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Ebola in West Africa: the outbreak able to change many things

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A huge Ebola virus disease (EVD) outbreak has been striking West Africa since December 2013. Virological investigation identified Ebola virus (EBOV; formely Zaire ebolavirus) as the causative agent; this is one of the five species of the genus *Ebolavirus*, which was also involved in the outbreaks in Central Africa from 1976 [1,2]. EBOV is characterized by an 80% fatality rate in humans, and is also responsible for the catastrophic decline in wild great ape populations in Central Africa [3,4]. The current EVD outbreak started in Conakry Guinea, and spread into Liberia, Sierra Leone, Nigeria, and finally Senegal, where one case has just been reported. Although this outbreak continues to expand, with more and more victims, on 7 September 2014 the WHO reported 4366 confirmed cases, including 2218 deaths, representing more than double the number of cases listed overall since 1976. To date, the reported numbers are as follows: in Conakry Guinea, 861 cases, including 557 deaths; in Liberia, 2081 cases, including 1137 deaths; in Sierra Leone, 1287 cases, including 478 deaths; and finally, in Nigeria, 21 cases, including eight deaths. The only case reported in Senegal appeared to be a patient who had escaped from Conakry Guinea. Meanwhile, in the Democratic Republic of Congo (DRC), a new outbreak, suspected to have emerged from an animal source, was confirmed on 26 August 2014.

The EVD crisis was minimized and underestimated for >30 years, mainly because the impact of EVD on public health was judged to be 'ridiculous' as compared with other infectious diseases such as AIDS, malaria, and Dengue. It was described as a 'little disease of poor countries', but the terrifying ongoing EVD outbreak in West Africa will certainly change the usual scientific, sanitary and political approaches.

Towards research guided by a public health approach

The impressive numbers of EVD cases and deaths, which are far from complete, led the WHO to proclaim this EVD outbreak in West Africa as a 'public health worldwide emergency with international impact and considerable sanitary risk for all other countries'. The new dimensions reached by EBOV will not only increase and diversify research teams, but will also result in more studies on treatment and the development of a vaccine, which currently does not exist. The actual public health dimension will become more important than the simple commercial considerations that have predominated so far. This will finally convince government and pharmaceutical firms to invest in the large-scale production of treatment agents and vaccines, even if these are not yet authorized [5,6].

Towards a diversification of diagnostic capabilities

The increase in the number of EBOV cases has resulted in a huge increase in the number of contacts, and thus an increase in the number of suspected cases. Although some clinical signs are easily identifiable and relatively specific, EVD can be confused with many other diseases. Indeed, fever, vomiting, diarrhoea and cutaneous rash are the symptoms that most frequently develop. In this context, laboratory diagnosis is essential. Despite hopes for future treatment agents and vaccines, reducing human-to-human transmission will always remain key in the fight against EVD outbreaks: isolation of suspected cases and medical care provided by completely protected competent staff; protected burial of dead EVD victims; and education of populations about routes of transmission and risk factors of EVD. To manage the multiplication of suspected cases, mainly resulting from the real increase in the number of contaminated people, but also from the imprecision in inclusion protocols for suspected cases, a decrease in the security level of laboratories authorized to manipulate such biohazardous material for diagnostic purposes is necessary, ethically justified, and even is required from the point of view of public health ethics. Achieving a diagnosis by real-time PCR methods in laboratories that are technically equipped, experienced in virological diagnosis and with a

class 3 security level will considerably decrease the associated costs, and will shorten the diagnostic delay, which is a crucial parameter in the fight against EVD outbreaks.

Towards an unavoidable evolution of EBOVs

EVD is a zoonosis that is accidentally transmitted to humans. The transmission can occur directly from natural hosts of EBOV [7], or indirectly from intermediate animal species such as gorillas and chimpanzees [3]. In its own reservoir, EBOV replicates very slowly in target organs such as the liver and spleen; viral load is often undetectable, and the animal does not usually show any symptoms. The genomic evolution of EBOV is therefore very slow. In humans, the situation is completely reversed. Indeed, EBOV finds a favourable environment for replication, and can reach extremely high viral loads (up to 10^9 particles/mL of blood). The high viral multiplication rate increases the probability of mutation. However, genomic studies performed on viruses isolated during outbreaks from 1976 to 2008 showed very low genetic diversity (approximately 3%) [8]. This relative genomic stability of EBOV can probably be explained by the small scale of these outbreaks to date. However, the exceptionally large-scale current outbreak could change this situation, and dramatically speed up the genomic evolution of EBOV [9]. The exponential increase in the number of detected cases, and thus of human-to-human transmission events, will increase the mutation rate of EBOV. All of these factors could finally induce phenotypic modifications in virulence or transmission mode in humans; airborne or vector-borne transmission could have catastrophic effects.

Towards an ecological continental approach

Although exceptional because of its large scale and its geographical expansion, the EDV outbreak in West Africa is not surprising. Indeed, the distribution of EBOV reservoir species (*Hypsignathus monstrosus*, *Epomops franqueti*, *Myonycteris torquata*, and probably *Rousettus aegyptiacus*) extends across all African forested regions, from the south of Senegal to the north of South Africa and the east of the DRC, including all countries along the coast of the Atlantic Ocean [10]. Under favourable conditions, the spill-over of EBOV from its natural host is likely to occur anywhere in all of these regions. In general, human contamination occurs during handling and butchering of these animals, which are widely consumed by local populations [7]. Today, the factors controlling this spill-over are not all known, but they can be divided into three categories: (i) social and behavioural factors that lead to exposure to viral agents; (ii) virological factors intrinsic to infected animals that affect viral load; (iii) and virological factors associated with the reservoir population, affecting the proportion of infected animals. Whereas the causes of variability in factors in the two first categories are partially known (e.g. an increase in the amount of consumption of bats because of the scarcity of other animals, or increases in viral load in breeding females, immunodepressed animals, or co-infected animals), there is still much to discover about the third category. The global pattern of EVD outbreaks seems to indicate that, at a continental scale, they have a cyclical nature, with low and high phases. This could suggest a periodic significant increase in infected animal rates in the continent overall that would result in higher rates of transmission to human populations. In fact, two outbreaks appeared at the same time in two distinct regions in 1976 (the DRC and Sudan); similarly, five outbreaks occurred in 1995–1996 in three different countries (Ivory Coast, the DRC, and Gabon); and there were numerous independent epidemic chains during the 2001–2002 outbreak in Gabon and Brazza Congo, and again in 2003 in Brazza Congo. Today, the occurrence of at least two EVD outbreaks in distant countries (Conakry Guinea and the DRC) tends to support this idea. Confirmation of this potential phenomenon and understanding the factors leading to the increase in the global infection rates in bat populations could be valuable for evaluating the risk of viral emergence and predicting EBOV outbreaks. Determination of an alert threshold will be crucial in the fight against EVD outbreaks, where rapidity and efficiency of action are fundamental.

Transparency Declaration

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