The 2013-2015 Ebola outbreak in West Africa

Ji-Hoon Kang, Weon young Chang, Sungwook Choi, Joseph Rho and Keun Hwa Lee*

Jeju National University School of Medicine, Jeju, South Korea

Zaire Ebola virus (EBOV) is a fatal human pathogen, with a high case fatality rate (CFR) averaging up to 78%. In March 2014, the World Health Organization (WHO) was made aware of a ZEBOV outbreak in rural Guinea, West Africa. Epidemiologic investigation linked the clinical and laboratory confirmed cases with the presumed first fatality of the outbreak in December 2013. EBOV from Guinea is a separate clade from other ZEBOV strains reported from the Democratic Republic of Congo (DRC) and Gabon. Since the outbreak in March, ZEBOV was also reported in Conakry, Guinea’s capital and spread to other neighboring countries. In its largest outbreak, ZEBOV disease expanded through Guinea, Liberia, Sierra Leone, and Nigeria and to Spain, the USA, and the UK. The WHO declared the 2013-2015 West African Ebola epidemic a public health emergency of international concern considering its presumable capacity for further international spread. Early manifestations of EVD (Ebola virus disease) include a high fever, body aches, malaise, and fatigue. Severe diarrhea and other gastrointestinal manifestations such as vomiting were common, while bleeding was a more sporadic finding. The fatality rate was 43% and highest in patients aged ≥ 45 years and the overall fitted mean incubation period was 10.3 days (95% CI 9.9~10.7). We present a review of the literature on the emergence of Ebola, and the epidemiologic, clinical, and laboratory records of patients in whom EVD was diagnosed in Sierra Leone, Guinea, Liberia, Mali, the USA, and Spain, its zoonotic origin, and the transmission of ZEBOV, as well as presenting original literature on the current Ebola outbreak.

Key Words: EBOV (Zaire Ebola virus), Epidemiology, Clinical features, Late complications, Zoonotic origin, Transmission

I. INTRODUCTION

A case fatality rate (CFR) of Ebola virus disease (EVD) is 30 to 90%, depending on the virus species (1). Specific conditions in hospitals and communities in West Africa contribute to the human-to-human contagion of the disease (1). EBOV (formerly Zaire Ebola virus), Sudan Ebola virus (SEBOV), and the recently described Bundibugyo Ebola virus (BEBOV) are the three Ebola virus species that have caused large outbreak in sub-Saharan Africa. The Democratic Republic of the Congo (DRC), Sudan, Gabon, and Uganda have all suffered from the epidemics. While the Reston Ebola virus (REBOV) is widespread in the Philippines, it has yet to cause disease in humans but has done so in nonhuman primates such as pigs. Tai Forest Ebola virus (TEBOV), the fifth species, was reported in a single human infection caused by direct contact with an infected chimpanzee from the Tai Forest in Ivory Coast. Such detection confirmed the presence of Tai Forest Ebola virus in West Africa. However, this subregion was not considered to be an EBOV endemic region (2).
The 2013–2015 Ebola outbreak in West Africa

EBOV is a lethal human viral pathogen that causes EVD with an average CFR of 78%. The World Health Organization (WHO) has recognized a total of 24 outbreaks of EVD responsible for approximately 2,400 reported cases that had occurred between the first recognized outbreak of in 1976 and the onset of the West Africa Ebola epidemic in 2013-2015 (1, 3). Prior to such epidemics, there were only outbreaks restricted to remote regions of Middle Africa; the largest, having 318 cases in 1976 (4).

In March 2014, the WHO was made aware of an outbreak of Ebola virus disease (EVD) in a remote area of Guinea. This outbreak then quickly spread to encircling areas, making it the largest EVD epidemic thus far (Fig. 1) (1). The 2013-2015 current outbreak was evoked in February 2014 in Guinea, West Africa. The epicenter and site of its first introduction was the Guéckédou region in Guinea, which is a remote southeastern forest region. It then spread to Liberia in March, Sierra Leone in May, Nigeria in late July, and Mali in late September. The 25th known outbreak of EVD is dissimilar to any of the previous epidemics. Between July and October 2014, there was an additional outbreak involving 69 cases that happened in the DRC (2, 3).

EVD is identified as the causative agent of Ebola hemorrhagic fever, a severe form of viral hemorrhagic fever in

Figure 1. Geographical distribution of new and total confirmed cases in Three Countries in Africa. The map shows the districts that have been affected by EVD in Guinea, Liberia, and Sierra Leone. Yellow circles indicated the total number reported during 21 days and red circles indicated the total number reported during 7 days leading up to October 25, 2015. ©2015 World Health Organization
human, and is endemic in regions of central Africa. Not only this alone constitutes an important local public health menace in West Africa, but raises concern for its worldwide effects through imported infections and the fear of biological terrorism. There are no prophylaxes or remedy available for the EBOV (only supportive treatment available) and the CFR of the African Ebola virus species in human is as high as 90%. The clinical manifestation of EVD is in some ways similar to septic shock, both fundamentally involving immune suppression and a systemic inflammatory response that cause the deterioration of the vascular, coagulation, and immune systems, ultimately leading to multiorgan failure (MOF) and shock (2).

We present a review of the literature on the epidemiologic and clinical presentation of EBOV, the zoonotic origin of the West African Ebola epidemic, and the transmission of EBOV from 2013, as well as introducing original literature on the current Ebola outbreak.

II. The Emergence of EVD in Guinea 2013

In March 2014, the WHO received report of an outbreak of an infectious disease in Guinea characterized by fever, emesis, severe diarrhea, and a high fatality rate. Clinical microbiologic studies identified EBOV as the causative agent. Full-length genome sequencing of viral pathogen and phylogenetic analysis showed that the EBOV from Guinea is in fact a separate clade from other known EBOV strains from the Gabon and DRC. Through epidemiologic investigation, the confirmed cases were connected to a 2-year-old boy (index case) in Meliandou, Guinea, the outbreak's presumed first fatality, in December 2013 (1).

The appearance of a new EBOV strain in Guinea was reported by Sylvain Baize et al. The high degree of likeness among the 15 partial L segment sequences, along with the 3 full-length sequences and the epidemiologic links between the cases, suggest a single introduction of the Ebola virus into the human population. It is possible that such introduction have occurred in December 2013 (1). There is an ongoing epidemiologic investigation to further identify the supposed animal reservoir of the outbreak. Clusters of cases in the hospitals of Guéckédou and Macenta may be clues to suspect that the EBOV was transmitted for months prior till the outbreak became apparent. Such lengths of exposure probably have allowed numerous chains of transmission, ultimately increasing the number of cases of EVD (1).

Phylogenetic analysis of the complete-length segment of EBOV established a separate clade for the EBOV strain from Guinea in a sister relationship with other known EBOV strains. This suggests that the Guinean EBOV strain evolved in parallel with the strains from DRC and Gabon from a recent ancestor and has not been introduced from the latter countries into Guinea. Possibility animal host of EBOV, such as fruit bats of the species Hypsignathus monstrosus, Epomops franqueti, and Myonycteris torquata, are being in large parts of West Africa. It is feasible that EBOV has circulated undetected in this area for some time. The worry for the risk of EBOV outbreaks in the whole West African subregion is legitimate considering the emergence of the EBOV in Guinea (1).

III. The zoonotic origin of the 2013-2015 West African Ebola epidemics

West African Ebola epidemics are of zoonotic origin and are thought to be transmitted to human populations by two possible routes. Either through direct contact with larger wildlife susceptible to EBOV infections or by direct contact with the suspected animal host, bats. This first infection route is responsible for the majority of zoonotic transmissions in Central Africa where EBOV have caused large epidemics in great primates and duikers, leading to an enhanced risk of exposure for humans population. Although we are aware that the current Ebola epidemic spreading through West Africa was initiated in southeastern Guinea, the nature of the initial zoonotic event has yet to be determined (3).

Marí Saéz A et al. studied the epidemic of the zoonotic origins using interviews, wildlife surveys, and analysis of molecular epidemiology of bat and environmental specimens. They surveyed wildlife in the two protected regions in southeastern Guinea and found no evidence of a concurrent outbreak in wildlife. They also led more detailed epidemi-
ology investigations in the epicenter of this outbreak. Intriguing, Meliandou is not located in or near a pristine forest but in a heavily artificial-modified landscape dominated by plantations, which represent "modern" African settings. Locals informed the researchers through interviews that they often encounter fruit bats while hunting, although no large colony was reported. Children were also reported to hunt bats, especially insectivorous bats living near or in villages. Interestingly, Meliandou's children, including the index case (a 2-year-old boy), used to play in and around a large hollow tree housing a colony of insectivorous freetailed bats (existing literature reports these strain of bats, *Mops condylurus* tested EBOV positive) (3, 5). This may have resulted in massive exposure to bats and may have created a situation similar to the one described for Marburg virus for which transmission from bats to humans has happened in caves occupied by large bat colonies (3).

Their results suggest an overview of the wildlife-human interface at the epicenter of the current EVD outbreak in West Africa and expand the range of plausible EBOV sources to include insectivorous bats (3).

**IV. Genomic surveillance elucidates the origin of Ebola virus and its transmission during the 2013-2015 outbreak**

Stephen K. Gire *et al.* sequenced around 100 EBOV genomes from around 80 patients in Sierra Leone and observed a fast accumulation of inter- and intrahost genetic mutation, allowing us to characterize patterns of EBOV spreading over the initial weeks of the epidemic. There is high probability that this West African variant likely diverged from Middle African lineages circa 2004, crossed from Guinea to Sierra Leone in May 2014, and has subsequently exhibited sustained human-to-human transmission. Their impact on diagnostics, vaccines, and therapies critical to outbreak responses should be monitored (4).

**V. Clinical manifestations in patients with Ebola**

Index cases of Guinea predominantly showed clinical features such as fever, severe diarrhea, and emesis in December 2013. Hemorrhage was not documented as one of the symptoms at the time of sampling but may have developed during the later course of the EVD. The term EVD (rather than the earlier term Ebola hemorrhagic fever) takes into account the fact that hemorrhage is not observed in all confirmed cases and may help clinicians and public health officials in the early identification of EVD. The CFR was 86% among the early confirmed cases and 71% among clinically suspected cases. This is consistent with the CFR observed in previous EBOV outbreaks (1), and several papers have reported the clinical manifestations and outcomes of patients in West Africa (6–8). We present original literature on the main clinical manifestations of patients with Ebola in Sierra Leone, Guinea, and Liberia.

**Clinical features and outcomes in EVD patients in Sierra Leone**

Schieffelin J.S. *et al.* reported the clinical manifestations and outcomes of patients with Ebola in Sierra Leone (6). Since the first outbreak in Sierra Leone in May 2014, the Kenema Government Hospital in Sierra Leone cared for EVD patients and they reviewed the clinical, laboratory data, and epidemiologic records of patients with EVD was diagnosed between May 25 and June 18, 2014. The viral load in a subgroup of patients was assessed by quantitative reverse-transcriptase-polymerase chain reaction (RT-PCR). Of the 106 patients diagnosed with EVD, 87 had a known outcome, and 44 were available detailed clinical information. The incubation period was 6 to 12 days, the CFR was 74%, and the incubation period and CFR among EVD patients in Sierra Leone are similar to those observed elsewhere in the 2014 outbreak and in previous outbreaks.

Clinical features of EVD patients included fever (89%), headache (80%), dizziness (60%), weakness (66%), abdominal pain (40%), diarrhea (51%), and emesis (34%). The clinical and laboratory factors on presentation that were associated with a deadly result included fever, dizziness, weakness, diarrhea, and elevated levels of blood urea nitrogen, creatinine, and aspartate aminotransferase. Results of analyses showed that patients with EVD presenting with
fewer than 100,000 EBOV copies per milliliter had a lower CFR than those with 10 million EBOV copies per milliliter or more (33% vs. 94%, \( p = 0.003 \)), and patients with EVD over the age of 45 years had a higher CFR than those under the age of 21 years (94% vs. 57%, \( p = 0.03 \)). Bleeding manifested in only 1 patient while severe gastrointestinal manifestations such as emesis and diarrhea were found in most patients with EVD (6).

Clinical features and outcomes in patients with EVD in Conakry, Guinea

Elhadj Ibrahima Bah et al. described the clinical features of patients who had EVD in Conakry, Guinea (7). From March 25 to April 26, 2014, they carried out the study of all patients with laboratory confirmed EVD in Conakry. The primary outcome was mortality and secondary outcomes included patient characteristics, complications, remedy, and comparisons between survivors and nonsurvivors. Of the 80 patients who presented with clinical manifestations, 37 had clinical and laboratory-confirmed EVD. Among the confirmed cases, the median age was 38 years (interquartile range, 28 to 46), 24 patients (65%) were male, and 14 (38%) were HCWs; among HCWs, nosocomial infection was implicated in 12 patients (32%). Confirmed patients with EVD presented to the hospital a median of 5 days (interquartile range, 3 to 7) after the onset of clinical manifestations, most commonly with fever (84%; mean temperature, 38.6°C), tachycardia (mean heart rate, >93 beats per minute), diarrhea (62%), and fatigue (65%). Of these patients, 28 (76%) were cured with intravenous fluids and 37 (100%) with antibiotics. 16 patients (43%) died, with a median time from sign onset to death of 8 days (interquartile range, 7 to 11). Patients who were 40 years of age or older, compared with those under the age of 40 years, had a relative risk of death of 3.49 (95% confidence interval, 1.42 to 8.59; \( p = 0.007 \)). EVD patients suffered from dehydration elicited by emesis and severe diarrhea resulting in CFR as high as 43% despite efforts of volume repletion and antibiotic remedy (7).

Clinical features and outcomes in EVD patients with EVD in Monovia, Liberia

Daniel S. Chertow et al. reported the clinical features and management of patients with EVD in Monrovia, Liberia (8). More than 700 patients with EVD were treated between August 23 and October 4, 2014 in the largest Ebola treatment unit in Monrovia, Liberia. The early clinical manifestations of EVD included a high fever (temperature of up to 40°C), fatigue, malaise, and body aches. The fever persists, and by day 3 to 5 of the disease, gastrointestinal signs typically begin, including nausea, emesis, epigastric pain, and diarrhea. Patients with EVD routinely presented to the facility after 2 or 3 days of severe emesis or severe diarrhea, during which they posed a substantial risk to their communities and had a high probability of testing positive for EBOV in the blood by RT-PCR. Although some patients tested positive by RT-PCR within 24 hours after the onset of manifestations, they found that a negative test result by RT-PCR could not be depended on to discount EVD until 72 hours after manifestations began. Daniel S. Chertow et al. observed that recurrent episodes of vomiting resulted in an inability to tolerate oral intake. Large volumes of watery diarrhea estimated at > 5 liters per day similar to that of cholera, presented suddenly, persisted for up to 7 days or longer (rarely), and steadily tapered off. The associated clinical manifestations and signs included torpor, a late finding. Hemorrhage in either upper or lower gastrointestinal tract or both was found in less than 5% pre mortem. Most passing occurred between days 7 and 12 of diseases. Clinical manifestations began to improve in approximately 40% of patients after approximately 10 days of EVD. Oral ulcers and aphtha developed around this time, along with dysphagia and throat pain. Mostly patients who survived to day 13 finally lived. Their discharge from hospital criteria included 3 days without gastrointestinal signs and a negative result for RT-PCR EBOV test. Patient groups that were identified as more weak were the elderly, pregnant women and children younger than 5 years-old.

Patients with EVD suffered from massive fluid loss such as emesis and severe diarrhea. Hence, oral antiemetics and
antidiarrheal therapies appear to be crucial early interventions that may limit shock and life-threatening dehydration. Such regimens successfully seemed to control symptoms, facilitate oral intake, reduce further loss of fluid, and reduce infecting the environment through body fluids from patients such as diarrhea. These observations support the aggressive use of antiemetics, antidiarrheal medications, and rehydration solution to reduce massive gastrointestinal losses and the consequences of hypovolemic shock. The selective use of intravenous fluid remedy in the patients that is most likely to benefit is a rational approach under the current situation. For a significant improvement of outcomes, a broader use of intravenous fluid remedy and electrolyte replacement is necessary (8).

Clinical features and outcomes in patients with EVD in the Freetown, Sierra Leone

Ansumana R et al. described similar data on the 631 patients with EVD, who were hospitalized to the EVD treatment centre at the Hastings Police Training School near Freetown, Sierra Leone, on or after September 20, 2014. The fatality rate was 31%, as reported by Ansumana R et al., which is lower than 74% rate reported by Schieffelin et al. (183 of the 581 patients for whom a final disposition is known died, representing a CFR of 31.5%). The most common manifestations reported at hospitalization were fever, headache, emesis, anorexia, and fatigue, joint and muscle pain, nausea, and severe diarrhea. Patients with EVD were usually admitted 3 or 4 days after the onset of signs. The average admission period of survivors from EVD was approximately 2 weeks; the inpatients who died usually did so within 3 or 4 days after hospitalization. Their current remedy protocol is as follows: For 72 hours after admission, all EVD patients receive 1 g of ceftriaxone intravenously every 12 hours and 500 mg of metronidazole intravenously every 8 hours, as well as 500 ml of Ringer's lactate every 8 or 12 hours and 500 ml of dextrose saline (5% and 0.9%, respectively) intravenously every 8 or 12 hours. All EVD patients also take 10 mg of vitamin K and 160 mg of artemether intramuscularly promptly on hospitalization, as well as a 20 mg zinc sulfate tablet every day, a 400-mg ibuprofen tablet every 12 hours, and 10 mg of metoclopramide intravenously as needed for nausea or emesis. After the first 3 days, uninterrupted remedy includes a 400 mg metronidazole tablet every 8 hours for 7 days, a 500 mg cefuroxime tablet every 12 hours for 5 days, an artesunate-lumefantrine combination-therapy tablet every day for 3 days, a 400-mg ibuprofen tablet every 12 hours, and one capsule of Immuno-Boost nutrition supplement (Novopharm Formulations) every day. Juice and other oral rehydration solutions were administered freely. It is uncertain why the CFR is reducing at Hastings. They could not assess any individual component of the remedy we used because they applied a package of meddle. The effectiveness of this remedy approach will need to be proved with clinical and laboratory study at other Ebola outbreak treatment facilities (9).

Late complications among survivors from patients with EVD

Jay B. Varkey et al. reported the clinical course of a male in whom acute, severe, unilateral uveitis developed during the convalescent phase of EVD and he also reported the detection of viable EBOV in aqueous humor acquired from the inflamed eye 14 weeks after the onset of the initial manifestations of EVD and 9 weeks after the clearance of viremia (10).

A 45-year-old male physician was a patient who was cured at Emory after he infected with EBOV in September during working in Sierra Leone. He started having ophthalmic manifestations soon after his leaving the hospital, which worsened over the course of 4 weeks, despite remedy. His medical team acquired aqueous humor specimens, which was positive for EBOV gene by RT-PCR. A viral culture did at the US Centers for Disease Control and Prevention (CDC) was positive for live EBOV, however the peripheral blood, tear, and conjunctiva tests were negative. His panuveitis and vision improved with continued remedy, and his medical teams continue to follow his progress (10).

Jay B. Varkey et al. described that the 45-year-old male physician's experience stresses an crucial complication of Ebola virus disease and give lessons medical staffs more
about Ebola virus endurance in an immune-protected organ such as eye (10).

**Possible Sexual Transmission of Ebola Virus**

Athalia Christie et al. described possible sexual transmission of EBOV from survivor on the MMWR website (http://www.cdc.gov/mmwr) (11). On March 20, 2015, 30 days after the most recent confirmed case in Liberia was isolated, EBOV was clinical and laboratory confirmed in a female in Monrovia (11). There was only one epidemiologic link identified by the investigation: unprotected sexual contact such as vaginal intercourse with a survivor (male).

MMWR reports from previous outbreaks described that survivors especially male from EVD can continue to harbor EBOV in immunologically privileged sites for a period of time after convalescence. EBOV has been isolated from semen as long as 82 days after manifestations onset and EBOV gene has been identified in semen up to 101 days after manifestation onset (11). One example of possible sexual intercourse transmission of EBOV has been reported, although the accompanying evidence was not decisive (11). On top of that, possible sexual intercourse transmission of Marburg virus, a filovirus related to Ebola virus, was documented in 1968 (11). Based on information gathered in this study, the US CDC is recommending that sexual contact with semen from male Ebola survivors should be avoided until more information regarding the duration and infectivity of viral shedding in semen is known. A condom should be used correctly and consistently every time in case of male survivors have coitus, regardless whether vaginal, oral, or anal with female or male (11).

**VI. The Transmission of Ebola Virus**

Existing evidence suggests that direct contact with a patient and contaminated body fluids are the primary ways EBOV is transmitted. However, this is supported by few studies (3).

Osterholm MT et al. suggested that fields requiring further study include (i) respiratory transmission (either through small or large droplets or droplet nuclei from patients with EVD), (ii) fomite transmission from environmental contaminants (iii) the degree to which minimally or mildly ill patient transmit infection, (iv) how long clinically related infectivity sustains, (v) superspreading events may play a role in spreading in regional communities or hospital settings (vi) whether differences among strands of EBOV or repeated serial passage in outbreak settings can impact spreading of EBOV, and (vii) what role animals, wild or domestic, may play in propagating an outbreak, particularly while a major outbreak such as the 2013-2015 Ebola outbreak in West Africa (3).

Osterholm MT et al. also emphasize what we know and what we do not know about EBOV transmission and also hypothesize that EBOV spreads through respiratory mechanisms (3).

Many scientists reached a conclusion that the large-scale transmission documented in the 2013-2015 Ebola outbreak in West Africa is due to societal factors such as urban density, migration pattern of people, penury, and poor health care facility and infrastructure rather than biological factors that are distinctive of EBOV (12, 13). Available data still limit, however, regarding mutation of EBOV genomics (affecting the phenotype/pathotype of Ebola virus), viral loads of patient, and epidemiological characters of EBOV. Moreover, human-to-human transmissions is yet to be fully understood due to the lack of number of cases of outbreak investigations prior to 2013-2015 Ebola outbreaks in West Africa, and as a result, unanswered questions remain (14).

The available data presented that direct physical contact including contact with infected body fluids is the major source of EBOV transmission (3). In support of this, EBOV has been identified from samples of semen, urine, breast milk, and saliva of patients with EVD; in addition, RT-PCR revealed viral genes in vaginal, rectal, stool, tears, conjunctival, sweat, and skin swabs (3). Fomite transmission could occur by environmental contamination. However, according to several epidemiological data, the role of fomites also appears to be relatively small and studies describe that EBOV can survive on solid surfaces and in liquids from several days to several weeks supporting that EBOV could spread via fomite transmission (3).
EBOV genes were detected by RT-PCR among multiple environmental sampling in 2014 at the Ebola treatment center in Kailahun, Sierra Leone. Interestingly, EBOV gene was detected by RT-PCR from the outer surfaces of 3 of 16 masks worn by HCWs that were not visibly bloody or soiled (J. Strong, unpublished data). Such findings could mean two things: cross-contamination of the masks (such as when workers peel off personal protective equipment (PPE)) or the presence of aerosols in the patient-care environment (3).

One dramatic epidemiological character of the 2013-2015 Ebola outbreak in West Africa is that a large number of HCWs were infected in a hospital (3). The WHO has hypothesized that inappropriate training in metier care, lack of PPE, the improper use of PPE, shortages of medical staff, and the misdiagnosis of EVD have contributed to this outbreak. However, the exact transmission mechanism of EBOV still unknown for two American nurses who acquired infection while caring for a patient in Dallas, TX, USA and for a nurse in Madrid, Spain, who cared for a returning priest (3). For the Dallas patient, intubation, an aerosol-generating procedure, was performed before a patient with EVD expired, but it is still unknown if these contributed to transmission to the HCWs in hospital.

Several studies have examined direct animal-to-animal EBOV transmission in various animal species. One study involving EBOV-inoculated rhesus monkeys and controls found that two three control monkeys caged in the same room developed Ebola disease 10 and 11 days after the inoculated rhesus monkeys had died; the control monkeys were housed approximately 3 m from the inoculated monkeys (15). The authors conjectured that the control apes became infected through conjunctival, oral, or aerosol exposure to EBOV-laden droplets. The pattern of respiratory antigen staining on pathology specimens suggested airborne (aerosol) transmission. Alternatively, spreading of EBOV could have happened through certain behaviors of caged apes for example, through routine animal husbandry or throwing feces and spitting (16). Droplet transmission spread through sneezing, coughing, talking, etc and virus-laden droplets that spread directly from the respiratory tract of the patient with EVD to susceptible mucosal surfaces of the uninfected person, generally over short distances. Airborne (droplet nuclei) transmission happens by spreading of either airborne droplet nuclei or small particles in the respirable size range containing EBOV that remain infective over time and distance. In further study of the complexities of EVD transmission, two standpoints should be deliberated. One is airborne transmission, which involves the inhalation of virus-laden aerosols suspended in the air either near a patient or at a distance and can involve aerosol particles of diverse sizes that either attach on mucosal surfaces, such as the mouth and snout, or are inhaled deep into the respiratory tract breathed (17). Both traditional models of droplet and droplet nuclei transmission can fit under the broader category of aerosol transmission. Aerosols can be generated from the respiratory tract, through the forceful emission of body fluids such as aerosol-generating procedures (intubation), or severe diarrhea or vomitus. This leads to the last concept, which is respiratory transmission. Respiratory transmission is limited to the generation of aerosols (either droplet or droplet nuclei aerosols) from the respiratory tract such as nasal passages, the trachea, or the lungs that then enter the airspace and, to use the traditional model, cause transmission by droplet or droplet nuclei transmission (3).

Roy and Milton suggested classifying the aerosol transmission of respiratory pathogens as obligate, preferential, or opportunistic, based on the ability of the pathogen to be transmitted through small-particle aerosols in 2004 (18). According to this system, Mycobacterium tuberculosis can transmit primarily through droplet nuclei aerosols and thus involves obligate airborne (aerosol) transmission. Microorganisms with preferential aerosol transmission include agents such as varicella zoster virus that can be transmitted in multiple ways but are transmitted primarily by small-particle (droplet nuclei) aerosols. Microorganisms with opportunistic aerosol transmission include those that are transmitted primarily by other routes but can be transmitted by droplet nuclei aerosols under certain conditions; as noted above, norovirus is an example. EBOV may also fit into this category because infectious aerosols (either in small or large droplets), which could result in transmission, may be generated and emitted during the course of disease (3).
EBOV is in macrophages and epithelial cells of humans. It could infiltrate the upper or lower respiratory tract and infect particles of various sizes, including fine mists particles that could infiltrate the upper or lower respiratory tract and infect macrophages and epithelial cells of the respiratory tract, and EBOV is in the respirable range (800 to 1,000 nm) (21).

Fifth, experience with the Reston Ebola virus (REBOV) suggests that the respiratory transmission of REBOV can happen between animals and possibly from animals to humans. Finally, people can generate and emit aerosols with viruses: what we know and what we do not know. mBio 2015;6:e00137.

The authors hypothesize that EBOV can spread as a respiratory pathogen (3). Despite the lack of solid and concrete epidemiological data, a key additional question is whether the respiratory transmission and primary pulmonary infections of EBOV could happen in the future. Evidence suggests that airborne transmission is possible, even without drastic changes in the EBOV genes, although evolution of EBOV could enhance the possibility. First, the identification of EBOV in the pulmonary alveoli from patient autopsies and the fact that it can be isolated from the saliva, suggest that virus-laden aerosols could be transmitted by respiratory mechanism. Second, EBOV is able to infiltrate macrophages and epithelial cells of the respiratory tract (19). Third, sneezing and coughing, a symptom of EVD, is known to generate aerosols (droplet nuclei) as often as 49% (20). Fourth, animal studies suggested that EBOV can be transmitted through aerosols (droplet nuclei) and that respiratory infection with pneumonitis can occur following this route of inoculation. Fifth, experience with the Reston Ebola virus (REBOV) suggests that the respiratory transmission of REBOV can happen between animals and possibly from animals to humans. Finally, people can generate and emit aerosols with particles of various sizes, including fine mists particles that could infiltrate the upper or lower respiratory tract and infect macrophages and epithelial cells of the respiratory tract, and EBOV is in the respirable range (800 to 1,000 nm) (21).

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