



‘Ebola Virus Disease’

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Abstract

Ebola virus disease was first identified in 1976 in Sudan and the Democratic Republic of the Congo (formerly Zaire). It is named after a river in the Democratic Republic of the Congo. Since its discovery, there have been several Ebola outbreaks, primarily limited to remote villages near tropical rainforests in Central and West Africa.

Keywords: Introduction, Causes, Symptoms, Diagnosis, Treatment, Prevention.

Introduction

A notoriously deadly virus that causes severe symptoms, the most prominent being high fever and massive internal bleeding. Ebola virus kills as many as 90% of the people it infects. It is one of the viruses that is capable of causing hemorrhagic (bloody) fever. Epidemics of Ebola virus have occurred mainly in African countries including Zaire (now the Democratic Republic of Congo), Gabon, Uganda, the Ivory Coast, and Sudan. Ebola virus is a hazard to laboratory workers and anyone who is exposed to it. Ebola virus is transmitted by contact with blood, faeces, or body fluids from an infected person or by direct contact with the virus, as in a laboratory. The incubation period --the period between contact with the virus and the appearance of symptoms -- ranges from 2 to 21 days. The initial symptoms are usually high fever, headache, muscle aches, stomach pain, and diarrhea. There may also be sore throat, hiccups, and red and itchy eyes. The symptoms that tend to follow include: vomiting, rash, and bleeding problems

that include bloody nose (epistaxis), spitting up blood from the lungs (hemoptysis).

Causes: Ebola outbreaks occur when the virus is transmitted first from an infected animal to a human and then between humans. The viral infection is spread from animals to humans through contact with infected wildlife such as fruit bats, chimps, and gorillas. Certain fruit bats are believed to be the natural hosts for the Ebola viruses.

EVD is transmitted from person to person by direct contact (through broken skin and mucous membrane) via bodily fluids or secretions from infected people, such as:

- blood
- breast milk
- semen (up to 61 days after infection)
- sweat
- stool
- urine
- vomit

Transmission can also occur through contact with objects contaminated with these fluids and the bodies of the deceased with EVD. Since the bodies of the deceased can infect those who handle them, safe burial practises are extremely important in containing outbreaks. The infection can be spread further by cultural burial practises such as ritual washings that bring people into close contact with infected bodies.

Ebola Symptoms & Signs

Symptoms of Ebola virus infection are similar to those produced by other hemorrhagic fever viruses and include

- fever,
- fatigue, malaise, and weakness,
- reddened eyes,
- joint and muscle pain,
- headache,
- nausea and vomiting.

Additional Ebola symptoms may include

- diarrhea,
- cough, sore throat, and difficulty swallowing,
- rash,
- hiccups,
- chest pain,
- breathing problems.

As the disease worsens in severity, symptoms can include bleeding at various sites within or outside of the body.

Diagnosis

Due to the fact that most Ebola infection symptoms such as weakness, fever, headache, and muscle pains are not specific to the disease, more common diseases need to be ruled out first, especially during the early stages of the infection when diagnosis is difficult to make. Common diseases with similar symptoms include malaria, typhoid fever, and cholera. The person's medical history is also looked at, with particular interest in whether the person was in contact with possible infected individuals or animals. People with suspected EVD should be quarantined while

waiting for definitive diagnosis by laboratory tests.

There are many laboratory tests that can be used to diagnose Ebola virus disease. It is commonly and quickly done through detection of RNA and antibodies of the Ebola virus in the blood. In simple terms, these tests detect traces of the virus itself or our bodies' defence response against the virus.

Ebola hemorrhagic fever

Ebola hemorrhagic fever is a viral disease caused by Ebola virus (a member of the *Filoviridae* family) that results in nonspecific symptoms (see symptom section of this article) early in the disease and often causes internal and external hemorrhage (bleeding) as the disease progresses. Ebola hemorrhagic fever is considered one of the most lethal viral infections; the mortality rate (death rate) may be very high during outbreaks (reports of outbreaks range from about 50%-100% of people infected, depending on the Ebola strain); consequently, the survival rate may range from about 50% to zero. Because most outbreaks occur in areas where high-level intensive care supportive services are not available, survival rates are difficult to translate to potential outbreaks in areas with more resources.

History of Ebola hemorrhagic fever

Ebola hemorrhagic fever first appeared in Zaire (currently, the Democratic Republic of the Congo or DRC or Congo) in 1976. The original outbreak was in a village named Yambuku near the Ebola River after which the disease was named. During that time, researchers identified the virus in person-to-person contact transmission. Of the 318 patients diagnosed with Ebola, 88% died.

Since that time, there have been multiple outbreaks of Ebola virus, and researchers have identified five strains; four of the strains are responsible for the high death rates. The four Ebola strains are termed as follows: Zaire, Sudan, Tai Forest, and Bundibugyo virus, with Zaire Ebola virus being the most lethal strain. Researchers have found a fifth strain termed Reston in the Philippines. The strain infects

primates, pigs, and humans and causes few if any symptoms and no deaths in humans. Most outbreaks of the more lethal strains of Ebola have occurred in sub-Saharan West Africa and mainly in small- or medium-sized towns. Health care professionals believe bats, monkeys, and other animals maintain the non-human virus life cycle in the wild; humans can become infected from handling and/or eating infected animals.

Once an Ebola outbreak is recognized, African officials isolate the area until the outbreak ceases. However, in the last outbreak that began in West Africa in March 2014, some of the infected people reached larger city centers before the outbreak was recognized; this caused further spread. The infecting Ebola virus detected during this outbreak was the Zaire strain, the most pathogenic strain of Ebola. Health agencies are terming this outbreak as an "unprecedented epidemic." This epidemic spread quickly in the West African countries of Guinea and Sierra Leone. In addition, countries of Liberia, Nigeria, Senegal, Uganda, and Mali all reported confirmed infections with Ebola. In addition, a few infections or flare-ups of Ebola virus infection appeared in the United States, Spain, and the United Kingdom; most of the people with Ebola in these countries either were imported infections from West Africa or were newly spread infections from treating patients who originally became infected in Africa. Another outbreak occurred in the DRC in May 2018 in Bikoro, a small town 80 miles from Mbandaka, with 46 reported infections and 26 deaths. Unfortunately, the large city of Mbandaka, with over 1 million people, has recorded at least three people with Ebola. The DRC hopes to isolate or stop the spread of Ebola in the two areas by vaccinating anyone who may have had some physical contact with an infected person with a new chimeric virus vaccine that in 2015 showed good results in Ebola-infected patients.

Ebola virus contagious

Ebola viruses are highly contagious once early symptoms such as fever develop. The infected patient sheds infectious viruses in all body secretions (bodily fluids); direct contact with any of these secretions may cause the virus

transmission to uninfected individuals. The Centers for Disease Control and Prevention (CDC) suggests that infection with Ebola that is airborne is theoretically possible but unlikely.

What causes Ebola hemorrhagic fever

The cause of Ebola hemorrhagic fever is Ebola virus infection that results in coagulation abnormalities, including gastrointestinal bleeding, development of a rash, cytokine release, damage to the liver, and massive viremia (large number of viruses in the blood) that leads to damaged vascular cells that form blood vessels. As the massive viremia continues, coagulation factors are compromised and the microvascular endothelial cells are damaged or destroyed, resulting in diffuse bleeding internally and externally (bleeding from the mucosal surfaces like nasal passages and/or mouth and gums and even from the eyes [termed conjunctival bleeding]). This uncontrolled bleeding leads to blood and fluid loss and can cause hypotensive shock that causes death in many Ebola-infected patients.

Contagious period for the Ebola virus - For those patients who survive infection, they may remain contagious for approximately 21-42 days after symptoms abate. However, health care professionals can remove the viruses from semen, breast milk, spinal column, and ocular fluids. It is unclear, according to the CDC, if these fluids can transmit viruses, although the CDC suggests that Ebola can be spread by semen and suggest male survivors of the disease abstain from sex or use a condom for all sexual activity.

Treatment and Prevention

There is currently no cure for Ebola virus disease, nor are there any vaccines available to prevent infection. Treatment is supportive and typically involves rehydration, nutrition, and medications to manage symptoms (pain, fever, vomiting, etc.). The majority of people with EVD die from severe dehydration, so early supportive treatment is critical in improving the chances of survival.

Since there is no cure for the disease, the key in limiting outbreaks is to prevent transmission from animals to humans and between humans. There are several measures that need to be in place, including:

- rapid quarantine of suspected infected animals – these animals should then be buried or burned promptly
- handling all animals and their waste with gloves and other protective clothing cooking animal products (meat and blood) thoroughly before eating
- safe burial practises
- wearing protective gear such as gloves and other personal protective equipment (such as face protection and long-sleeved gowns) when dealing with infected patients
- safe injection practises
- regular hand washing
- sanitation and sterilization of the environment and instruments
- identification and isolation of infected individuals from the community
- tracing contacts, including those during the incubation period

Ebola Vaccines:

Ebola virus disease (EVD) emerged at unprecedented epidemic levels in West Africa in 2014. Whereas previous EVD outbreaks were contained fairly quickly, this epidemic spread to crowded urban areas where transmissions continued unabated for many months.

Retrospective analysis indicates that the first case of the disease may have occurred at the end of 2013. An 18-month-old boy in a small village in Guinea became ill and died in late December, and the disease began to spread. It wasn't until late March 2014 that the disease-causing agent was identified as Ebola virus. Through the fall of 2014, the epidemic was ongoing in Sierra Leone, Guinea, and Liberia. Nigeria and Senegal had small outbreaks related to importations from neighboring countries, but public health authorities there were able to contain spread of the disease. Several cases and deaths were reported from Mali, but spread was limited. In total, by the time the epidemic was over in March

2016, 11,325 confirmed, probable, and suspected deaths occurred. Total EVD cases numbered 28,652. Transmission of the disease was limited to West African countries, with the exception of several transmissions in healthcare settings in Europe and the United States. Two U.S. nurses and one Spanish nurse became ill from contact with patients who acquired the disease in West Africa. The nurses recovered.

Ebola virus disease has no cure, but supportive care in a hospital setting can increase a patient's chance for survival. Additionally, plasma transfusions from convalescent patients and an experimental antibody preparation have been used to treat certain patients. It is not possible to say at this time whether these treatments have had an effect on the course of the disease in the patients who received them.

Ebola virus was first identified in 1976. By the end of that year, two related strains of the virus were known--Ebola Zaire and Ebola Sudan. Three other strains are now known to exist. Vaccine development began in the late 1970s:

results from a test of inactivated Ebola vaccine in guinea pigs were published in *Lancet* in 1980. Because EVD outbreaks are rare and have, until 2014, been controlled quickly, commercial vaccine manufacturers have demonstrated little urgency in advancing vaccines through clinical trials. That changed in 2014: several vaccines previously tested only in animals are being fast-tracked into Phase 1 clinical trials.

ClinicalTrials.gov, a global registry of trials involving human subjects, lists several Ebola vaccine trials in progress. Ebola Zaire is the strain of the virus that is responsible for the 2014 outbreak; accordingly, all of the vaccine candidates being advanced are designed to prevent that strain. If these vaccines work for Ebola Zaire, it is very likely that the same principles can be applied to the other strains.

The two front-running vaccine candidates are a GSK chimpanzee adenovirus vector vaccine (including several versions of it) and a Merck/NewLink Genetics recombinant vaccine. Both are being tested in a single Phase 2 trial in

Liberia in those at risk for EVD. The trial is being run by NIAID/NIH and began recruiting participants in fall 2015.

The Ebola vaccine licensed by NewLink Genetics in Ames, Iowa, was originally developed by the Public Health Agency of Canada, which still holds intellectual property rights for it. The vector for this monovalent Ebola Zaire vaccine is an attenuated vesicular stomatitis virus -- a virus, like rabies virus, in the *Rhabdoviridae* family. Vesicular stomatitis virus (VSV) can infect humans though this is a self-limited infection. A safe VSV vaccine for animals has been developed for animal use but it is not currently marketed in the United States.

The version of the GSK Ebola vaccine in the Phase 2 trial is monovalent and offers protection from Ebola Zaire only. This vaccine uses an adenovirus to deliver key Ebola antigens to human cells. Adenoviruses can cause a variety of diseases, but attenuated adenoviruses are safe and have been studied as vaccine vectors. A related bivalent (Ebola Zaire and Ebola Sudan) chimpanzee adenovirus vaccine is being tested in a Phase 1 trial at the NIH Clinical Center.

A vaccine candidate originating from Thomas Jefferson University's Vaccine Center may advance to clinical trials in humans. This vaccine, developed by Jefferson's Matthias Schnell, delivers Ebola antigens with an inactivated rabies virus vector. Versions of the vaccine, which have also delivered both Ebola Zaire and Ebola Sudan antigens as well as Marburg virus antigens, have been tested in macaques. Funding from the National Institute of Allergy and Infectious Diseases and the Department of Defense allowed production of a clinical lot of the vaccine for a potential Phase 1 trial.

Johnson & Johnson has a prime-boost Ebola vaccine in development. This two-phase strategy starts with direct exposure to DNA (the "prime") followed by offering the same or similar antigen in a virus that does not replicate well in human tissue ("the boost"). This approach has been shown in a variety of settings to yield a robust immune response to the antigen of interest.

The Phase 1 trial starts in January 2015 in the United States and Europe. The first dose of the vaccine uses a DNA vaccine that primes the immune system to make Ebola Zaire and Ebola Sudan surface proteins; the boost vaccine is based on a recombinant adenovirus vector that delivers an Ebola Zaire surface protein.

More Phase 2 and 3 vaccine trials are already being planned. In many cases, trial participants will be those at high risk of contracting the disease, such as healthcare workers and family members of people who have EVD.

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Ashikujaman Syed. (2019). Ebola Virus Disease. Int. J. Curr. Res. Med. Sci. 5(3): 18-23.
DOI: <http://dx.doi.org/10.22192/ijcrms.2019.05.03.004>