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Ebola Virus Disease

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Abstract: *The epidemic of Ebola haemorrhagic disease in West Africa is the most extensive to date, where the outbreak notably involved three West African countries with distant spread to other countries. There are five identified subspecies of Ebola virus. The first viral species reported to have infected humans was in 1976 in what is now the Democratic Republic of the Congo near the Ebola River. Ebola virus is an enveloped RNA virus about 80 x 800-1400 nm in size whose survival is dependent on an animal reservoir. An international team of researchers have sequenced 99 Ebola virus genomes and also observed a rapid increase in its genetic variation. There are several ways in which the virus can be transmitted to others. Symptoms of EVD may appear anytime from 2 to 21 days after exposure to the virus, although 8-10 days is most common. Making a diagnosis of EVD in individuals with early infection is very difficult. It is strongly recommended that diagnostic tests, which have undergone an independent and international evaluation, be considered for use. Samples collected from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions. Despite the use of experimental drugs during the outbreak, which included monoclonal antibodies (ZMapp), the WHO, identified that the reason most patients in American and European hospitals survived was due to the use of intravenous fluids and other supportive therapy, along with adequate monitoring, control of blood chemistry and other parameters. Results of an interim analysis of trial show vaccine to be highly efficacious, but more conclusive evidence is needed on its capacity to protect populations through herd immunity. Finally, addressing the challenges of EVD is largely dependent on the creation of infection control awareness with the contribution of all members of the community.*

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I. Introduction

Ebola virus disease (EVD) is a severe; potentially life threatening illness caused by Ebola virus.[1, 2] Ebola virus is one of the causes of the dreaded Viral Haemorrhagic Fevers (VHF). Viral Haemorrhagic Fevers are caused by viruses of five distinct virus families: Arenaviridae, Bunyaviridae, Filoviridae, Flaviviridae and Paramyxoviridae. Each of these families shares a number of features:

1. They are all Ribonucleic Acid (RNA) viruses and are all covered, or enveloped, in a fatty (lipid) coating.
2. Their survival is dependent on an animal or insect host, called the natural reservoir.
3. The viruses are geographically restricted to the areas where their host species live.
4. Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.
5. Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.
6. With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs.

Data and relevant information were extracted from relevant publications and bulletins about the Ebola epidemic in West Africa and other outbreaks of EVD.

Ebola Virus

Ebola virus disease is often a fatal disease that normally occurs in primates (such as monkeys, gorillas and Chimpanzees) and recently in humans. Ebola virus disease is caused by an infection with a virus of the family *Filoviridae*, genus *Ebola virus*.[1, 2] The first viral species reported to have infected humans was in 1976 in what is now the Democratic Republic of the Congo near the Ebola River.[3] Ever since then, outbreaks have been reported sporadically. There are five identified subspecies of *Ebola virus.* Four of the five have caused disease in humans: Ebola virus (Zaire *Ebola virus*); Sudan virus (Sudan *Ebola virus*); Tai Forest virus (Taï Forest *Ebola virus*, formerly Côte d'Ivoire *Ebola virus*); and Bundibugyo virus (Bundibugyo *Ebola virus*).[1,2,3] The fifth, Reston virus (Reston *Ebola virus*), has caused disease in nonhuman primates, but not in humans.[3,4] However,

the natural reservoir host of Ebola virus still remains unclear. Although, on the basis of available evidence, scientists believe that the virus is zoonotic (animal-borne) with fruit bats being the most likely reservoir.[4,5] Four of the five subtypes occur in animal host native to Africa while the Reston virus subtype was isolated from specimens collected from the Philippines, however, this subtype is not known to cause human illness.

Ebola virus is an enveloped RNA virus about 80 x 800-1400 nm in size whose survival is dependent on an animal reservoir.[6] An international team of researchers have sequenced 99 *Ebola virus* genomes and also observed a rapid increase in its genetic variation.[7] In total, 99 EBOV genome sequences were generated from 78 confirmed EVD patients, representing more than 70% of the EVD patients diagnosed in Sierra Leone from late May to mid-June; using multiple extraction methods or time points for 13 patients.[8] Genetic similarity across the sequenced 2014 samples suggests a single transmission from the natural reservoir, followed by human-to-human transmission during the outbreak.[8] However, more recent molecular data obtained from the outbreaks in Kikwit and Gabon did not find any molecular evidence for adaptation during human to human transmission.[9] Infection results in severe disease with high mortality rate among infected humans and other primates.[10] It has no known cure or vaccine; treatment is only supportive.[11] Ebola virus is considered a potential biological weapon candidate.[6]

***Ebola Virus* Disease**

Transmission occurs mainly in acutely ill patients.[1,2] There are several ways in which the virus can be transmitted to others, these include:

1. Direct contact with blood or body secretions such as sweat, saliva, semen or vaginal fluids of an infected person
2. Exposure to objects (such as needles and other sharps) that have been contaminated with infected secretions.
3. Exposure through friends and family members who are often the first care givers of cases.
4. Through health care personnel who are at risk of contracting the disease from cases in healthcare facilities.

Human to human transmission is usually a sequel to this by direct contact with the bodily fluids of symptomatic infected persons, these accounts for the high rate of infection of health workers and subsequently nosocomial infection.[12]

Clinical Presentation

Symptoms of EVD may appear anytime from 2 to 21 days after exposure to *Ebola virus*, although 8-10 days is most common.

Typical symptoms include:

1. Headache, fever and chills
2. Malaise and weakness
3. Joint and muscle aches
4. Diarrhea and loss of appetite
5. Abdominal pain and vomiting

Diagnosis

Making a clinical diagnosis of EVD in individuals with early infection is difficult.[3] However, having a high index of suspicion would aid during outpatient triaging. If an individual presents the early symptoms of EVD and there is suspicion of visit to or exposure to EVD exposed case, EVD should be considered, the patient must be isolated and other health professionals notified. Confirmation that symptoms are caused by Ebola virus infection are made using the following diagnostic methods:[3]

1. antibody-capture enzyme-linked immunosorbent assay (ELISA)
2. antigen-capture detection tests
3. serum neutralization test
4. reverse transcriptase polymerase chain reaction (RT-PCR) assay
5. electron microscopy
6. virus isolation by cell culture.

Careful consideration should be given to the selection of diagnostic tests, which take into account technical specifications, disease incidence and prevalence, and social and medical implications of test results. It is strongly recommended that diagnostic tests, which have undergone an independent and international evaluation, be considered for use. Current WHO recommended tests include:[3]

1. Automated or semi-automated nucleic acid tests (NAT) for routine diagnostic management.

2. Rapid antigen detection tests for use in remote settings where NATs are not readily available. These tests are recommended for screening purposes as part of surveillance activities; however reactive tests should be confirmed with NATs.

The preferred specimens for diagnosis include:[3]
1. Whole blood collected in ethylenediaminetetraacetic acid (EDTA) container bottle from live patients exhibiting symptoms.
2. Oral fluid specimen stored in universal transport medium collected from deceased patients or when blood collection is not possible.

Samples collected from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions. All biological specimens should be packaged using the triple packaging system when transported nationally and internationally.

Treatment

Standard treatment for EVD is still limited to supportive efforts, although medications and vaccines are still undergoing clinical trials. Therapy consists of:
1. balancing the patient's fluids and electrolytes,
2. maintaining their oxygen status and blood pressure, and
3. treating them for any other complicating infections

Note that oral or topical salt and water therapy does not give any benefit to the patient. Despite the use of experimental drugs during the outbreak, which included monoclonal antibodies (ZMapp), the WHO, identified that the reason most patients in American and European hospitals survived was due to the use of intravenous fluids and other supportive therapy, along with adequate monitoring, control of blood chemistry and other parameters.[12] There is however hope for EVD management as researchers announced on 31st July, 2015 that a vaccine trial in Guinea had been completed that appeared to give protection from the virus. The vaccine is a recombinant replication-competent vesicular stomatitis virus-based vaccine, expressing a surface GP of Zaire Ebola virus (rVSV-ZEBOV).[12] The vaccine, rVSV-ZEBOV, was studied in a trial involving 11 841 people during 2015. Among the 5837 people who received the vaccine, no Ebola cases were recorded 10 days or more after vaccination.[3] Results of an interim analysis of the trial show the vaccine to be highly efficacious, but more conclusive evidence is needed on its capacity to protect populations through herd immunity.[12]

Prevention

Prevention remains the major strategy in combating the spread of EVD. A number of measures aimed at containing the spread of EVD at the individual, health facility and community levels include:

a) Individual level:
1. Individuals should observe a high index of suspicion for people (including friends and family members) who are sick and suffer very high fever and anyone of the above mentioned symptoms.
2. Recent contacts with someone who had EVD or visited a community where there is outbreak of EVD calls for caution.
3. Increased personal hygiene practice such as regular hand washing, bathing and use of personal protective equipment.

b) Health Facility level:
1. Infection control measures/standard precautions should be taken in cases suspected to be EVD.
2. Enforce the use of personal protective equipment i.e, hand gloves, face mask and eye goggles by all healthcare personnel at risk of exposure to blood and body fluids.
3. Suspected cases should be isolated and barrier nursed.
4. Appropriate disposal of all biological waste especially blood, body fluids, sharps and needles.

c) Community Level:
1. Increased community hygiene and environmental sanitation
2. Community members should notify health care workers (facilities) and appropriate authorities of any suspected case(s).
3. Community should be educated properly about EVD and mobilized to observe safer cultural practices e.g. circumcision, tattoo and traditional surgical practices.
4. Immediate burial of dead bodies should be practiced and the practice of touching dead bodies with bare hands be avoided.

Finally, addressing the challenges of EVD is largely dependent on the creation of infection control awareness with the contribution of all members of the community. All healthcare personnel, non-governmental

organization staff and medical students should lead information dissemination in the community and in private discussions wherever they find themselves. Health care facilities personnel must insist that protective measures are instituted in all healthcare facilities and hospitals.

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