WHY IS IT AN EMERGING ISSUE?

Since the first few cases of suspected hemorrhagic fevers were reported in a remote forested area of the south-eastern region of Guinea in February 2014, > 9000 clinical cases have been identified, and the outbreak has claimed more than 4500 lives and jumped borders to Sierra Leone, Liberia, Mali and Nigeria.

EBOLA HEMORRHAGIC FEVER

Guinea in West Africa is currently suffering from one of the largest outbreaks of ebola virus disease in history.

By Thea Fischer

The fear is that the outbreak will sweep through a region with weak public health infrastructure, where basic control measures such as prevention and quarantines of suspected cases are challenged by decades of political dictatorship, strong fear and lack of trust in national governmental injunctions.

SIGNS AND SYMPTOMS

Ebolavirus constitutes together with *Marburgvirus* and *Lassafevervirus* the three African hemorrhagic fever viruses. *Ebolavirus* leads to a severe, often fatal hemorrhagic fever disease in humans and nonhuman primates. Ebola virus disease (formerly known as ebola hemorrhagic fever) has an incubation period of 2 to 21 days though 8-10 days are most common. The infected person will typically suffer from an array of symptoms such as fever, chills, breathing difficulties, joint and muscle pain (influenza-like illness),

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vomiting, diarrhea and renal impairment. As the infection progresses, cases will typically experience a rash over their entire body, swelling of the eyes and genital area, unstoppable bleeding from the mouth, nose, eyes, ears, and rectum, followed by shock, coma, and death in many cases. Currently neither a vaccine (development ongoing) nor an effective treatment is available. Severely ill patients require intensive supportive care.

EBOLA VIRUS DISEASE

- Ebolavirus causes a severe, often deadly disease, which is characterized by fever and bleeding. (= hemorrhagic fever disease)
- Once humans are infected with Ebolavirus, they become very contagious
- Currently no vaccine or effective treatment is available.
- Epidemics have occurred in the Democratic Republic of Congo, Sudan, Gabon, Republic of Congo, and Uganda.
- Healthcare facilities are often involved in outbreaks: close human-to-human interactions and challenging hygienic conditions provide a perfect environment for rapic virus spread.
- Where Ebolavirus is hiding in between outbreaks is still a mystery

VIROLOGY

Ebolavirus is named after a river in what is now known as the Democratic Republic of Congo where one the world's first Ebola outbreak occurred in 1976. Since then 5 species of *Ebolavirus* each named after a geographical location (most often in remote African villages in near proximity to a tropical rainforest) have been identified: Zaire, Sudan, Taï Forest (formerly Ivory Coast), Bundibugyo and Reston.

Ebola virus disease is caused by a single-stranded RNA virus belonging to the *Filoviridae* family. Filoviruses are characterized with a filamentous virion and the threadlike structure appearing on electron micrographs .

Ebola virus disease is associated with a case fatality rate of 30 to 90%, depending on the virus species, with the Zaire ebola virus being associated with the highest case fatality. Specific conditions in hospitals and communities in Africa facilitate the spread of the disease from human to human.

Three ebolavirus species have caused large outbreaks in sub-Saharan Africa: *Zaire ebolavirus (EBOV)*, *Sudan ebolavirus,* and the recently described *Bundibugyo ebolavirus*. Epidemics have occurred in the Democratic Republic of Congo, Sudan, Gabon, Republic of Congo, and Uganda. *Tai Forest ebolavirus* was documented in a single human infection caused by contact with an infected chimpanzee from the Tai Forest in Ivory Coast. Although this event indicated the presence of *Tai Forest ebolavirus* in West Africa, this subregion has not been considered to be an area in which *Zaire ebolavirus/EBOV* was endemic.

Ebola-Reston is the only known Filovirus that does not cause severe disease in humans; and it was discovered in a laboratory outbreak of monkey imported from the Philippines in the town Reston in USA. Ebola-Reston proved fatal in monkeys and has recently been recovered from infected swine in South-east Asia (China).

Although the *Ebolavirus* detected in Guinea shows a very high genetic similarity (>98%) to the *Zaire ebolavirus*/EBOV, full-length genome sequencing and phylogenetic analyses have demonstrated that the new Guinea *Ebolavirus* strains form a separate clade in relationship to the known *Zaire Ebolavirus*/EBOV strains from the Democratic Republic of Congo and Gabon. In other words Guinea is most likely facing an outbreak of an entirely new *Ebolavirus* strain.

TRANSMISSION

The natural reservoir host of *Ebolavirus* is unknown although bats, and in particular fruit bats of the *Pteropodidae* family are suspected to be involved in the transmission of virus to human and nonhuman primates such as monkeys, gorillas, and chimpanzees. *Ebolavirus* has been documented to be introduced into the human population through close contact with blood, body-fluids, or organs of infected animals. 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.

Ebola then spreads in the community through human-to-human transmission, either through direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, or indirect contact with contaminated environments. Burial ceremonies in which mourners have direct contact with the body of the deceased and/or the body fluids while participating in ritual washing procedures of the deceased person can also play a role in the transmission of *Ebolavirus*. Men who have recovered from the disease can

FACT BOX

Case fatality rate: Proportion of individuals with a particular condition (cases), who die from that condition.

IgM: Immunoglobulin M is the largest antibody and circulates in blood and lymph.

IgG: Immunoglobulin G is the most abundant antibody found in circulation.

MERS-CoV: Middle East Respiratory Syndrome coronavirus

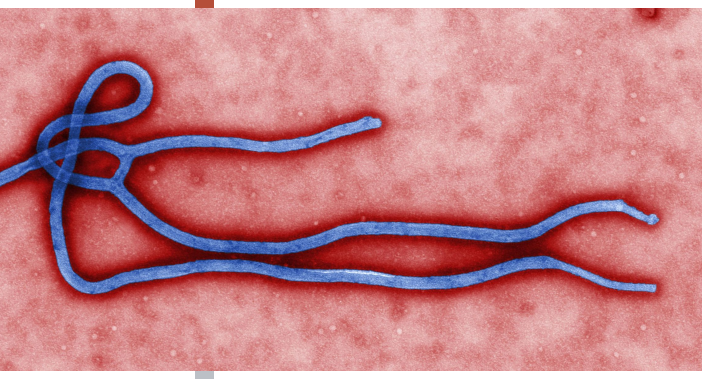
PCR: Polymerase chain reaction, is a method for fast amplification/copying small segments of DNA

RNA: Ribo-nucleic-acid

SARS: Severe Acute Respiratory Syndrome

still transmit the virus through their semen for up to 2 months after recovery from illness.

Healthcare facilities are often involved in the major hemorrhagic fever outbreaks as they often present the perfect environment for rapid virus spread with close human-to-human interactions and challenging hygienic conditions. This is often the case particularly in the early phases of the outbreak before proper personal protection equipment such as masks, goggles, gowns and gloves are in place. Once humans are infected with *Ebolavirus*, they become highly contagious and the infectivity increases towards the final stage of the disease where viruses are replicating at high speed in their host's organs while disintegrating these.



Ebola virus virion

This colorized transmission electron micrograph (TEM) revealed some of the ultrastructural morphology displayed by an Ebola virus virion.

Photo Credit: DCD/Cynthia Goldsmith

The first known outbreaks of ebola virus disease occurred simultaneously in 1976 Nzara, Sudan and in Yambuku, the Democratic Republic of Congo (then known as Zaire). Approximately 300 people became infected during both outbreaks and the case fatality rate was 53% in Sudan and 88% in Zaire making the Zaire *Ebolavirus* strain the most deadly. The outbreak in Yambuku occurred in a small clinic and hospital driven by catholic nuns. Here 11 of the 17 nuns and missionary health care professionals died during the outbreak which otherwise mainly affected local pregnant women and young children. The outbreak was traced to the nun's use of contaminated needles used during the mission's vaccination campaigns. A total of 318 cases were identified of which 280 died (case-fatality: 88%) before the outbreak was contained by quarantining local villagers in their communities and sterilizing all medical equipment and ensuring personal protective gear to all professionals serving in the control of the outbreak.

Smaller outbreaks have occurred in 1977 and 1979 in the same regions and sporadic outbreaks of the Zaire and Sudan Ebola subtypes have erupted over the succeeding

years in the Democratic Republic of the Congo, Gabon, Uganda, and Sudan. *Ebolavirus* most recently resurfaced in September of 2007 in the Democratic Republic of the Congo. In total, there have been over 1800 cases of human Ebola infections and nearly 1300 deaths.

DIAGNOSIS

Biological sample material from ebola patients constitutes an extreme biohazard risk and testing should therefore only be conducted under maximum biological containment conditions.

During the early phase of disease either reverse transcriptase polymerase chain reaction (RT-PCR), antigen-capture enzyme-linked immonosorbent assays (ELISA), IgM ELISA or virus isolation can be used. Later in disease course or during recovery IgM and IgG ELISA can be used. The most commonly differential diagnoses include malaria, severe gastrointestinal bacterial infections (e.g. typhoid fever, shigellosis, and cholera), leptospirosis, meningitis, hepatitis and other viral hemorrhagic fevers as Marburg and Lassavirus fever.

THE MYSTERY OF EBOLAVIRUSES

Where are *Ebolavirus* hiding in between outbreaks? The knowledge of the natural reservoir is of great importance in order to establish the geographic range and ecological areas where humans need to be conscious about the risk and need to take preventive measures in order to avoid contact with insects and/or animals which might be transmitting the virus. Furthermore, this insight will allow governments and health professionals to move fast and rapidly implement relevant outbreak containing measures.

Since 1994 *Ebolavirus* has been known to infect and kill gorillas. In particular the Western lowland gorillas have suffered severely from ebolavirus disease. During the years of 2001 – 2003 researchers use traps to catch small rodents and other animals caught in close proximity to corpses of

Ebolavirus-infected gorillas and chimpanzees. Here three species of captured fruit bats showed evidence of asymptomatic infection with the Zaire and Tai Forest *Ebolavirus* subtypes. Fruit bats are common in the geographical regions where ebola outbreaks have occurred. Fruit bats are considered a delicacy as bats are often grilled over an open flame or boiled in a spicy soup with peppers and other ingredients. Bats have been implicated as a reservoir of other deadly viruses such as SARS,MERS-CoV, Nipah virus and Marburgvirus.

To combat the spread of this deadly disease, Guinean officials took the unusual step of banning the consumption of bat soup, grilled bat and other local delicacies in March 2014. More recent prevention and control initiatives include mobilization of expertise (in the areas of coordination, medical anthropology, clinical case management, data management and health informatics, surveillance and epidemiology, infection prevention and control, laboratory services, logistics, risk communications, social mobilization, finance and administration) providing a suite of innovative community sensitizations and social mobilization activities with mining companies, community leaders, educational institutions as well as local non-governmental organizations.

Further, dissemination of information about EVD disease and prevention of disease transmission via rural community radio broadcastings of awareness messages and public informative posters and door-to-door education about EVD in affected villages has also been introduced. However, so far the preventive measures have not proven sufficient to stop the outbreak which is still spreading, and hopefully sooner than later other and more effective preventive measures will succeed in containing this devastating ebola outbreak in West Africa.

1976 photograph of two nurses standing in front of a patient with Ebola virus disease. She died only a few days later due to severe internal hemorrhaging.
Photo Credit: Wikipedia

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