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As if the Ebola outbreak was not enough to convince the biomedical, public health and pharmaceutical communities to prepare vaccines in advance of epidemics, we now have the Zika virus. The media have raised justifiable concern about the spread of this mosquito-borne virus throughout much of the western hemisphere. The virus originated in Africa and like many other agents of disease, has migrated from one continent to distant parts of the world. As is now well known, Zika is associated with severe abnormalities in babies born to mothers infected by the virus early in pregnancy, notably microcephaly. In this regard it resembles rubella and cytomegalovirus, and although Zika is unrelated to those viruses some evidence suggests that like them Zika crosses the placenta to infect the fetus. And as with Ebola at the start of the West Africa epidemic we have no vaccine.

The problem is that commercial vaccine companies are not going to spend the millions of dollars necessary to bring a vaccine to use in humans unless there is a market for them. Previous experience shows that at least half a billion dollars are spent to license a single vaccine. As the size of a market for emerging infections is likely to be small in the absence of an epidemic, vaccine development is usually confined to animal studies. Fortunately scientists almost always embark on vaccine development as soon as a pathogen is identified. The objective of those early studies of experimental vaccines is to demonstrate protection in animals. But success in animals cannot be transposed immediately to allow use in humans when an epidemic strikes. The path from an experimental vaccine that is successful in animals to one shown to work in humans is long, expensive, and has a high failure rate [1,2]. The candidate vaccine must be produced in a safe and reproducible manner involving detailed process development. Then it must be progressively tested in increasing numbers of humans to show safety and efficacy, usually referred to as phases I, II and III. This path is reliably estimated to be 3–5 years long after coming from the laboratory and may be longer if unexpected problems arise.

Those of us who are vaccine developers have long deplored this situation, and after the Ebola epidemic sensitized the world to the absence of prevention, Dr Adel Mahmoud (formerly President of Merck vaccines), Jeremy Farrar (Director of the Wellcome Trust) and I wrote a proposal in the New England Journal of Medicine to establish a Global Fund for Vaccine Development [3]. This fund would reimburse companies to bring a vaccine against a potentially epidemic infection through the so-called Valley of Death, the transition from successful prevention in animals to some proof of safety and efficacy in humans. At that stage, a vaccine could be pursued for licensure or at least a stockpile put away for emergency use. Of course, vaccines are not the only means of prevention, as exemplified by the need for mosquito control in the case of Zika.

Financing is not the only obstacle to developing vaccines for epidemic and emerging diseases. As Ebola showed, there are complex issues of ethics, trial design and legal liability to think through before a trial vaccine can be deployed in large populations. In Ebola, the time taken to work these issues through delayed trials until the epidemic was already waning, which undermined efforts to demonstrate efficacy. Zika presents an additional challenge if trials are conducted in women of reproductive age, as safety for the fetus must be assured.

Both the Foundation for Vaccine Research, of which I am a member, and the World Health Organization have created lists of known pathogens that cause what are usually called emerging or neglected diseases. The list includes haemorrhagic fever viruses other than Ebola, the Middle East respiratory syndrome coronavirus that spread from Saudi Arabia to South Korea, the enterovirus 68 that causes neurological disease in children, the bacterial cause of paratyphoid fever and other pathogens for which we do not have vaccines for human use (Table 1). One can argue about the content of the list or the priority of one candidate or another. However, decisions regarding funding could be made by committees of experts using collected information. The difficulties of making vaccines under emergency conditions are further compounded when a pathogen emerges with little or no prior awareness of its potential for global spread.
Conditions, with the medical, legal, ethical and regulatory constraints of good practice were amply demonstrated in the recent Ebola crisis. When new agents are discovered they can be considered for investment in vaccine development. If a profitable market for a vaccine developed using the fund’s money becomes evident, the manufacturer may sell it according to a prearranged formula that rewards the fund and maintains a reasonable price.

Fortunately, the idea of making vaccines in advance of epidemics has gained some traction. Many experts in public health have agreed that the idea of the proposed fund is basically sound and most of the major vaccine manufacturers agree that something along these lines must be done. At the recent World Economic Forum in Davos, Switzerland, this proposal and others were discussed by representatives of governments, vaccine manufacturers, philanthropic organizations and private donors. There was general agreement that a new structure is needed to change the situation for the future. Now the task is to obtain the required funds to create a fund and a structure to manage it. We have estimated that 100 million dollars are necessary to bring a single vaccine to a usable point, and that a fund of 2 billion dollars would cover the immediate threats. The money would be sought from governments of developed countries and from philanthropies, but governments of developing countries like Brazil, India and China should also contribute to protect their citizens.

Success would allow the world to react quickly to the next outbreak caused by an infectious agent, whereas failure will leave us in the same vulnerable position as were West Africa in the face of Ebola and Brazil in the case of Zika. We cannot allow these devastating occurrences to happen without preventive vaccines prepared in advance.

**References**

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