No room for blame after our surprise from Ebola

LONDON, UK----1st October 2014----ExpertREACT. Unless we fund significantly every possible rare pathogen associated with outbreak potential and high mortality, we will always be caught short by our inherent nature to prioritise precious resources. The Ebola headlines are chilling, especially the first US imported case – but blaming ourselves is futile.

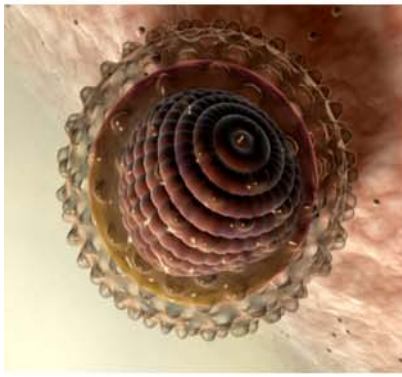
Ebola virus disease (EVD) has always been in the back of our minds, but as some rare, exotic disease affecting only a minority in deepest Africa. The first significant outbreak in Zaire, 1976 measured 318 cases albeit with high mortality (88%) (1) - a well known characteristic of this lethal *Filoviridae.* Now in 2014, infectious diseases continue to surprise us with their unpredictability. The latest Ebola outbreak, which began in March 2014, dwarfs all outbreaks so far recorded with 6553 probable and suspected cases and 3083 deaths. Countries so far affected are Guinea, Liberia, Sierra Leone, Nigeria, Congo and Senegal; the most widespread and intense transmission occurring in the first three of this list. Experts estimate that between 550,000 and 1.4 million people could be infected in the West Africa region by January 2015. This makes chilling headlines and causes fingers to point (2).

Ebola is transmitted through direct contact with infected blood or bodily fluids and fortunately, is not airborne as in the case of measles, diphtheria and whooping cough. The natural reservoir of the virus has not yet been identified, although it is suspected it is an animal, possibly members of the *Pteropodidae* family (fruit bats). Symptoms generally occur after 2 to 21 days with appearance signifying infectiousness. A similarity with other infectious diseases such as malaria, typhoid fever and meningitis hampers rapid disease identification of EVD with laboratory tests being necessary to confirm EVD and involve an extreme biohazard risk for field personnel. Good outbreak control with community engagement has been cited to be the key to successfully controlling Ebola outbreaks; hence, countries with more advanced primary health care systems have been better prepared. The WHO has published the Ebola Response Roadmap (3), which has the goal of stopping Ebola transmission in affected countries within 6 to 9 months and preventing international spread. The estimated cost of the roadmap is $490 million.

As is often the case, Western countries are concerned that EVD can spread beyond Africa, especially since some infected personnel have been transported to their home countries. In fact, the first imported US case was reported in Dallas, 1st October. The US Centers for Disease Control and Prevention states that any US hospital that is following their infection control recommendations (4), and can isolate a patient in their own room with a private bathroom, is capable of safely managing a patient with Ebola. Indeed thus far, two out of four US health workers infected with the virus have recovered after US treatment. Overall, experts state that the risk of a U.S.-based Ebola outbreak is very low but for precaution, a level 3 travel alert to affected countries is in place. A confused public remain wary and suspicious.

With many rare pathogens that do not pose a continual threat, the healthcare community, once again, is caught short in terms of specific therapies. No vaccine or anti-viral has been proven to be effective against Ebola. Treatment is therefore symptomatic i.e. providing intravenous fluids and balancing electrolytes, coupled with the maintenance of oxygen status and blood pressure. Co-infections are treated with antibiotics as they occur. The WHO Ebola Response Roadmap, aside from cataloguing the huge range of human and logistical activities does include a section on research and product development. This section has the objective to fast track treatment of vaccine options with guidance on safety, efficacy, quality, regulatory standards and ethical use of therapies in the pipeline (3).

Before this latest outbreak, some entities within the public and private sector had programs, focused on the Ebola virus. One good example has been the collaborative development of ZMapp™, a blend of three monoclonal antibodies manufactured in Nicotinia directed against Ebola like the Zaire virus strain identified in January 2014. ZMapp™ is being by San Diego company, Mapp pharmaceuticals Inc (5) and contains MB-003, another serum, developed by Mapp in collaboration with USAMRIID. MB-003 has been shown to protect nonhuman primates (43%) against EBV within one or two days of viral challenge (6). ZMapp™ also contains Zmab developed by Toronto based Dreyfus Inc in collaboration with the Public Health Agency of Canada. ZMapp™, despite never being shown to be safe and effective in humans, has been granted emergency use authorisation by the US FDA.



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Supplies of ZMapp™ are currently exhausted although the manufacturers are working with the US government to scale up production. People are asking why large supplies of ZMapp™ aren't being shipped to Africa.

The apparent lack of past urgency to focus on Ebola treatments such as ZMapp™ is a controversial topic, covered in depth elsewhere **(7)**. Possibly, in response to this lack of action, in early September, US BARDA announced an 18-month contract with Mapp to advance ZMapp™ worth a total of $42.3 million **(8)**. President Obama assures us of his grave concern.

In terms of active vaccines, a number of programs have recently been discussed. The NIH's National Institute of Allergy and Infectious Diseases announced they are expediting their work and are launching phase 1 clinical trials of an Ebola vaccine (ChAd3) along with GlaxoSmithKline Biologicals as part of a wider international consortium **(9)**. Similarly, the NIH is supporting a Crucell (Johnson & Johnson) candidate that most likely lay dormant. Other companies involved in early-stage treatments include BioCryst, Newlink (PHAC), Inovio, Profectus and Tekmira **(10)**.

Ebola has ignited a call to arms among international politicians and champions of the public and private sector with some hubris. But let's be realistic, unless we fund significantly every possible rare pathogen associated with outbreaks potential and high mortality we will always be caught short by our inherent nature to prioritise precious resources. We shouldn't use Ebola as a reason to apportion blame but get to work on pushing forward.

***Top 5 companies:** GSK Biologicals, Sanofi Pasteur, Merck & Co, Pfizer (Wyeth) and Novartis Vaccines and Diagnostics

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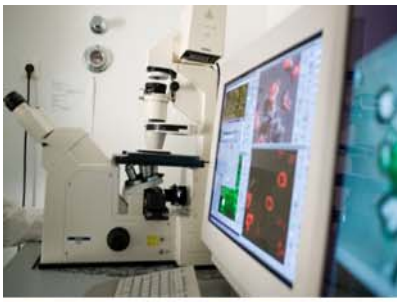

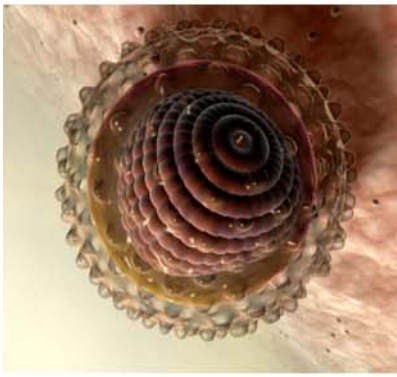

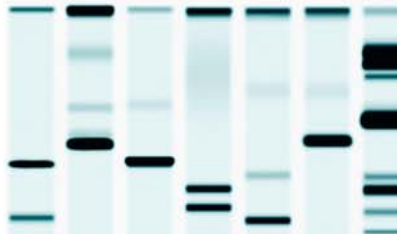

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