further investigations, part of the pathogenesis has been elucidated. Clinical infection in human and nonhuman primates is associated with rapid and extensive viral replication in all tissues. Viral replication is accompanied by widespread and severe focal necrosis. The most severe necrosis occurs in the liver and this is associated with the formation of Councilman-like bodies similar to those seen in yellow fever. In fatal infections, the host's tissues and blood contain large numbers of Ebola virions and the tissues and body fluids are highly infectious [8].

While disseminated intravascular coagulation (DIC) is often viewed to be a prominent manifestation of Ebola virus infection in primates, the presence of DIC in human filoviral infections has been a controversial topic; cultural mores and logistical problems have hampered systematic studies [25].

Ebola in Humans: When the disease does manifest, clinical symptoms range from mild illness to swift and fatal conditions. The IP lasts about a week and onset is sudden with fever and headache. A large proportion of patients experience thoracic pain, diarrhea, vomiting, dry and sore throat and an erythematous maculo-papular eruption on the trunk, which rapidly spreads to other parts of the body and tends to become confluent. The erythema may not be noticed on dark-skinned individuals. Desquamation ensues after 3 or 4 days [14].

Four or five days after onset of the disease, patients develop extreme lethargy and changes in their mental state, gravely ill patients exhibit restlessness and confusion and then lapse in to a deep coma before they die [26].

The high fever continues for a week, after which it gradually subsides. Data from past cases show that more than 90% of the patients who died, as well as 48% of those who recovered had hemorrhagic symptoms. Among the latter, melena was the most common and hematemesis, epistaxis and bleeding in other organs and tissues were also frequently observed. Convalescence was slow and in some cases took up to two months. The hemorrhagic manifestations are less severe at the end of the outbreak than they are at the beginning [27].Pregnant women usually abort their fetus and have copious hemorrhaging. There are no known cases of human disease caused by the Reston strain of the virus [3].

Ebola virus outbreaks provide dreadful publicity for Tourism and Investment. Bush-meat is an essential component of Congolese eating habits, particularly in areas with highest risks for Ebola virus outbreaks. Hence, during outbreaks Government and international organization must provide for all the food which is imported from outside the area. However, inhabitants are not interested in alternatives to readily available traditional foods such as Gorilla or Chimpanzee meat as part of tradition and social maturation. Some traditional customs incite young men to hunt down apes and thereafter consume their heart to gain bravery and demonstrate hunting skills. During outbreaks women are not allowed go to the fields to maintain crops and fish [20].

Ebola in Animals: Non-human primates are in general highly susceptible to Filovirus infections. Large outbreaks of lethal Ebola virus infection have been reported in wild populations of gorillas (*Gorilla gorilla*) and chimpanzees (*genus pan*). In rhesus monkeys (*Macaca mulatta*), cynomolgus monkeys (*Macaca fascicularis*), African green monkeys (*Cercopithecus aethiops*) and baboons (*Papio species*) inoculated with Marburg virus or Zaire Ebola virus the incubation period of 4-6 days is followed by an abrupt onset of clinical disease marked by petechiae, ecchymosis, hemorrhagic pharyngitis, hematemesis, melena and prostration. Infection nearly always ends in death. The pathogenesis of filovirus infections is apparently similar in those non-human primates and humans. Mice and guinea pigs are not highly susceptible to field isolates of filoviruses but rodent adapted strains of the viruses do induce uniformly lethal disease and have been utilized for testing vaccines and therapeutic agents [15].

When inoculated experimentally in various monkey species, the Ebola virus causes severe disease characterized at first by fever and depression followed by diarrhea, petechiae, languor, shock and finally death [28].In the *Cynomolgus macaques* imported in to Italy and the United States from the Philippines, the infection caused by the Reston strain of the virus produced disease and a high case fatality rate. Antibodies have also been found in other old world primates [21]. The Sudan and Reston subtypes of Ebola virus are least pathogenic for primates and guinea pigs, killing only a fraction of animals inoculated with un-passaged virus. Serial passage increases the virulence of these viruses for these hosts [29].

Table 3: Laboratory tests used in diagnosis with respective time of infection

Timeline of Infection	Diagnostic Tests Available
Within a few days after symptoms begin	-Antigen capture ELISA testing
	-IgM ELISA
	-PCR
	Virus Isolation
Later in disease courseor after recovery	-IgM and IgG antibodies.
Retrospectively in diseased patients	-Immuno-histochemistry testing
	-PCR
	-Virus isolation

Source: CDC Ebola Hemorrhagic Fever factsheet, 2002

Diagnosis: The ability of diagnosing diseases both old and emerging, in humans and in animals often is overlooked. Basic anatomic pathology involves analyzing tissues from dead specimens, making observations, interpreting those findings and following up with histopathology studies of samples under a microscope. In recent years, the advent of molecular pathology has heightened the power of diagnostic pathology. Using such tools as immunohistochemistry, in situ hybridization and polymerase chain reaction (PCR) assays, pathologists now can identify the etiology, or cause of death, faster than ever before and, in many cases, where it would otherwise have been impossible. However, current disease surveillance systems, for human diseases and zoonoses alike, fail to make adequate use of diagnostic pathology [1].

Diagnosing EHF in an individual who has been infected only a few days is difficult because early symptoms, such as red eyes and a skin rash, are nonspecific to the virus and are seen in other patients with diseases that occur much more frequently. Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing, IgM ELISA, polymerase chain reaction (PCR) and virus isolation can be used to diagnose a case of EHF within a few days of the onset of symptoms. Persons tested later in the course of the disease or after recovery can be tested for IgM and IgG antibodies; the disease can also be diagnosed retrospectively in deceased patients by using immunohistochemistry testing, virus isolation, or PCR [17].

Treatment: There is no standard treatment for EHF. Patients receive supportive therapy. This consists of balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure and treating them for any complicating infections [17].

Treatment is symptomatic predominantly to preserve hemostasis and to control the hemorrhagic diathesis and shock. Fresh blood transfusions are recommended to control the hemorrhagic diathesis under African

conditions. Exchange transfusion should be strictly avoided. It has not yet been proven that hemodialysis is beneficial. Treatment with serum from recovered patients or Equine hyper-immune serum is recommended but has not yet been thoroughly tested. Experimentally, Filoviruses are susceptible to ribavirin and interferon. Replication of Filoviruses in cell culture can be inhibited by lysosomotropic agents' chloroquine and quinine [15].

Prevention and Control: Prevention measures should be directed above all toward avoiding inter-human transmission. It is necessary to isolate the patient and take immediate steps to institute strict containment nursing practices. In addition, all samples taken for diagnostic purposes, excreta and any other materials that may have been in contact with the patient should be regarded as infectious and handled and decontaminated using the appropriate procedures [28].

To prevent the spread of infection to their partners, males should not engage in sexual intercourse until three months after clinical recovery, or until semen is shown to be free of the virus [17]. The number of health workers assigned to the patients care should be restricted and all such individuals should be dually trained and provided with complete protective gear, including gowns, gloves, masks, goggles, caps and overshoes [29]. Deceased victims should be promptly cremated or buried, preferably in a plastic bag by persons wearing protective clothing [14].

The prevention of EHF in Africa presents many challenges. Because the identity and location of the natural reservoir of Ebola virus are unknown, there are few established primary prevention measures [17].

Current Status in Africa: In 1967, 31 cases of Hemorrhagic fever with seven deaths, occurred among laboratory workers in Germany and Yugoslavia who were processing kidneys from African green monkeys (Cercopithecus aethiops) that had been imported from Uganda [3].

In 1976, two severe epidemics of hemorrhagic fever occurred in Sudan and Zaire. The virus responsible was named Ebola virus after a river in Zaire. The outbreaks involved more than 500 cases and at least 400 deaths due to clinical hemorrhagic fever. Another epidemic occurred in Kikwit, Zaire in 1995. There were at least 315 identified cases with 80% mortality. The causative agent was the Zaire sub-type of Ebola virus. Outbreaks of EHF occurred in Uganda in 2000 and the DRC in 2003. The Ugandan epidemic was caused by the Sudan subtype; there were 425 cases with 53% deaths. The outbreak in 2003 was first recognized by a large number of dead gorillas and chimpanzees. It was caused by the Zaire subtype; of 143 human cases, 89% were fatal [30].

On February 27, 2001, Uganda was declared officially to be free of Ebola hemorrhagic fever, following a 42-day period, twice the maximum incubation period, during which no new cases had been reported. According to the World Health Organization (WHO), 20 cases, including 5 deaths, from Ebola hemorrhagic fever (EHF) have been reported from Yambio County in southern Sudan. On August 28, 2007, CDC was notified of cases of an unidentified disease in a remote area of Kasai Occidental Province in the Democratic Republic of Congo (DRC). The onset of the latest laboratory-confirmed case was on September 29, 2007. On October 1, 2007, the total of suspected cases was 249 with 183 deaths. On November 26, 2007, CDC received blood samples from the Ugandan Ministry of Health, taken from 20 of the 49 patients involved in an outbreak of an unknown illness in Bundibugyo district in western Uganda. Patients reported fever, enteritis and bleeding. Of the 49, 14 have died. Genetic sequencing of a small segment of viral RNA from samples indicated the presence of a previously unknown strain of Ebola virus. At the invitation of the Ugandan Ministry of Health, CDC, WHO, MSF and other collaborators deployed field investigators to the affected region; additionally, a laboratory was set up in Entebbe at the Uganda Virus Research Institute (UVRI). As the outbreak neared conclusion in January 2008, the total number of suspected cases was 149, with 37 deaths. On May 14, 2011, the Ugandan Ministry of Health informed the public that a patient with suspected Ebola Hemorrhagic fever died on May 6, 2011 in the Luwero district, Uganda. CDC-Uganda confirmed a positive Ebola virus test result from a blood sample taken from the patient. The quick diagnosis of Ebola virus was provided by the new CDC Viral Hemorrhagic Fever laboratory installed at the Uganda Viral Research Institute (UVRI) [31].

On July 28, 2012, the Uganda Ministry of Health reported an outbreak of Ebola Hemorrhagic Fever in the Kibaale District of Uganda. A total of 24 human cases (probable and confirmed only), 17 of which were fatal, were reported starting at the beginning of July. Laboratory tests of blood samples, conducted by the Uganda Virus Research Institute (UVRI) and the U.S. Centers for Disease Control and Prevention (CDC), confirmed Ebola virus in 11 patients, four of whom died. Reported numbers are subject to change [28-30].

On October 4, 2012, the Uganda Ministry of Health declared the outbreak ended. The DRC Ministry of Health has declared an end to the most recent Ebola outbreak in DRC's Province Orientale. The November 26 Press Release reports a final total of 77 cases, including 36 laboratory-confirmed cases, 17 probable and 24 suspect cases, with a total of 36 deaths. As of December 2, 2012, the Ugandan Ministry of Health reported 7 cumulative cases (probable and confirmed) of Ebola virus infection, including 4 deaths, in the Luwero District of central Uganda [30-31].

According to the World Health Organization (WHO), the Ministry of Health (MoH) of Guinea reported 236 probable and suspect cases, including 158 deaths on April 10, 2014. Of these suspect cases, 66 have been laboratory confirmed positive cases of Ebola hemorrhagic fever (EHF). One additional health care worker with clinical symptoms has been reported since April 7, increasing the total to 15 health care workers. All cases reported in Conakry (20) have been laboratory confirmed. Other districts with confirmed and suspected cases remain Guekedou, Macenta, Kissidougou, Dabola and Djingaraye. UNICEF of Liberia reported on April 9, 2014, 22 probable and suspect cases of EHF, including 14 deaths and 5 laboratory-confirmed cases. Four of these confirmed cases were reported from Lofa County and 1 from Margibi County according to WHO. Other Counties in Liberia under further investigation now include Bong, Nimba, Montserrado and for the first time, Grand Cape Mount County. Additional reports of suspect cases in Sierra Leone and Mali are under investigation [31].

CONCLUSION AND RECOMMENDATIONS

Ebola hemorrhagic fever is a severe viral disease caused by three of the four species of Ebola viruses, Epidemics occur when an infectious case-patient is introduced into a susceptible population. The first recognized epidemics occurred almost simultaneously in 1976 in southern Sudan and in a nearby region of the DRC. The major mode of transmission is within hospitals, especially in the early stages of the outbreaks. Person-to-person transmission also occurred outside the hospital setting, with numerous community acquired cases. Generally the potential for global spread via transportation networks, large scale epidemic potential given short incubation period, severity of illness and wide transmission patterns,potential for impact on non-human primate populations, limited treatment options and its concern for development as bioterrorism agents make the disease an economically important emerging disease being the hot issue for mass medias and different organizations.

Based on the above conclusion the following recommendations are forwarded:

- Awareness should be created about the disease to prevent its spread.
- As the disease has no effective treatment prevention and control measures based on further investigations should be implemented to mitigate the disease.
- Those that are at high risk like health professionals should take appropriate care when handling patients.
- Hunters, laboratory workers and those having contact with primates or secretions should also be protected when handling animals and specimens.
- Dead persons and animals should be buried appropriately to avoid potential source of infection.
- As the disease is the current issue worldwide, thorough studies on the disease like on vaccine development should be done.
- Men infected with Ebola virus should not have sex for 3 months or until tests Show that semen is free of the virus.
- As the disease is not reported in Ethiopia appropriate measures should be taken to the movement of animals and people from abroad.

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