

USA focuses on Ebola vaccine but research gaps remain

As the hunt for an Ebola vaccine receives a boost, experts say that other avenues of research also need to be explored to help tackle the highly virulent disease. Talha Khan Burki reports.

WHO describes Ebola Haemorrhagic Fever (EHF) as “one of the most virulent viral diseases known to man”. The US Centers for Disease Control and Prevention (CDC) classifies Ebola virus as a category A bioterrorism agent. If the theoretically possible (but enormously difficult) task of aerosolising the virus were to be achieved, it would be a fearsome weapon. Then again, the Ebola virus cannot easily survive outside the body—it is quickly killed by sunlight—and the rapid progression to death among those infected restricts its ability to cause mass destruction.

Nonetheless, the potential risk is serious enough for the US Department of Defence to fund research efforts. It has provided US\$291 million for the US Army Medical Research Institute for Infectious Diseases (USAMRIID) to continue its work on a promising pair of drugs targeting the Ebola virus and the closely related Marburg virus. In May, USAMRIID announced a joint venture with biotechnology company Medicago to develop an Ebola vaccine.

Momentum has been building for some time. “There have been quite a few promising vaccine candidates in post-exposure treatment strategies that have successfully protected non-human primates”, explains Thomas Geisbert from the University of Texas Medical Branch, Galveston, TX, USA. His team, working with USAMRIID, demonstrated 100% efficacy in one such candidate in a study published last year in *The Lancet*. A successful vaccine could be used to inoculate laboratory workers and health-care professionals in endemic areas, and for post-exposure prophylaxis (the rabies vaccine is used in a similar manner). But transferring a prospective vaccine to the field is difficult.

There are ethical issues associated with licensing this kind of product. The Zaire strain of the Ebola virus can result

in a mortality rate of 90%. In which case, how can one arrange a placebo-control group? The FDA’s 2002 Animal Rule provides a way round this, allowing for certain demonstrably safe drugs to be licensed with the backing of efficacy data from a well characterised animal model. But this is a tiny global market—funding for any vaccine will inevitably require a donor government, probably the USA. “I would think we’re years away from a licensed product and bringing the kinds of vaccines or therapeutics into the regions that actually need them”, asserts Heinz Feldmann from the US National Institutes of Health. Therapeutics are likely to be particularly expensive, because of their steep production costs.

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Feldmann believes the emphasis should be placed on prevention. “It’s cheaper and likely to be more effective in the long-run.” This requires research. “One of the biggest challenges is to understand how the virus is being transmitted from the putative reservoir species to humans; or to other wildlife which then transmit it to humans”, Feldmann told *The Lancet*. Ebola has been found in chimpanzees and gorillas as well as forest antelopes. But the suspicion is that bats represent the natural reservoir, perhaps transmitting it to humans through fruit contaminated with faeces, saliva, or urine.

“It’s a totally understudied subject”, says Feldmann. Aside from confirming the key agent in the transmission chain and its living habits, there are all kinds of other questions: for example,

whether the virus is activated or reactivated at certain times in the animal’s life cycle. Answering such questions would require large-scale ecological studies, and these are expensive. Feldmann thinks it is worth it. “Understanding how Ebola is transmitted and where it is hiding is one of the handles to control the disease”.

“It’s a pity that so much research has the biological weapon aspect in mind rather than helping the affected population”, adds Esther Sterk from Médecins Sans Frontières. She points to difficulties dealing with an Ebola outbreak on the ground. “If we had more diagnostic possibilities at field level, that would help.” The CDC and the Public Health Agency of Canada have mobile laboratories that can be deployed to offer on-site diagnostic support, and there are several laboratories dotted around Africa which can diagnose Ebola. But the situation is far from ideal. “We’re still suffering from the fact that diagnosis, and confirmation of diagnosis, takes too long”, agrees Feldmann. This is a particular problem if a suspected patient is held in a hospital without the capacity to prevent human-to-human transmission. Sterk cites outbreaks where it has taken 10 days to receive diagnostic results. “We’re lacking a biochemical and haematological test adapted to the field situations in which outbreaks usually occur”, she adds.

Meanwhile, Geisbert speculates that vaccines and treatments in development might be deployed on compassionate grounds if a serious outbreak were to hit central Africa; but certainly in the short-medium term, control measures offer the region its best chance of combating the virus.

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This online publication has been corrected. The corrected version first appeared at www.thelancet.com on October 7, 2011