Perspective

EBOLA VIRUS DISEASE (EVD)

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Introduction

Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a severe, often fatal illness in humans.[1] EVD outbreaks have a case fatality rate of up to 90%.[1] EVD outbreaks occur primarily in remote villages in Central and West Africa, near tropical rainforests.[1] The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission.[1,2] Fruit bats of the *Pteropodidae* family are considered to be the natural host of the Ebola virus.[1,2] Severely ill patients require intensive supportive care. No licensed specific treatment or vaccine is available for use in people or animals.[1]

History of EVD

Ebola first emerged in 1976 in two simultaneous outbreaks, in Nzara, Sudan, and in Yambuku, Democratic Republic of Congo (DRC), then Zaire. The latter was in a village situated near the Ebola River, from which the disease takes its name.[1] There has been several sporadic outbreaks since then. The largest outbreak as of 2014 is the ongoing 2014 West Africa Ebola outbreak , which is affecting Guinea, Sierra Leone, Liberia, Nigeria and Senegal. DRC in Central Africa is also affected.

Types of Ebola virus

Genus Ebolavirus is one of two members of the *Filoviridae* family, along with genus Marburgvirus.[3] Genus Ebolavirus comprises 5 distinct species:

1. Bundibugyo ebolavirus.
2. Zaire ebolavirus.
3. Reston ebolavirus.
4. Sudan ebolavirus.
5. Taï Forest ebolavirus.

Bundibugyo ebolavirus, Zaire ebolavirus, and Sudan ebolavirus have been associated with large EVD outbreaks in Africa.[1] The Reston species, found in Philippines and the People's Republic of China, can infect humans, but no illness or death in humans from this species has been reported to date.[1] The Zaire ebolavirus has the highest case fatality rate and is responsible for the ongoing outbreak in West Africa.[2,4] The ebolavirus has been classified as a biosafety level 4 agent, as well as a Category A bioterrorism agent by the Centre for Disease Control and Prevention (CDC).[2]

Mode of transmission

Ebola is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals.[1,2] In Africa, infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.[1] Ebola then spreads in the community through human-to-human transmission, with infection resulting from direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and indirect contact with environments contaminated with such fluids.[1,2]

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. Men who have recovered from the disease can still transmit the virus through their semen for up to 7 weeks after recovery from illness.[1,2] 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.[1]

Pathogenesis of EVD

After infection, a secreted glycoprotein (sGP) known as the Ebola virus glycoprotein (GP) is synthesized. Ebola replication overwhelms protein synthesis of infected cells and host immune defenses. The GP forms a trimeric complex, which binds the virus to the endothelial cells lining the interior surface of blood vessels. The sGP forms a dimeric protein that interferes with the signaling of neutrophils which allows the virus to evade the immune system by inhibiting early steps of neutrophil activation.The presence of viral particles and cell damage resulting from budding causes the release of cytokines (to be specific, TNF-α, IL-6, IL-8, etc.), which are the signaling molecules for fever and inflammation. The cytopathic effect, from infection in the endothelial cells, results in a loss of vascular integrity. This loss in vascular integrity is furthered with synthesis of GP, which reduces specific integrins responsible for cell adhesion to the inter-cellular structure, and damage to the liver, which leads to coagulopathy.[5]

Signs and symptoms of EVD

Manifestation of Ebola begins abruptly with a sudden onset of common symptoms including general malaise, fever with chills, sore throat, severe headache, weakness, joint pain, muscle pain, and chest pain.[1,2] This is followed by vomiting, diarrhoea, rash, impaired kidney and liver function, and in some cases, both internal and external bleeding.[1,2] Respiratory tract involvement is characterized by pharyngitis with sore throat, cough, dyspnea and hiccups.[2] The central nervous system affectation is characterized by the development of severe headaches, agitation, fatigue, depression, seizures, and sometimes coma.[2]

Cutaneous manifestation may include: maculopapular rash, petechiae, purpura, ecchymoses, and haematomas especially around needle injection sites. In general, development of hemorrhagic symptoms is indicative of a negative prognosis. However, contrary to popular belief, hemorrhage does not lead to hypovolemia and is not the usual cause of death (total blood loss is low except during labour).[2] Instead, death occurs due to multiple organ dysfunction syndrome (MODS) due to fluid redistribution, hypotension, disseminated intravascular coagulation, and focal tissue necroses.[2]

The incubation period is 2 – 21 days.[1,2]

Diagnosis of EVD

Ebola virus infections can be diagnosed definitively in a laboratory through several types of tests: antibody-capture enzyme-linked immunosorbent assay (ELISA), antigen detection test, serum neutralization test, reverse transcriptase polymerase chain reaction (RT-PCR) assay, electron microscopy, and virus isolation by cell culture.[1,2] Samples from patients are extreme biohazard risk and testing should be conducted under maximum biological containment conditions.[1] The most important method of diagnosis of EVD is the medical history, especially travel to an endemic area and occupational history and the person's exposure to a case of EVD and wildlife.[2]

Treatment

No proven Ebola virus-specific treatment exists as of August 2014.[1,2,6] Treatment is primarily supportive in nature and includes minimizing invasive procedures, balancing fluids and electrolytes to counter dehydration, administration of anticoagulants early in infection to prevent or control disseminated intravascular coagulation, administration of procoagulants late in infection to control hemorrhaging, maintaining oxygen levels, pain management, and administration of antibiotics or antimycotics to treat secondary infections.[7,8] Early supportive treatment may increase the chance of survival.

The unavailability of treatments in the most-affected regions has spurred controversy, with some calling for experimental drugs to be made more widely available in Africa on a humanitarian basis, and others warning that making unproven drugs widely available would be unethical.[4] As a result of the controversy, an expert panel of the world health organization (WHO) on 12 August 2014 endorsed the use of interventions with as-yet-unknown effects both for treatment and for prevention of Ebola, and also said that deciding which treatments should be used and how to distribute them equitably were matters that needed further discussion.[9]

Subsequently the WHO assistant director-general for health systems and innovation said on 5 September 2014 that transfusion of whole blood or purified serum from Ebola survivors is the therapy with the greatest potential to be implemented immediately on a large scale in West Africa, although there is little information on the efficacy of such treatment.[4] The experimental treatments include ZMapp (a monoclonal antibody vaccine), TKM-Ebola (an RNA interference drug), Favipiravir.[4]

Prevention

Ebola viruses are highly infectious as well as contagious.[2] The aim of prevention is to interrupt transmission of the virus and contain the disease since there is no proven specific licensed treatment currently available for EVD. Frequent hand washing with soap and flowing water is advocated as a major preventive measure. Isolation of all affected persons and strict barrier nursing procedures are all effective preventive measures.[2] The WHO in collaboration with CDC has outlined steps to aid in prevention of EVD and other viral hemorrhagic fevers (VHFs)[10]:

- ❑ Use Standard Precautions with All Patients.
- ❑ Identify Suspected Cases of EVD.
- ❑ Isolate the Patient.
- ❑ Wear Protective Clothing.
- ❑ Disinfect Reusable Supplies and Equipment.
- ❑ Dispose of Waste Safely.
- ❑ Use Safe Burial Practices.
- ❑ Mobilize Community Resources and Conduct Community Education.
- ❑ Make Advance Preparations to Use EVD Isolation Precautions.

Case definition recommendations for EVD by WHO[11]

Suspected case: Illness with onset of fever and no response to treatment for usual causes of fever in the area and one of the following signs: bloody diarrhoea, bleeding from the gums, purpura, bleeding into the eyes and urine.

Probable case: Any suspected case evaluated by a clinician, or any deceased suspected case having an epidemiological link with a confirmed case.

Laboratory confirmed case: Any suspected or probable case with a positive laboratory result.

Non-case: Any suspected or probable case with a negative laboratory result.

Current status of the ongoing Ebola outbreak in Africa

The current Ebola outbreak is literally the worst outbreak of the virus in history in regard to the number of human cases and fatalities with the number of cases from the current outbreak now outnumbering the combined cases from all known previous outbreaks.[4] The outbreak began in Guinea in December 2013 after which it spread to Liberia, Sierra Leone, Nigeria and Senegal.[4] Another outbreak in the Democratic Republic of the Congo, which has 62 possible and confirmed cases and 35 deaths as of 9 September 2014, is believed to be unrelated to the West African outbreak.[4]

As of 10 September 2014, the World Health Organization and the Centers for Disease Control reported a total of 4,846 suspected cases and 2,375 deaths (2,898 cases and 1,386 deaths being laboratory confirmed).[4] Past EVD outbreaks have been localized to small rural villages but this has spread to multiple countries, including large cities.[4]

Various aid organisations and international bodies, including the Economic Community of West African States (ECOWAS), US Centers for Disease Control and Prevention (CDC), and the European Commission have donated funds and mobilised personnel to help counter the outbreak; charities including Médecins Sans

Frontières, the Red Cross, and Samaritan's Purse are also working in the area.[4] At the end of August 2014, the WHO reported that the loss of so many health workers was making it difficult for them to provide sufficient numbers of foreign medical staff, and the African Union launched an urgent initiative to recruit more health care workers from among its members.[12] The outbreak was formally designated as a public health emergency of international concern on 8 August 2014.[13]

Cases / Death (as of 10th September, 2014)[4]
Total: 4,846 / 2,375

- Guinea: 899 / 568
- Liberia: 2,415 / 1,307
- Nigeria: 22 / 0
- Senegal: 3 / 0
- Sierra Leone: 1,509 / 493

Challenges to containment efforts in West Africa

Difficulties faced in the effort to contain the outbreak include the multiple locations across country borders that are affected. Adequate equipment has not been provided for medical personnel, with even a lack of soap and water for hand-washing and disinfection.[4] Containment efforts are further jeopardized due to ignorance among country people to recognize the danger of infection related to person-to-person spread of disease, such as burial practices which include washing of the body of one that has died.[4]

A condition of dire poverty exists in many of the areas that have experienced a high incidence of infections, with poor living conditions and lack of water and sanitation.[4] Denial in some affected countries has often made containment efforts impossible.[4] Language barriers and the appearance of medical teams in protective suits has sometimes magnified fears of the virus.[4]

Healthcare providers caring for Ebola patients and family and friends in close contact with Ebola patients are at the highest risk of getting sick because they may come in direct contact with the blood or body fluids of sick patients.[4] As of 11 August 2014, healthcare workers have represented nearly 10 percent of the cases and fatalities, significantly impairing the ability to respond to the outbreak in a country which already faces a severe shortage of doctors.[4]

Comparing the present Ebola outbreak to some in the past, the WHO notes that many of the most recent districts in which epidemics have occurred were in remote areas where the transmission had been easier to track and break. This outbreak is different in that large cities have been affected as well, where tracking has been difficult and medical staff may not suspect Ebola disease when they make a diagnosis. Several infectious diseases endemic to West Africa, such as malaria and typhoid fever, mimic the symptoms of Ebola disease, and doctors and nurses may see no need to take protective measures.[12] Also, without recent past experience with the disease, people have become intensely fearful and have, in some cases, attacked medical staff, believing that they cause the disease.[12]

Recommendations/way forward

- ❑ Strengthening of the National Routine Surveillance and Notification system (IDSR).
- ❑ Revitalizing the health sector: infrastructural development, provision of basic amenities, conflict resolution/management etc.
- ❑ Capacity building and re-orientation of port health officials.
- ❑ Capacity development of healthcare workers on diagnosis, case management and infection prevention and control.
- ❑ Other Resources (isolation centres, ambulances, PPEs, body bags, consumables etc.) should be provided in readiness for an outbreak.
- ❑ Public information and community mobilization.
- ❑ Contact tracing system to be put in place.
- ❑ Intersectoral collaboration and coordination.
- ❑ Setting up of Outbreak Response Committee that should be functional before an outbreak.

Conclusion

Tom Frieden, Director of the Center for Disease

Control, stated: "The bottom line with Ebola is we know how to stop it: traditional public health. Find patients, isolate and care for them; find their contacts; educate people; and strictly follow infection control in hospitals. Do those things with meticulous care and Ebola goes away."[14]

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