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Ebola virus disease: a highly fatal infectious disease reemerging in West Africa

Kelvin K.W. To [a,b,c,d], Jasper F.W. Chan [a,b,c,d], Alan K.L. Tsang [d], Vincent C.C. Cheng [d], Kwok-Yung Yuen [a,b,c,d,*]

[a] State Key Laboratory for Emerging Infectious Diseases, The University of Hong Kong, Hong Kong, China
[b] Carol Yu Centre for Infection, The University of Hong Kong, Hong Kong, China
[c] Research Centre of Infection and Immunology, The University of Hong Kong, Hong Kong, China
[d] Department of Microbiology, The University of Hong Kong, Hong Kong, China

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Abstract

Ebolavirus can cause a highly fatal and panic-generating human disease which may jump from bats to other mammals and human. High viral loads in body fluids allow efficient transmission by contact. Lack of effective antivirals, vaccines and public health infrastructures in parts of Africa make it difficult to health workers to contain the outbreak.

Keywords: Ebolavirus; Ebola virus disease; West Africa; Outbreak

Ebolavirus has been known to cause outbreaks of severe hemorrhagic fever with high fatality in Africa since 1976 [1]. However, *ebolavirus* has been out of the spotlight of the clinical and scientific community because it mainly affects remote villages involving at most few hundred people, and these outbreaks often stopped spontaneously. In 2014, a large *ebolavirus* outbreak occurred in West Africa. This outbreak was first reported from Guinea in March 2014, although epidemiological investigation suggested that the first fatal case had occurred in December 2013 [2]. The outbreak then spread to Liberia, Sierra Leone, Nigeria, Senegal, and Mali in Africa. The first case diagnosed outside Africa was reported from USA on September 30, 2014 [3]. In October 2014, three nurses acquired *ebolavirus* locally in the United States and Spain which has generated huge media attention and public panic. The 2014 West Africa *ebolavirus* outbreak is unprecedented in many ways. Firstly, this is the largest *ebolavirus* outbreak recorded in history, with over 10,000 cases and a mortality rate of 48.5% [4]. Secondly, the outbreak involved major cities, including Conakry in Guinea, Free-town in Sierra Leone, Monrovia in Liberia, and Lagos in Nigeria [5,6]. The involvement of major cities increases the risk of rapid local dissemination, spread to neighboring countries, and trans-continental spread by air travel, and therefore presenting a major health threat to the entire world [7]. Here, we review the basic science, epidemiology and clinical aspects of *ebolavirus* which are relevant for the control of the current outbreak.

1. Taxonomy

Ebolavirus, together with *Marburgvirus* and *Cuevavirus*, are the three genera belonging to the family *Filoviridae* in the order *Mononegavirales* [8]. Four species within the *ebolavirus* genus can cause fatal human disease, including *Sudan*

* Corresponding author. Carol Yu Centre for Infection and Division of Infectious Diseases, Department of Microbiology, The University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Pokfulam, Hong Kong Special Administrative Region, China.
E-mail address: kyyuen@hku.hk (K.-Y. Yuen).

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ebolavirus, *Zaire ebolavirus*, *Taï Forest ebolavirus* (also known as *Ivory Coast ebolavirus* or *Cote d'Ivoire ebolavirus*), and *Bundibugyo ebolavirus*. *Reston ebolavirus* can cause disease in pigs and monkeys but only asymptomatic infections in humans.

Although *ebolavirus* is the accepted terminology for the virus genus according to both ICTV and NCBI, the World Health Organization (WHO) and the Centers for Disease Control and Prevention have used the term "Ebola virus disease" (EVD) to describe the clinical disease caused by *ebolavirus*. In this review, we will use the term "*ebolavirus*" when referring to the virus, and EVD when referring to the clinical disease.

2. Epidemiology

Ebolavirus was first discovered in 1976 during an outbreak in Ebola River valley in Zaire (now Democratic Republic of Congo [DRC]) in Central Africa. Another simultaneous outbreak occurred in Sudan [9]. It was postulated that two earlier cases of EVD may have occurred in 1972. The evidence came from the investigation of the 1977 outbreak in Zaire [10]. A serum sample obtained from a physician was found to be seropositive. In 1972, that physician developed a febrile illness associated with sore throat, headache, myalgia, vomiting, diarrhea, rash and leukopenia about 2 weeks after he lacerated his finger during an autopsy on a Zairois student who died from hemorrhagic illness.

Since then, there have been numerous outbreaks in Africa, affecting six countries (Table 1). Most of the outbreaks occurred after 1994 in Sudan, Congo, DRC, Uganda, and Gabon, which are located in Central and East Africa. *Zaire* and *Sudan ebolavirus* are responsible for most outbreaks, and these species are associated with highest case-fatality rates, ranging from 44–100% and 41–69%, respectively. *Taï Forest ebolavirus* caused illness in an ethnologist who performed a necropsy on an infected chimpanzee in 1994 in Cote d'Ivoire of West Africa [11]. *Bundibugyo ebolavirus* has only been associated with two outbreaks since 2007, with relatively low case-fatality rate [12]. *Reston ebolavirus* can cause disease in pigs and be fatal in monkeys [13], but has not been definitively associated with any human disease, although asymptomatic infection, diagnosed with serological test, was identified in persons with contacts with infected monkeys and pigs [13,14].

Table 1
Ebola virus disease outbreaks from 1976 to 2012 [1].

Year	Place	*Ebolavirus* species	Number affected (case-fatality)
1976	Sudan	Sudan	284 (53%)
1976	DRC	Zaire	318 (88%)
1977	DRC	Zaire	1 (100%)
1979	Sudan	Sudan	34 (65%)
1994	Gabon	Zaire	52 (60%)
1994	Cote d'Ivoire	Taï Forest	1 (0%)
1995	DRC	Zaire	315 (81%)
1996 (Jan–Apr, Jul–Dec)	Gabon	Zaire	91 (73%)
1996	South Africa (ex-Gabon)	Zaire	1 (100%)
2000	Uganda	Sudan	425 (53%)
2001–2002	Gabon, Congo	Zaire	124 (78%)
2003 (Jan–Apr, Nov–Dec)	Congo	Zaire	178 (88.2%)
2004	Sudan	Sudan	17 (41%)
2005	Congo	Zaire	12 (83%)
2007	DRC	Zaire	264 (71%)
2007	Uganda	Bundibugyo	149 (25%)
2008	DRC	Zaire	32 (44%)
2011–2012	Uganda	Sudan	32 (69%)
2012	DRC	Bundibugyo	57 (51%)

DRC, Democratic Republic of Congo.

In addition to clinically apparent EVD outbreaks, seroepidemiology studies showed that there is a high prevalence seropositive individuals, suggesting that asymptomatic or mild infection can occur [15]. In a study testing blood samples collected from 4349 individuals from 220 randomly selected village in Gabon between 2005 and 2008, 15.3% of samples were found have *ebolavirus*-specific antibodies using ELISA [16]. *Ebolavirus*-specific antibodies can also be found in individuals from areas without apparent EVD outbreak. For example, *ebolavirus*-specific antibodies, detected using indirect immunofluorescence slide test, were found in 13.4% of healthy individuals from a rainforest area of Liberia in the early 1980s [17]. Though these serological test results have not been confirmed by neutralization antibody study, it is highly likely that asymptomatic and mildly symptomatic infections are much more common than severely symptomatic and fatal illness.

The current West Africa EVD outbreak started in December 2013, when cases first appeared in Meliandou Village, Guéckédou of Guinea (Table 2) [5]. The index patient was a 2-year-old child with fever, black stool, and vomiting, with symptom onset on December 2, 2013, and died 4 days later. The disease then spread to other villages of the Guéckédou district, and also Macenta and Kissidougou district. The first peak occurred in March 2014 when patients were diagnosed with EVD in Liberia. The second peak occurred in May and June 2014, coinciding with the first report of cases from Sierra Leone. Contact tracing found that the initial cases in Sierra Leone attended a funeral of a highly respected "traditional healer", who has treated patients with EVD in Guinea [6,18]. There was a large increase in cases since July 2014. The first case in Nigeria was a traveler from Liberia, who has caused an outbreak involving 19 laboratory-confirmed cases from July to September [19]. Senegal and Mali reported the first imported cases on August 29 and October 22, 2014, respectively [20]. The first case of EVD diagnosed outside Africa was confirmed on September 30, 2014 [3]. The patient, from Liberia, arrived in USA on September 20, and developed symptoms on September 24. A separate EVD outbreak, also caused by *Zaire ebolavirus*, has occurred in DRC since July 2014 [21]. As of October 25, 2014, the DRC outbreak has involved 67 cases with 49 deaths [22].