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38 years after its discovery, Ebola virus spins out of control

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In 1976, two outbreaks of a previously unknown disease occurred almost simultaneously in northern Zaire (now Democratic Republic of Congo) and southern Sudan. They were dramatic: Most of those afflicted died, often with severe haemorrhagic disease; the disease spread to family members and other close contacts; and dramatically also in and through healthcare settings. (Peter Piot provides a vivid account of events in his book "No time to lose" (1).) Two different filoviruses, Zaire ebolavirus and Sudan ebolavirus, were identified as aetiological agents.
The evolutionary origin of Ebolaviruses is not very clear. The simple notion that these viruses have been circulating for many millennia in wildlife in tropical parts of Africa, occasionally spilling over into human populations, often brought on by human activities, may not be correct or at least incomplete (2,3).

Since then there have been a number of Ebola disease outbreaks reported (4). Over time, a pattern in the outbreak response seemed to have been established, consisting of relatively prompt notification and deployment of specialised teams, typically provided by Médecins Sans Frontières (5) (MSF, Doctors Without Borders) and other NGOs with support from agencies such as the World Health Organization (WHO), the U.S. Centres for Disease Control and Prevention (CDC) etc. These efforts typically succeeded in bringing the outbreak under control through measures including adequate precautions against blood-borne virus transmission, quarantining of exposed individuals, isolation units for treating the diseased, etc. (6,7).

A lot was also learnt about Ebolaviruses, their epidemiology and ecology: The natural reservoir seem to be frugivorous bats (8,9); outbreaks pose an acute threat not only to human beings but also to Great Apes (10); their geographic distribution extends beyond Central and East Africa: Taï Forest ebolavirus occurs in Côte d'Ivoire (Ivory Coast) and Reston ebolavirus in the Philippines (with importation from there into the USA and Italy); Reston ebolavirus causes asymptomatic infection in human beings and can infect pigs; and in 2007, a fifth Ebolavirus species, Bundibugyo, was discovered in Uganda (11).

However, the 2014 Ebola outbreak challenges our understanding in many respects. It started in Guinée forestière (Forested Guinea) in West Africa, far away from regions previously known to harbour Ebola viruses, toward the end of 2013, apparently through one zoonotic transmission event followed by generation upon generation of human-to-human transmission (12). Whether human influences may be to blame is being disputed (13). The outbreak has so far (as of 2nd September 2014) spread to Sierra Leone, Liberia and Nigeria, with most recently an imported case being reported from Senegal.

The outbreak is continuing and clearly out of control. The number of probable and confirmed cases is 3069, with 1552 deaths, but there are fears that many cases go unreported. Its burden is already greater than that of all previous outbreaks combined, and no end is in sight: Over 40% of cases have occurred within the past 3 weeks (14).

Sadly, neither Liberia (1378 cases with 694 deaths) nor Sierra Leone (1026 cases with 422 deaths) were able to learn from the events unfolding over months just across their borders in Guinea (648 cases with 430 deaths) and now carry the greatest burden. Especially troublesome is the high number of infected health care workers (more than 240 of whom about half have died), leaving already struggling health care systems even worse off. However, this does not mean that established infection control measures are insufficient; a lack of personal protective equipment, its improper use, and the sheer burden of many critically ill patients and far too few staff account for this tragedy. That a single infected traveller from Liberia to Nigeria caused 17 direct and subsequent transmissions points to serious flaws with applying very basic protective measures.

While MSF had repeatedly issued dire warnings months ago already, official agencies were overly complacent. It seems that only the medical evacuations of several foreigners to their home countries served as wake-up calls to

the international community. While this is useful in that finally sufficient resources are being devoted to the issue, the sense of panic about the possible importation and subsequent spread of Ebola virus in industrialised countries is unjustified and counterproductive (as so beautifully expressed by Zapiro recently (15)).

Apart from a belated and panic-driven response, there is a very active discussion of specific treatment options. Ebola is a classical neglected tropical disease; these diseases occur in resource-poor settings and thus offer little financial incentives for research and development to be undertaken by drug companies, as the vast majority of those who would benefit from such drugs would not be able to afford them. Luckily though (odd as it may sound), filoviruses are regarded as potential biowarfare or bioterrorism agents under the highest priority Category A (16) which has triggered major government investment into vaccine and drug development (17). This is at the origin of many of the treatment modalities currently being discussed and, in some cases, even administered although none of these has undergone a phase 3 clinical trial. However, most of these discussions do not take cognisance of the extremely limited clinical care most Ebola patients currently receive which certainly contributes to the high fatality rate. This needs to be addressed and improved very urgently, not least to increase community confidence in the health care system (18-20)). Furthermore, it is also sad that although after the SARS outbreak in 2003 (21), the "swine 'flu" pandemic of 2009, and on other occasions, there have been discussions around the need to prepare in advance so that controlled clinical trials can be instituted rapidly once outbreak situations occur, none of this seems to have been translated into practice (22). In any case, the key to controlling the outbreak will not lie in providing specific therapies (even if safe and effective) to a few (for sufficient quantities of these compounds will not be available for months to come) but in implementing an effective response as outlined in WHO's "roadmap" (23).

The magnitude and propensity to spread of the current outbreak have been seriously underestimated (24). Most experts expect it to get a lot worse before it will be brought under control. Missed opportunities abound. Lack of preparation for the event of cases reaching industrialised or middle income countries such as South Africa is not one of them. Although one can never exclude the possibility of limited onward transmission, especially when the index patient's Ebola diagnosis is not made in time, it is highly unlikely that even such an unfortunate event would result in a larger outbreak. While the recent events in Nigeria may serve as a warning I believe that places like Cape Town are as safe as most European or American cities, as long as complacency does not set in.

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