An Overview Of Ebola Virus Disease

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Abstract

Ebola virus is an aggressive pathogen that causes a highly lethal hemorrhagic fever syndrome in humans and nonhuman primates. Ebola Virus Disease (EVD) is characterized by the sudden onset of fever and malaise accompanied by other nonspecific signs and symptoms such as myalgia, headache, vomiting, and diarrhea. Among EVD patients, 30%–50% experience hemorrhagic symptoms. In severe and fatal forms, multiorgan dysfunction including hepatic damage, renal failure, and central nervous system involvement occur, leading to shock and death. The wildlife reservoir has not been definitively ascertained; however evidence supports fruit bats as one reservoir. The virus initially spreads to the human population after contact with infected wildlife and is then spread person-to-person through direct contact with body fluids. The incubation period is 2–21 days. Prevention includes decreasing the spread of disease from infected animals to humans. Properly cooking meat and wearing protective clothing when handling meat may also be helpful. Samples of bodily fluids and tissues from people with the disease should be handled with special caution. There is currently no antiviral therapy or vaccine that is effective against Ebola virus infection in humans. Efforts to help those who are infected are supportive and include giving either oral rehydration therapy or intravenous fluids. The disease has a high risk of death, mortality between 50% and 90% of those infected with the virus.

Key words: Ebola virus, Ebola hemorrhagic fever.

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Introduction

Ebola virus are members of the Filovirus family, most similar to the Paramyxoviridae contain linear nonsegmented, single-stranded non-infectious RNA genomes of negative polarity that possesses inverse-complementary 3' and 5' termini.[1] Ebola virus genomes are approximately 19 kilobase pairs long and contain seven genes . Of the four identified strains of Ebola virus, three—the Zaire, Ivory Coast, and Sudan strains—have been shown to cause disease in both humans and nonhuman primates, with the Zaire strain exhibiting the highest lethality rate.[2]

Ebola virus was first isolated in 1976 during outbreaks of Ebola hemorrhagic fever in the Democratic Republic of the Congo (then Zaire)[3] and Southern Sudan.[4] The name of the disease originates from the first recorded outbreak in 1976 in Yambuku, Democratic Republic of the Congo, which lies on the Ebola River.[3] This genus was introduced in 1998 as the "Ebola-like viruses".[5,] In 2002 the

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name was changed to Ebolavirus [6] and in 2010, the genus was amended. The genus Ebola virus is closely related to the Marburg virus.[7]

Epidemiology

The disease typically occurs in outbreaks in tropical regions of Sub-Saharan Africa.[8] From 1976 (when it was first identified) through 2013, the World Health Organization (WHO) reported 1,716 confirmed cases. The largest outbreak to date is the ongoing 2014 West Africa Ebola virus outbreak, which is affecting Guinea, Sierra Leone, Liberia and Nigeria. [9] As of 13 August, 2014, 2,127 cases have been identified, with 1,145 deaths.[10]

Symptoms of Ebola Virus Disease

Typically, Ebola virus infection runs its course within 14 to 21 days. Infection initially presents with nonspecific flu-like symptoms such as fever, myalgia, and malaise. As the infection progresses, patients exhibit severe bleeding and coagulation abnormalities, including gastrointestinal bleeding, rash, and a range of hematological irregularities, such as lymphopenia and neutrophilia.[11] Cytokines are released when reticulo-endothelial cells encounter virus, which can contribute to exaggerated inflammatory responses that are not protective. Damage to the liver, combined with massive viremia, leads to disseminated intravascular coagulopathy. The virus eventually infects microvascular endothelial cells and compromises vascular integrity. The terminal stages of Ebola virus infection usually include diffuse bleeding, and hypotensive shock.[12]

Transmission

It is not entirely clear how Ebola is spread. Human-to-human transmission can occur via direct contact with blood or body fluids from an infected person (including embalming of an infected dead person) or by contact with contaminated medical equipment, particularly needles and syringes.[13] Because dead bodies are still infectious local traditional burial rituals may spread the disease. Semen may be infectious in survivors for up to 50 days. Medical workers who do not wear appropriate protective clothing may also contract the disease. In the past, hospital-acquired transmission has occurred in African hospitals due to the reuse of needles and lack of universal precautions.[14] Air borne transmission has not been documented during EVD outbreaks. They are, however, infectious as breathable 0.8– to 1.2-µm laboratory-generated droplets. Bats drop partially eaten fruits and pulp, then land mammals such as gorillas and duikers feed on these fallen fruits. This chain of events forms a possible indirect means of transmission from the natural host to animal populations, which has led to research towards viral shedding in the saliva of bats.[15]

Reservoir

Bats are considered the most likely natural reservoir of the Ebola virus. Plants, arthropods, and birds have also been considered.[16] Transmission between natural reservoir and humans is rare, and outbreaks are usually traceable to a single case where an individual has handled the carcass of gorilla, chimpanzee or duiker.[17]

Pathophysiology

Endothelial cells, mononuclear phagocytes and hepatocytes are the main targets of infection. 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. These white blood cells also serve as carriers to transport the virus throughout the entire body to places such as the lymph nodes, liver, lungs, and spleen.[18] The presence of viral particles and cell damage resulting from

budding causes the release of cytokines like TNF- , 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.[19]

Diagnosis

The medical history, especially travel and work history along with exposure to wildlife are important to suspect the diagnosis of EVD. The diagnosis is confirmed by isolating the virus, detecting its RNA or proteins, or detecting antibodies against the virus in a person's blood. Isolating the virus by cell culture, detecting the viral RNA by polymerase chain reaction (PCR) and detecting proteins by enzyme-linked immunosorbent assay (ELISA) is effective early and in those who have died from the disease. Detecting antibodies against the virus is effective late in the disease and in those who recover.[20]

During an outbreak, virus isolation is often not feasible. The most common diagnostic methods are therefore real time PCR and ELISA detection of proteins, which can be performed in field or mobile hospitals.[21] Filovirions can be seen and identified in cell culture by electron microscopy due to their unique filamentous shapes, but electron microscopy cannot tell the difference between the various filoviruses despite there being some length differences.[22]

Differential diagnosis

The symptoms of EVD are similar to those of Marburg virus disease.[23] It can also easily be confused with many other diseases common in Equatorial Africa such as other viral hemorrhagic fevers, falciparum malaria, typhoid fever, shigellosis, rickettsial diseases such as typhus, cholera, gram-negative septicemia, borreliosis such as relapsing fever. Other infectious diseases that should be included in the differential diagnosis include the following: leptospirosis, scrub typhus, plague, Q fever, candidiasis, histoplasmosis, trypanosomiasis, visceral leishmaniasis, hemorrhagic smallpox, measles, and fulminant viral hepatitis.[24] Non-infectious diseases that can be confused with EVD are acute promyelocytic leukemia, hemolytic uremic syndrome, snake envenomation, clotting factor deficiencies/platelet disorders, thrombotic thrombocytopenic purpura, hereditary hemorrhagic telangiectasia, Kawasaki disease and even warfarin poisoning.[25]

Infection control

Ebola viruses are highly contagious. Prevention predominantly involving behavior changes, proper full-body personal protective equipment, and disinfection. Techniques to avoid infection involve not contacting infected blood or secretions, including from those who are dead. This involves suspecting and diagnosing the disease early and using standard precautions for all patients in the healthcare setting.[26] Recommended measures when caring for those who are infected include isolating them, sterilizing equipment, and wearing protective clothing including masks, gloves, gowns, and goggles. Hand washing is important but can be difficult in areas where there is not even enough water for drinking. The Ebola virus can be eliminated with heat (heating for 30 to 60 minutes at 60 °C or boiling for 5 minutes). On surfaces, some lipid solvents such as some alcohol-based products, detergents, sodium hypochlorite (bleach) or calcium hypochlorite (bleaching powder), and other suitable disinfectants at appropriate concentrations can be used as disinfectants.[27]

Quarantine

Quarantine, also known as enforced isolation, is usually effective in decreasing spread. Governments often quarantine areas where the disease is occurring or individuals who may be infected. In the United States, the law allows quarantine of those infected with Ebola.

During the 2014 outbreak, Liberia closed schools. [28]Those who have been exposed to someone with the disease should be closely observed for 21 days.

Treatment

No Ebola virus-specific treatment exists. Treatment is primarily supportive in nature. These measures may includes: pain management, medications for nausea, fever and anxiety, as well as fluids by mouth or by intravenous. Blood products such as packed red blood cells, platelets or fresh frozen plasma may also be used. Other regulators of coagulation have also been tried including heparin in an effort to prevent disseminated intravascular coagulation and clotting factors to decrease bleeding.[29] Early treatment may increase the chance of survival.

A number of experimental treatments are being studied. In the United States, the food & drug administration's (FDA) animal efficacy rule is being used to demonstrate reasonable safety to obtain permission to treat people who are infected with Ebola. It is being used as the normal path for testing drugs is not possible for diseases caused by dangerous pathogens or toxins. Experimental drugs are made available for use with the approval of regulatory agencies under named patient programs, known in the US as "expanded access".[30] The FDA has allowed two drugs, ZMapp and an RNA interference drug called TKM-Ebola, to be used in people infected with Ebola under these programs during the 2014 outbreak.

Prognosis

The disease has a high mortality rate: often between 50 percent and 90 percent. As of April 2014, information from WHO across all occurrences to date puts the overall fatality rate at 60%-65%. There are indications based on variations in death rate between countries that early and effective treatment of symptoms (e.g., supportive care to prevent dehydration) may reduce the fatality rate significantly.[31] If an infected person survives, recovery may be quick and complete. Prolonged cases are often complicated by the occurrence of long-term problems, such as inflammation of the testicles, joint pains, muscle pains, skin peeling, or hair loss. Eye symptoms, such as light sensitivity, excess tearing, iritis, iridocyclitis, choroiditis, and blindness have also been described. Ebola virus may be able to persist in the semen of some survivors for up to seven weeks, which could give rise to infections and disease via sexual intercourse. [32]

Vaccine

No vaccine is currently available for humans. The most promising candidates are DNA vaccines or vaccines derived from adenoviruses, vesicular stomatitis Indiana virus (VSIV) or filovirus-like particles (VLPs) because these candidates could protect nonhuman primates from ebolavirus-induced disease. DNA vaccines, adenovirus-based vaccines, and VSIV-based vaccines have entered clinical trials.[33]

Research

A 2013 study isolated antibodies from fruit bats in Bangladesh, against Ebola Zaire and Reston viruses, thus identifying potential virus hosts and signs of the filoviruses in Asia.[34]

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