Re-emergence of the deadly Ebola virus disease: A Global Health Threat

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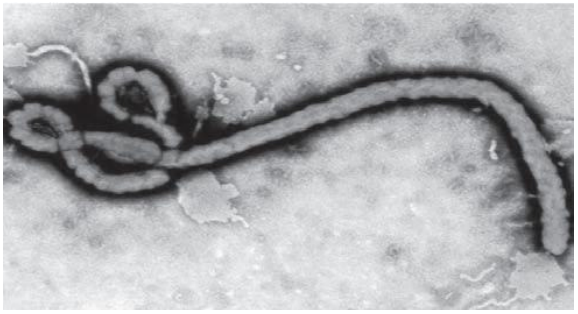
Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a severe, often-fatal disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees). It was initially recognized in 1976 in the Democratic Republic of the Congo (formerly Zaire) in Africa where the causative virus was named "Ebola" (named after a river in Zaire). Ebola virus belongs to a family of RNA viruses called the Filoviridae. Ebola viruses are nonsegmented, negative-sense, single-stranded RNA viruses.



Ultra structure of Ebola virus

The genus Ebola virus is divided into five different species which vary in their virulence and are named after the areas where they were first detected (Zaire, Sudan, Ivory Coast, Bundibugyo, and Reston agents).[1]

Zaire species was first recognition in 1976, since then it has caused ten large outbreaks, ranging from 30 to more than 300 cases, with mortality rates of 57 to 88 %.[2]

Sudan virus has been associated with four epidemics (two in Sudan in 1970s, one in Uganda in 2000, and again in Sudan in 2004) with 50 percent case fatality rate in.

The ***Ivory Coast virus*** (Taï Forest) has only been identified only in one person (ethnologist), who survived .[7]

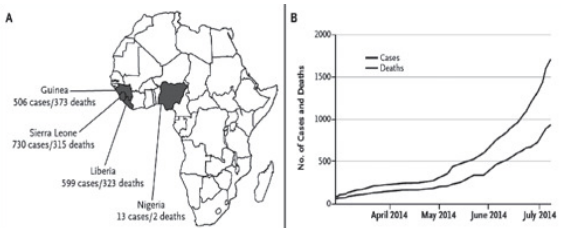
The ***Bundibugyo virus*** emerged in Uganda in 2007, causing an outbreak with case fatality rate (approximately 30 percent) than has typically been caused by the Zaire and Sudan viruses.

The ***Reston virus*** has not been found in Africa and is apparently maintained in an animal reservoir in the Philippines and. Ebola Reston have been reported to infect humans but, there have been no cases of human illness or death from this sub-type.[1]

Current scenario regarding 2014 outbreak

The World Health Organization, in partnership with the Ministries of Health in Guinea, Sierra Leone, Liberia, and Nigeria announced a cumulative total of 1975 suspect and confirmed cases of Ebola virus disease (EVD) and 1069 deaths, as of August 11, 2014. Of the 1975 cases, 1251 have been laboratory confirmed for Ebola virus infection. EVD outbreaks occur primarily in remote villages in Central and West Africa, near tropical rainforests.[3]

The strain currently circulating in West Africa bears 97% homology to ***Zaire species*** found in the Democratic Republic of Congo and Gabon.This strain has historically resulted in the highest mortality (90%), although the estimated case fatality rate in the current outbreak is less than 60%.[3,4]



Ebola Virus Cases and Deaths in West Africa (Guinea, Liberia, Nigeria, and Sierra Leone), as of August 11, 2014 (Panel A), and Over Time (Panel B).[13] Data are from the World Health Organization (www.who.int/csr/don/archive/disease/ebola/en/).

The mechanism of viral outbreaks in humans is unknown

as the natural reservoir of Ebola viruses has not yet been proven. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal. In Africa, infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found in the rainforest alive or dead. When an infection does occur in humans, the virus can be spread in several ways to others. Ebola spreads in the community through human-to-human transmission through direct contact (through broken skin or mucous membranes) with sick person's blood or body fluids (urine, saliva, faeces, vomit, and semen), objects (as needles) that have been contaminated with infected body fluids. Corpse handlers who contact infected deceased bodies are at risk of getting infected too.[5,6,7]

The incubation period is usually 8–10 days (ranging from 2 to 21 days). Virus can be transmitted during febrile state, through late stages of disease and infected bodies of the deceased. Men who have recovered from the disease can still transmit the virus through their semen for up to 7 weeks after recovery.

Healthcare workers and the family and friends in close contact with Ebola patients are at the highest risk of getting sick because they may come in contact with infected blood or body fluids. During outbreaks of Ebola HF, the disease can spread quickly within healthcare settings (such as a clinic or hospital), especially when the staffs are not wearing 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 reused. Without adequate sterilization of the instruments, virus transmission can continue and amplify an outbreak. Other potential routes of transmission include the following: accidental infection of workers in any Biosafety-Level-4 (BSL-4) facility where these viruses are being studied, use of filoviruses as biological weapons.[5,6,7]

The natural reservoir of Ebola virus and the mode of transmission from the reservoir to wild apes and humans are yet to be known. Bats are a prime suspect, due to the similar location of their natural habitat and filovirus outbreaks sites. In Africa, fruit bats, particularly species of the genera *Hypsignathus monstrosus, Epomops franqueti* and *Myonycteris torquata*, are considered possible natural hosts for Ebola virus. As a result, the geographic distribution of Ebola viruses may overlap with the range of the fruit bats.[7]

Pathogenesis - because of the difficulty of performing clinical studies under Ebola outbreaks, most data on pathogenesis of EVD have been obtained from laboratory experiments employing mice, guinea pigs, and various nonhuman primates. Whatever the point of entry into the body, macrophages and dendritic cells are probably the first cells to be infected, where the first round of replication occurs. Spread to regional lymph nodes results in further rounds of replication, followed by dissemination of virus to dendritic cells and fixed and mobile macrophages in the liver, spleen, thymus, and other lymphoid tissues. Rapid systemic spread is aided by virus-induced suppression of Type I interferon responses.

Although Ebola virus does not infect lymphocytes, their rapid loss by apoptosis is a prominent feature of disease. The substantial loss of lymphocytes probably results from a combination of factors including infection-mediated impairment of dendritic cells and release of soluble factors from monocytes and macrophages. Soluble factors released from target cells also contribute to the impairment of the vascular system leading to vascular leakage. The systemic virus spread and replication, the general derangement of the host immune response, the coagulation abnormalities, the impairment of the vascular system, and hypotension all together result in shock and multiorgan failure. It is thus the host response to infection, rather than any toxic effect of the virus, that is responsible for the fever, malaise, vasodilatation, increased vascular permeability, hypotension, and shock of filoviral HF.[8,9]

Clinical manifestations of the diasease, incubation period from 2 to 21 days, the following symptoms can occur: ***Fever*** (greater than 38.6°C or 101.5°F) sometimes with relative bradycardia, ***severe headache***, ***muscle pain***, ***weakness***, ***diarrhoea***, ***vomiting, abdominal pain, lack of appetite***. Some patients may experience ***nonpruritic maculopapular rash*** on the upper body during the first week of illness, ***conjunctival injection*** and ***dark red discoloration of the soft palate***, ***hiccups, cough, sore throat, chest pain ,difficulty breathing, difficulty swallowing***. These symptoms persist over several days, accompanied by the onset and progressive worsening of ***prostration, stupor, hypotension, impaired kidney and liver function, and internal and external haemorrhages*** (conjunctival haemorrhages, easy bruising, and failure of vein puncture sites to clot). Gross bleeding is common only in moribund patients, who often have blood in urine and faeces and may bleed from the gastrointestinal tract.[1,6,7]

Diagnosis of Ebola in an individual who has been infected for only a few days is difficult, because the early symptoms are similar to commonly occurring diseases. However, if a person has the early symptoms of Ebola HF and there is reason to believe that Ebola HF should be considered, the patient should be isolated and public health professionals notified. Samples from the patient can then be collected and tested to confirm infection. Laboratory tests used in diagnosis includes:

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 Ebola HF 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.

Confirmatory diagnosis of Ebola HF relies on replication of the causative agent in cell culture (in a BSL-4 containment laboratory) and visualization of the characteristic viral particles by electron microscopy. [1,6,7,9]

Other Laboratory abnormalities : Low white blood cell and platelet counts, elevated serum aspartate (AST) and alanine aminotransferase (ALT) levels, with the former typically increasing more than the latter, coagulopathy, and the presence of disseminated intravascular coagulation (DIC). A marked decrease in total plasma protein, reflective of a capillary leak syndrome. Proteinuria has also been a common finding; renal insufficiency occurs with progression of illness. Elevated amylase level has also been described. [1,6,7]

No specific therapy is available at present. Standard treatment is limited to supportive care which consists of: balancing the patient's fluids and electrolytes, maintaining oxygen status and blood pressure and treating infections.

Timely treatment is important but challenging since the disease is difficult to diagnose clinically in the early stages. Because early symptoms such as headache and fever are nonspecific to Ebola infection, many cases may be initially misdiagnosed. However, if a person has the early symptoms of Ebola HF and there is reason to believe that Ebola HF should be considered, the patient should be isolated and public health professionals notified. Supportive therapy can continue with proper protective clothing until samples from the patient are tested to confirm infection[6,7]. Experimental treatments have been tested and proven effective in animal models but their effect in humans are unknown. One drug "cocktail" of humanized-mouse antibodies "ZMapp" being developed is an experimental treatment for Ebola infection. It has not yet been tested in humans for safety or effectiveness. [4,6,7] Other candidate therapeutics include RNA-polymerase inhibitors and small interfering RNA nanoparticles that inhibit protein production.[10]

There are currently no FDA approved vaccines for Ebola. The NIH's National Institute of Allergy and Infectious Diseases is working on developing an Ebola vaccine. NIH recently announced they are expediting their work, and aiming to launch phase 1 clinical trials of an Ebola vaccine.[4,6,7]

Prevention and Control : Exact cure for this disease is still unknown; hence strict prevention plays a crucial role. However, the prevention of Ebola HF faces many challenges as the precise mechanism of infection with Ebola HF are still to be unravelled. The most effective way to stop the current Ebola outbreak in West Africa is meticulous work in finding Ebola cases, isolating and caring for those patients, and tracing contacts to stop the chains of transmission. It means educating people about the nature of the disease and about outbreak containment measures, including safe burial practices and having health care workers strictly follow infection control in hospitals. This is how all previous Ebola outbreaks have been stopped.

When cases of the disease do appear, there is increased risk of transmission within health care settings. Therefore, health care workers must be able to recognize a case of Ebola HF and employ practical viral haemorrhagic fever isolation precautions or barrier nursing techniques and universal precaution. Health-care workers caring for patients with suspected or confirmed Ebola virus should apply, in addition to standard precautions, other infection control measures to avoid any exposure to the patient's blood and body fluids and direct unprotected contact with the possibly contaminated environment. When in close contact (within 1 metre) of patients, health-care workers should wear face protection (as a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures). Laboratory workers are also at risk. Samples taken from suspected human and animal Ebola cases for diagnosis should be handled by trained staff and processed in suitably equipped laboratories. The aim of all of these techniques is to avoid contact with the blood or secretions of an infected patient. If a patient with Ebola HF dies, it is equally important that direct contact with the body of the deceased patient be prevented. Even though there is no evidence Ebola virus is transmitted among humans by the airborne route, precautions must be taken. The patient should be placed in a private room under negative pressure, when available. All patient care should be performed in strict accordance with CDC directives. [6,7]

Ebola has been declared as an international emergency and hence every country needs to raise the level of vigilance on the deadly virus. Nepal should also be on alert and prepared to detect, investigate, and manage Ebola cases; this should include access to a qualified diagnostic laboratory for Ebola virus detection and where appropriate, the capacity to manage travellers originating from known Ebola-infected areas who arrive at international airports or major land

crossing points with unexplained febrile illness. Proper investigation of the people travelling to Nepal from Ebola affected African countries should include filling a checklist health form and should remain under the observation of the health institute for 21 days. The government should set an emergency 24-hour helpline, strong alerts should be issued at airports and ports, and active surveillance and tracking system should be established, separate healthcare centre for the treatment and management EVD cases, public education. Government should contact Nepalese resident in the affected countries and supply all instructive materials so that they can take preventive measures. Travellers' address records should be maintained so as to track them easily if symptoms are detected, help desks should be set up at airports and ports to deal with travellers showing any potential Ebola symptoms.

The preventive measures set up by the Ministry of Health seem reassuring and we hope that things will be brought under control if at all the disease is detected in the country. However, considering past record in dealing with other diseases as swine flu, dengue, the situation does not appear promising. Will we be able to cope with such a dangerous disease outbreak bearing in mind that we lack adequate isolation and containment and treatment facilities?.

References

1. Feldmann H, Geisbert TW. Ebola haemorrhagic fever. Lancet 2011; 377:849.
2. Khan AS, Tshioko FK, Heymann DL, et al. The reemergence of Ebola hemorrhagic fever, Democratic Republic of the Congo, 1995. Commission de Lutte contre les Epidémies à Kikwit. J Infect Dis 1999; 179 Suppl 1:S76.
3. Chronology of Ebola hemorrhagic fever outbreaks. Atlanta: Centers for Disease Control and Prevention (http://www.cdc.gov/ vhf/ebola/resources/outbreak-table.html)
4. Anthony S. Fauci . Ebola — Underscoring the Global Disparities in Health Care Resources N Engl J Med DOI: 10.1056/NEJMp1409494
5. Dowell SF, Mukunu R, Ksiazek TG, et al. 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 1999; 179 Suppl 1:S87.
6. Centers for Disease Control and Prevention (CDC). Ebola hemorrhagic fever. http:// www.cdc.gov/vhf/ebola
7. World Health Organisation Ebola virus disease Fact sheet No.103 Updated April 2014 http://www.who.int/mediacentre/factsheets/fs103/en/
8. Bray M, Mahanty S. Ebola hemorrhagic fever and septic shock. J Infect Dis 2003; 188:1613.
9. Geisbert TW, Young HA, Jahrling PB, et al. Pathogenesis of Ebola hemorrhagic fever in primate models: evidence that hemorrhage is not a direct effect of virus-induced cytolysis of endothelial cells. Am J Pathol 2003; 163: 2371.
10. Feldmann H. Ebola — a growing threat? N Engl J Med. DOI: 10.1056/NEJMp1405314