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EDITORIAL
Ebola: when a nightmare becomes reality

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BACKGROUND INFORMATION

Ebola virus disease (EVD) was firstly identified in the Democratic Republic of Congo (DRC) and in Sudan in 1976, about nine years after the identification of the hemorrhagic fever due to the Marburg virus, another member of the Filoviridae family. Since most patients affected by Ebola do not develop frank hemorrhages, the formerly known term "Ebola hemorrhagic fever" has been replaced by "EVD", to raise clinical suspicion and facilitate early recognition of the disease in absence of hemorrhagic symptoms.

The ebolavirus genus includes five different species: Zaire, Sudan, Taï Forest , Bundibugyo, and Reston [1].

During less than four decades, between 1976 and 2012, 24 Ebola outbreaks have occurred in several Central African countries: DRC, Sudan, Gabon, the Republic of Congo (RC), and Uganda. Interestingly, the number of cases and outbreaks of EVD increased since the year 2000. Registered outbreaks, involving from a minimum of one up to a maximum of 425 individuals, were mainly caused by two different Ebola species: Zaire ebolavirus and Sudan ebolavirus. Such Ebola outbreaks are devastating in terms of high case-fatality rates (ranging from 25% to 51% for Bundibugyo ebolavirus, from 41% to 71% for Sudan ebolavirus, from 44% to 90% for Zaire ebolavirus), but they are usually controlled by applying public health measures consisting in early isolation of patients, contact tracing and quarantine of exposed people and/or entire villages (*cordon sanitaire*). A lower case-fatality rate was observed in one outbreak which occurred in Uganda and was caused by the so-called Bundybugio strain. Another Ebola species, Reston ebolavirus, causing viral disease among simians and pigs in Asia, may infect also humans but without causing disease. Finally, before the current outbreak, only one case of Ebola due to a different virus species (Taï Forest ebolavirus), was reported in Western Africa, in a researcher dissecting an affected ape in Ivory coast [2].

Traditionally, Ebola outbreaks origin from a single case (*i.e.*, a man going into the forest to hunter wild animals), which is followed by nosocomial amplification. Although fruit bats of the Pteropodidae family are assumed to represent the natural reservoir of the infection, other animal species living in the tropical rainforest, such as non-human primates (gorillas and chimpanzees) and antelopes, may acquire and introduce the infection into human populations through close contact with blood, secretions, organs or bodily fluids [3]. Then Ebola may spread through human-to-human transmission via direct contact with the body and/or bodily fluids of infected deceased persons, especially in the health care setting or in the household, or during traditional burial ceremonies. In such cases, the virus is supposed to enter human body through broken skin or mucous membranes. Infected persons develop EVD symptoms after an incubation period of about 4-11 days (range: 2 to 21 days) [1, 2, 4].

THE 2014 OUTBREAK IN WEST AFRICA

On March 2014, when Ebola cases were identified in a remote area of Guinea, there was no much concern about this news. At most, Ebola experts were a bit surprised by the geographical location of the outbreak epicenter. In fact, West Africa was not considered an area at high risk for EVD.

Although unexpected in terms of geographical localization, the Ebola outbreak in Guinea was initially considered just a further episode of the historical series of reappearance and disappearance of Ebola in Africa. Thus, for few months, it was almost ignored or, at least, underestimated.

The site of emergence of this outbreak was the region of Guéckédou, in the Guinea's remote southeastern forest area, near the border with Liberia and Sierra Leone. In a few months, Ebola crossed the borders ravaging the three countries, and reaching the capital cities of Conakry, Monrovia and Freetown. By October 29, 2014, a cumulative number of more than 13 700 cases was reported by WHO. The case-fatality in the current West African outbreak appears to be around 50% when based on WHO official data, but it may be as high as 70% in hospital case series [2, 4].

LESSONS TO BE LEARNT

Four major issues and caveats regarding the past and the future of this epidemic need to be discussed. In particular, we may take advantage from possible answers to questions raised by the emergence and the rapid spread of Ebola in West Africa:

i) what is the extent of the areas at risk for Ebola emergence in Africa?

As mentioned before, with the exception of a single human case caused by the Taï Forest species of Ebola virus, this is the first outbreak which occurred in Western Africa. The agent involved in the current outbreak is Zaire ebolavirus, which was previously isolated in the DRC, RC, and Gabon. Phylogenetic analyses suggest that the Zaire ebolavirus strain found in Guinea is a distinct strain from that identified in Central Africa [5]. Further analyses of Ebola virus genomes from patients in Sierra Leone showed that

the West African variant diverged from central Africa lineages around 2004. The genetic similarity across the strains sequenced during the outbreak suggests a single cross-species passage from the natural reservoir followed by sustained human-to-human transmission [6]. Thus, these data suggest the presence of natural reservoirs for Zaire ebolavirus in West Africa;

ii) why did the first Ebola outbreak in West Africa become so large?

There may be several answers to this question. First of all, Ebola was not expected to emerge in this area of the African continent, which is instead affected by the continued reemergence of another hemorrhagic fever: Lassa fever. Secondly, the original epicenter of the outbreak in Guinea was localized near the highly porous borders with the other two countries; the high human mobility across borders and from remote to urban areas might have influenced epidemic dynamics favoring the rapid spread of the infection [1, 7]. On the other hand, public health response was impaired by the need of intergovernmental coordination, along with logistical problems caused by poor infrastructures in areas devastated by civil wars [7]. Thus, delayed intervention due to logistical problems in the context of high population mixing may explain the rapidly growing epidemic dimensions;

iii) can we quantify the risk of Ebola spreading beyond the borders of currently affected countries?

Since the beginning of the outbreak, few cases of Ebola have been reported in other African countries, in Europe, and in the US.

In Nigeria, a cluster of 20 cases followed the introduction of the virus through a traveler who left Liberia after developing symptoms suggestive of EVD. However, the outbreak was rapidly contained. Single cases were also imported in Senegal (where there were no secondary cases) and in Mali, through people traveling from Guinea.

Another outbreak due to Zaire ebolavirus has been reported in Northern DRC this year, causing 66 cases of EVD before being contained; phylogenetic analyses have shown that it is not related to the West Africa outbreak.

In Spain, a nurse acquired Ebola after caring a missionary repatriated from Sierra Leone, whereas two cases were identified in Dallas, Texas, in health care workers who treated a traveler from Liberia who developed EVD symptoms after arriving in the US [8].

These findings suggest that Ebola may be contained when single cases are imported in other African countries. Although the introduction of single cases of EVD from affected countries to industrialized countries may occur, a large outbreak in a completely different context is unlikely. Moreover, exit screening of travelers from affected countries may reduce the risk of importation of Ebola cases [9];

iv) how can we deal with Ebola in terms of treatment and prevention?

Although there is no cure available at the moment, there are several experimental treatments that should be rapidly assessed, from antiviral drugs to monoclonal antibodies (*i.e.*, the so-called ZMapp). Moreover, vaccine candidates which have proved to be effective in animal trials are being tested in humans [10-12]. The need for effective drugs and vaccines claims for accelerated testing procedures and relaxed ethical considerations. Meanwhile, traditional public health measures should be strengthened in order to contain the outbreak in countries with sustained transmission of the infection.

CONCLUSIONS

The Ebola outbreak in West Africa has been defined by WHO as a "public health emergency of international concern" and urges to be brought under control. To this end, international response is necessary to support affected African countries, providing more hospital beds, individual protective equipment, and technical assistance, in order to improve outbreak management and supportive care.

In West Africa, a nightmare has become reality, and we cannot remain asleep: leaving Africa alone for too long would have unpredictable consequences, not only for poor-resource countries, but for the entire world.

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