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Ebola viral disease: a review literature

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ABSTRACT

Ebola virus is transmitted to people as a result of direct contact with body fluids containing virus of an infected patient. The incubation period usually lasts 5 to 7 d and approximately 95% of the patients appear signs within 21 d after exposure. Typical features include fever, profound weakness, diarrhea, abdominal pain, cramping, nausea and vomiting for 3-5 days and maybe persisting for up to a week. Laboratory complications including elevated aminotransferase levels, marked lymphocytopenia, and thrombocytopenia may have occurred. Hemorrhagic fever occurs in less than half of patients and it takes place most commonly in the gastrointestinal tract. The symptoms progress over the time and patients suffer from dehydration, stupor, confusion, hypotension, multi-organ failure, leading to fulminant shock and eventually death. The most general assays used for antibody detection are direct IgG and IgM ELISAs and IgM capture ELISA. An IgM or rising IgG titer (four-fold) contributes to strong presumptive diagnosis. Currently neither a licensed vaccine nor an approved treatment is available for human use. Passive transfer of serum collected from survivors of Junin virus or Lassa virus, equine IgG product from horses hypervaccinated with Ebola virus, a "cocktail" of humanized-mouse antibodies (ZMapp), recombinant inhibitor of factor VIIa/tissue factor, activated protein C, RNA-polymerase inhibitors and small interfering RNA nano particles are among the therapies in development. Preclinical evaluation is also underway for various vaccine candidates. One is a chimpanzee adenovirus vector vaccine; other vaccines involve replication-defective adenovirus serotype 5 and recombinant vesicular stomatitis virus.

1. Epidemiology

Ebola virus (EBOV) and Marburg virus (MARV), members of the Filoviridae virus family, are known as emerging and re-emerging zoonotic pathogens causing acute hemorrhagic fever with a high case-fatality rate in humans (up to 90%)[1].

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Ebola hemorrhagic fever (EHF) was first reported in 1976 during the Ebola outbreak in the Democratic Republic of the Congo (formerly Zaire), and the virus is named after the Ebola River where it was discovered. Since then, 21 additional Ebola virus disease (EVD) outbreaks among humans have occurred in the tropical regions of sub-Saharan Africa. The largest one to date took place in the Gulu District of Uganda in 2000-2001 caused by Sudan virus (SUDV). This outbreak resulted in 425 cases, of which 216 were laboratory confirmed, and the overall case fatality rate was 53%[2]. The Ebola strain that is now circulating in West Africa bears shows the homology of 97% with Zaire Ebola virus samples found in the

Democratic Republic of Congo and Gabon[2]. Historically, this strain has caused the highest mortality (90%), while the current estimate of case fatality rate is less than 60%[3].

During December 2013, the epidemic of EVD started in Guinea[2], and the World Health Organization (WHO) received official notification of a rapidly evolving outbreak of EVD on March 23, 2014. In August 2014, WHO declared this epidemic to be a "public health emergency of international concern"[3]. In mid-September 2014, the case fatality rate among patients with definitive outcomes was 70.8% [95% confidence interval (CI), 68.6 to 72.8] and was consistent among Guinea, Liberia, and Sierra Leone. Nigeria's case fatality rate was lower at 45.5%, although the current estimate is based on only 11 recent cases. The in-hospital case fatality rate was 64.3% (95% CI, 61.5 to 67.0), which was lower than those for all patients with definitive outcomes, and this rate was consistent among countries. A range of 56.1% (95% CI, 41.0 to 70.1) in Guinea to 80.0% (95% CI, 68.7 to 87.9) in Liberia of health care workers died. Despite multinational and multisectoral responses to the disease, a growing number of new cases and deaths were reported every week[4].

There is no change in the control measures for this epidemic and by November 2, 2014, the cumulative reported numbers of Ebola confirmed and suspected cases for Guinea, Liberia, and Sierra Leone are predicted to be 5 740, 9 890, and 5 000, respectively, exceeding 20 000 cases in total[4]. The majority of cases are between 15 to 44 years old (49.9% male). In terms of reported morbidity and mortality, the current EVD epidemic is much greater than all previous outbreaks combined. The real number of those who have been infected and died is likely much higher[4].

This time, the outbreak has become so large that the three most-affected countries, namely, Guinea, Liberia, and Sierra Leone, face numerous challenges for the implementation of rigorous control measures at the scale needed to prevent transmission and to supply all EVD patients with clinical care[4].

2. Species of ebola viruses

The genus Ebolavirus is classified into five different viruses: SUDV, Tai Forest virus, Reston virus, EBOV, and Bundibugyo virus. Among them, EBOV causing the EHF is associated with the highest fatality rate in humans (57%-90%), followed by SUDV (41%-65%) and Bundibugyo virus (40%). To date, Tai Forest virus has only been known to cause two nonfatal human infections, while Reston virus causes asymptomatic infection in humans[5,6]. The viral hemorrhagic fevers (VHFs) represent a group of diverse animal and human diseases caused by RNA viruses belonging to four distinct families

including Arenaviridae, Filoviridae, Bunyaviridae and Flaviviridae. The severity and clinical symptoms of VHFs may significantly change depending on different factors: the type of causative agent, and the epidemiological and clinical features of host. In general, all patients show evidences of fever and coagulation abnormalities that may lead to disseminated intravascular coagulation, multiple organ failure, signs of shock and eventually death. The VHF can be severe and life-threatening, and it may occur as isolated cases, such as cases imported from endemic areas, or may cause a devastating lethal outbreak. Human sporadic and outbreak cases have been reported with high case-fatality rates, involving social and economical disruption[7].

2.1. Structures

Filoviruses are enveloped particles with a non-segmented, single-stranded, negative-sense RNA genome, approximately 19 kb in size. EBOV and MARV genomes encode seven structural proteins, and also EBOV encodes two nonstructural soluble glycoproteins (GP): soluble GP and small soluble GP. All known MARV strains consist of one species *Lake Victoria marburgvirus*, while EBOV strains consist of four different species: *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus* (SEBOV), *Côte d'Ivoire ebolavirus* (CIEBOV) and *Reston ebolavirus* (REBOV). The newly discovered *Bundibugyo ebolavirus* (BEBOV) has been proposed as the fifth species. The species vary in their apparent pathogenicity in humans; ZEBOV is the most pathogenic (up to 90% case fatality rate), followed by SEBOV (approximately 50% case fatality rate) and BEBOV (approximately 40% case fatality rate). CIEBOV and REBOV cause lethal infections in nonhuman primates, but not being associated with fatal human cases yet[1,8].

By systematic viral replication, EBOV and MARV result in the release of high levels of inflammatory cytokines, coagulation abnormalities and fluid distribution problems. These processes are observed as hemorrhage and vascular leakage; ultimately these may lead to multiple organ failure and shock[9,10].

ZEBOV was first discovered in 1976, being the most virulent species with case fatality rates in humans up to 90% and as high as 100% lethality in experimental macaque models, the current gold standard animal model for ZEBOV among other established models[11].

2.2. Reservoir

Recent evidence has confirmed the importance of bats as potential reservoir species of filoviruses; however, it is unclear whether other species are also involved or how transmission to humans and/or