Ebola Virus Infection: An Overview

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Introduction

Of the more than two dozen or so viruses known to cause Viral Haemorrhagic Fever (VHF) syndrome, Ebola virus with a mortality rate of up to 90%, is the deadliest. The present outbreak, which appears to be the worst in history, started in the remote forests of South East Guinea in March 2014 and, up to the time of writing this review (December 2014), has already affected more than 17000 individuals with over 6000 deaths in six countries of West Africa including Guinea, Liberia, Sierra Leone, Senegal, Nigeria and Mali, with cases appearing in the United States and Spain. New infections and deaths are occurring on a daily basis. Countries worst affected in the present outbreak are Guinea, Sierra Leone & Liberia, where transmission remains persistent and widespread. The genus Ebolavirus which, along with Marburgvirus, belongs to the family Filoviridae, is classified into 5 separate species or strains that are named after the countries where most of the documented outbreaks have occurred; these include: Zaire ebolavirus, Sudan ebolavirus, Bundibugyo ebolavirus, Tai Forest (Ivory Coast) Ebolavirus and Reston ebolavirus. The first three are African strains and have been responsible for the majority of recorded outbreaks that occurred primarily in countries of sub-saharan Africa.

Based on genetic analysis, the present outbreak has been shown to be caused by Zaire Ebolavirus which is the most lethal of all the Ebola strains having the highest mortality of up to 90%.

Virus Structure

Ebolavirus, in common with all the Filoviruses, has a unique and characteristic filamentous form, with a uniform diameter of approximately 80 nm but a highly variable length. Filaments may be straight, but they are often folded on themselves (Figure 1).

Historical perspective

Ebolavirus was discovered by Peter Piot of the London School of Hygiene and Tropical Medicine in 1976 and named so after the Ebola river valley in Dr Congo where the infection was detected for the first time in a village. The virus has a non-segmented negative-stranded RNA genome containing 7 structural and regulatory genes. Most important of these is the GP gene which controls the production of sGP, a small (50-70 kd), soluble nonstructural secretory glycoprotein responsible for some of the most serious pathological effects of the virus.

Since the discovery of Ebolavirus in 1976, major documented outbreaks recorded up to 2012 have been caused mostly by the three African strains and include: Zaire Ebola–14 outbreaks with 1490 infections and 1141 deaths, Sudan Ebolavirus- 6 outbreaks, 762 cases with 405 deaths, and Bundibugyo strain -185 infections with 50 deaths. Based on available evidence, African fruit bats of the Order Pteropodidae, known to be a delicacy for some West African communities, are considered to be the likely reservoir of Ebolavirus. Host range of Ebolavirus is limited to humans and non-human primates like monkeys, gorillas and Chimpanzees.

Clinical infection

Patients may contract Ebolavirus infection either through primary exposure while traveling to or working in an endemic area like West Africa where virus activity is going on or through secondary exposure by human to human contact in which health care workers (HCW), family members caring for an Ebola patient or those burying Ebola dead are at maximum risk. Reportedly more than 520 HCWs have so far been affected in the present outbreak.
Transmission
Infection is transmitted by direct contact with body fluids of an infected host – saliva, blood, infected tissues, mucous membrane, conjunctiva, pharyngeal or GIT surfaces and skin. Direct contact via skin route is the major form of transmission followed by the respiratory route, the virus gaining entry through small breaks in the skin or through aerosols via respiratory tract. Admission to a hospital without strict barrier precautions amplifies the chances of transmission.

During late stages of the disease, large numbers of virus particles are present in the body fluids, tissues, and, particularly skin. Saliva of the infected host may be a major source of transmission. During an earlier outbreak in Congo in 1995, using RT-PCR assay, Ebolavirus RNA was identified in 100% of oral secretions from patients who had viral RNA in their serum.

Infectivity: Ebola patients are highly infective as soon as the symptoms become manifest. There is no evidence that patients can transmit infection before the appearance of symptoms.

Incubation period is up to 21 days with an average of 3-8 days.

Onset is sudden with fever, pharyngitis, severe constitutional signs and symptoms, maculopapular rash (best seen in fair skinned patients) and bilateral conjunctival injection. The most common symptoms of patients in the current outbreak have been fever, fatigue, vomiting, diarrhoea, and loss of appetite in that order.

Late findings may include expressionless facies, bleeding from puncture sites and mucous membranes, myocarditis and pulmonary edema. In terminally ill patients, there is tachypnea, hiccups, hypotension, anuria, and coma followed by death.

Pathogenesis
After infection, the victims experience an early period of rapid viral multiplication which, in lethal cases, is accompanied by an ineffective immune response. Although a full understanding of Ebolavirus disease demands further investigations, some aspects of pathogenesis have been partly elucidated.

1. sGP, the secretory glycoprotein mentioned above, is produced in large quantities during the initial phase of Ebolavirus infection. sGP prevents the appearance of an early and effective immune response through inhibition of neutrophil activation and production of profound lymphopenia
2. The virus invades, replicates in and destroys the endothelial cells of the patient. This leads to disseminated intravascular coagulation (DIC) which largely contributes to the haemorrhagic manifestations so characteristic of many but not all Ebola infections.

3. Ebolavirus infection is characterized by rapid and extensive viral replication in all tissues resulting in widespread focal necrosis, most severe in liver but also seen in spleen, lymph nodes, kidneys, lungs and gonads.
4. Host tissues and body fluids including semen and blood contain huge quantities of virus particles and are highly infectious.

Laboratory Diagnosis
Routine laboratory findings are characterized by thrombocytopenia, leucopenia and lymphopenia followed by neutropenia. ALT and AST may be elevated. Later blood urea nitrogen and serum creatinine increase. Terminally ill patients may develop a metabolic acidosis that may explain the frequent occurrence of tachypnea as an attempt for compensatory hyperventilation.

Definitive Diagnosis
The modalities available for definitive diagnosis include:
- RT-PCR: Currently the method of choice. It takes 3-10 days to become positive after the appearance of symptoms
- Virus isolation in Vero cells – an extremely dangerous procedure which can be undertaken only in a few selected high containment laboratories in the world.
- Antigen detection by ELISA
- Detection of IgG and IgM antibodies by ELISA – the appearance of these antibodies may be delayed.

Prognosis
Prognosis is extremely poor; patients usually succumb to infection within 2 weeks. Those who survive for more than 2 weeks usually make a slow recovery which often requires months before full resumption of normal activities.

Mortality: The case-fatality rate of the current outbreak has been approximately 71%.

Infectivity: Dead bodies can remain contagious for up to 60 days after death. Male patients who recover can transmit Ebolavirus infection through semen for up to 7 weeks after recovery.

Prevention and Control
Strict and intensive barrier protection is required for infection control both inside and outside of medical facilities. According to the latest CDC guidelines, physicians, nurses, and other clinicians caring for Ebola patients should wear personal protective equipment (PPE) that does not leave any skin exposed. This supersedes an earlier recommendation that allowed for a small degree of skin exposure and requires the use of a surgical hood that completely covers the head and neck, and a single-use, full-face shield instead of goggles. In addition, the CDC recommends vigorous training of HCW with regards to both
wearing and removing PPE. The latter step (i.e. taking off PPE), as if done improperly, puts an HCW at high risk for contracting infection.

**Treatment considerations:** No specific therapy is currently available for Ebolavirus infection.

**Supportive measures:** Intravascular volume repletion is critical. Others include electrolytes, nutrition, and comfort care. Survivors can produce infectious virions for prolonged periods. Strict barrier isolation in a private room must be maintained throughout the illness. Patient’s urine, stool, sputum, and blood, along with any objects that have come in contact with the patient or the patient’s body fluids (such as laboratory equipment), should be disinfected with 0.5% sodium hypochlorite solution. Patients who have died of Ebolavirus disease should be buried promptly and with as little contact as possible.

**WHO Initiative:** “The World Health Organization (WHO) has initiated expert assessment missions to assess Ebola preparedness of several member states. The mission aims to assess the medical capabilities an event of Ebola outbreak, recognize gaps in their preparedness and response plans and take steps to fill in the gaps. In each country, a team of WHO experts will review the assessment with national experts, United Nations Country Teams and other relevant partners.” The missions have been completed in Morocco and Somalia. Other countries that will undergo this exercise include Afghanistan, Bahrain, Djibouti, Egypt, Islamic Republic of Iran, Iraq, and occupied Palestinian territory, Pakistan, Sudan and Yemen”.

**Vaccine:** Intensive efforts had long been underway at vaccine production for Ebola. Two candidate vaccines, one each in Switzerland and Canada, appear to show some promise. Safety and immune response data may be available by the beginning of 2015. Because of the urgency of the situation, there being no time for phase III trials, the vaccine would probably be evaluated at the same time as being deployed in the field for use in the human subjects.

**Travel Advisory:** WHO recommends that travelers who have traveled from or through Guinea, Liberia or Sierra Leone should be screened on arrival at the airport.
- They should be asked questions to define any potential risk
- Have their temperature taken
- Observed for other symptoms suggestive of Ebola.

- Should be advised to observe themselves during the next 21 days and if they become febrile during this period, they should immediately report to the nearest hospital or a centre designated by the Health authorities.

If arriving passengers have symptoms, have a history of exposure to suspected case of Ebola or have recently been in West Africa, they should be:
- Taken to the hospital for evaluation, testing and, if required, treatment.
- Observed for 21 days for fever, headache, body aches and other symptoms suggestive of Ebola.

**References**