Innovation brief

KEY MESSAGES

East Coast fever (ECF), a parasitic disease of cattle, has a major impact on livestock farming in sub-Saharan Africa, killing over one million animals a year.

Losses caused by ECF are particularly devastating for smallholder farmers. The reduction in productivity and income can push poor households deeper into poverty.

A live vaccine has provided protection for over 1.5 million cattle and benefited 150,000 farming households so far. The vaccine provides life-long immunity after a single inoculation.

The live vaccine is expensive to produce, store and deploy. As a result, scientists are searching for other methods of control.

Extensive research, including the mapping of the parasite genome and gaining an understanding of the mechanisms through which cattle develop immunity to infection, is helping scientists to develop a subunit vaccine.

Scientists at the International Livestock Research Institute (ILRI) are exploring other methods of tackling the disease. These include co-infecting cattle with a less virulent strain of the parasite and identifying the genes which confer resistance to ECF.

SUMMARY

Livestock are vitally important for the welfare and survival of hundreds of millions of households in Africa. Not only do they provide meat, milk and draught power, but they are often the main source of income. Because of their importance, considerable effort has been put into tackling East Coast fever (ECF), a tick-borne parasitic disease that kills one animal every 30 seconds. A live vaccine has provided immunity for some 1.5 million cattle so far, but its production is expensive and time-consuming. Scientists at ILRI are researching other methods of controlling the disease, including a subunit vaccine that could be made widely available to pastoralists and dairy farmers.

A woman milks a cow in Nyandarua, Kenya. Tackling East Coast fever is a priority because of the potential devastating effects the disease has on smallholder farmers.

Banner photo: A woman dairy farmer, with her dairy cattle.
INTRODUCTION

ECF is caused by the protozoan parasite *Theileria parva* (*T. parva*), which is transmitted to cattle by the brown-ear tick, *Rhipicephalus appendiculatus*. The disease occurs in 12 countries in eastern, central and southern Africa and kills over one million cattle a year. It affects both dairy cows and zebu cattle in pastoral systems. For smallholder farmers, the losses caused by ECF can be devastating.

In herds of cattle that have not been previously exposed to or infected by *T. parva*, over 80% die within three to four weeks of infection. Animals become listless and anorexic, while the infection rapidly spreads to the lungs, liver, kidneys and sometimes the brain. In the Ngorongoro Conservation Area and a trans-border study site in northern Tanzania where indigenous Maasai zebu calves were the target of an immunization programme, ECF was responsible for 80% of deaths in the non-immunized population. It is estimated that 40 million of the 75 million cattle in eastern, central and southern Africa are at risk of catching the disease.

The direct impact of ECF includes the loss of livestock, the stunting of calves, reduced milk production among the survivors and the considerable costs of preventing and controlling the disease. A 1992 ILRI-led study estimated that ECF caused annual economic losses amounting to USD 170 million. A decade later, cattle deaths alone were thought to account for losses of more than USD 300 million. The costs today would be higher, especially when considering other factors such as the purchase of tick-killing acaricides. Smallholder farmers whose cattle are affected by the disease suffer from reductions in productivity and reduced incomes, which can make poor households even more vulnerable and food insecure.

The disease also has some significant indirect impacts. As local indigenous breeds of cattle are more resistant to ECF than imported breeds, farmers are deterred from adopting more productive modern breeds, which could provide higher yields of meat and milk. Many cattle farmers use acaricides to kill ticks and mites, but their widespread use has led to problems of resistance.

The early work on developing a vaccine for ECF took place at the East African Veterinary Research Organisation (EAVRO), based at Muguga, Kenya. This led to the creation of the Muguga cocktail, derived from three different strains of the parasite. This is delivered to cattle using the infection-and-treatment (ITM) method of vaccination, whereby cattle are infected with the live parasite and simultaneously treated with an antibiotic.

The ITM vaccine has provided immunity to some 1.5 million cattle and increased the incomes of 156,000 rural households, the majority in Tanzania, by an estimated USD 74 million. Vaccination programmes conducted between 1997 and 2014 prevented the premature deaths of some 400,000 cattle. However, the manufacture, cold-storage requirements and delivery of the ITM vaccine are complicated and expensive. As a result, donors and researchers continue to pursue the development of a cheaper recombinant subunit vaccine which could be easily deployed.

Less visible to the farming community, but highly significant in terms of scientific impact, has been work by ILRI scientists and their colleagues which has shown that T cells and antibodies play a key role in resisting infection by protozoan parasites like *T. parva*. This has provided valuable insights into the immunobiology of the host-parasite relationship. In collaboration with researchers elsewhere, ILRI scientists have also developed DNA-based methods to characterise *Theileria* parasites and they have mapped the parasite genome. The research into ECF helped to improve scientific understanding of the role of a specific enzyme in certain human cancers.
DEVELOPING A LIVE VACCINE

An early observation of ECF was that cattle which had survived one episode of the disease developed lasting immunity. This implied that vaccination against the disease was possible. The development of a live vaccine required technical innovations, including the ability to harvest the parasite’s sporozoites – the stage in the lifecycle that infects the host – from batches of infected ticks; the ability to preserve sporozoite stabilates – a purée of crushed parasite-infected ticks – in liquid nitrogen without affecting their infectivity; and the ability to induce immunity in cattle by injecting the stabilates together with a long-acting antibiotic. Without the latter – the antibiotic of choice being oxytetracycline – the inoculation of the sporozoites, which infect the white blood cells of the host, would almost certainly lead to death.

The parasite’s genetic diversity initially posed a serious challenge. Scientists at EAVRO found that an ITM vaccine using just one strain of *T. parva* would not provide immunity against other strains. What was needed was a mixture. This led to the development of a vaccine which used a combination of three different strains of the parasite, known as Muguga, Serengeti-transformed and Kiambu 5. The Muguga cocktail provided very good protection against the parasite both in the laboratory and in the field in many parts of East and Central Africa.

The Muguga cocktail vaccine has proved to be highly effective. In field trials carried out under the regional Tick and Tick-borne Disease Programme of the Inter-African Bureau for Animal Resources in Hanang and Handani districts in northern Tanzania, involving the immunization of 1,434 crossbred calves between 1997 and 2000, the vaccine reduced calf mortality rates from as high as 80% to just 2%. Pastoralists have reported that cattle with ear tags denoting that they have been vaccinated against ECF attract higher prices in the market than those of similar size which have not. In a survey conducted among pastoralist households, those whose incomes had increased after taking advantage of the ITM vaccination spent the extra money on school fees, staple foods and commercialising their livestock enterprises.

Unfortunately, cattle which have naturally survived a dose of ECF or been immunised with the live vaccine can become carriers of the disease. This has become an obstacle to the widespread deployment of the Muguga cocktail in areas where its three strains are not found. Although years of observation suggest that the use of the Muguga cocktail is safe, many countries beyond Kenya and Tanzania have resisted its use. Efforts have therefore been made to develop vaccines based on their own indigenous parasite strains. For example, in Zambia, the Katete and Chitongo stocks of *T. parva* have been used to develop a local vaccine for the control of ECF.

CONCOCTING THE COCKTAIL

ILRI has not only played a major role in conducting research on ECF, but ILRI was previously the centre of production for the first two large batches of the Muguga cocktail – 600,000 doses in 1996 and a further 1.2 million doses in 2007. A primary drawback of the ITM vaccine is that its manufacture is complicated, expensive and raises questions about animal welfare. The production of one million doses requires 130 cattle, 500 rabbits and at least 600,000 infected ticks. Each batch takes around 18 months to produce. Storage and transport require a liquid nitrogen cold chain, which poses a major challenge in Africa, and imposes significant costs when delivering the vaccine to rural areas.

The vaccine is contained in plastic straws containing 30 to 40 doses, suitable for immunizing large herds in a single location. Once thawed, the doses must be used within a few hours. To make the doses more readily available for smallholder farming systems, where fewer animals are vaccinated at a time, ILRI scientists developed a procedure to thaw, dilute, refreeze and repackage straws containing a small number of doses, without affecting the efficacy of the vaccine. However, this procedure has yet to be established commercially.

Although the Muguga cocktail provides good protection against cattle-derived parasites, this is not the case with parasites which come from African buffalo, which often graze in the company of domestic stock. This suggests that scientists need to develop a vaccine stabilate containing buffalo-derived parasites. This will not be easy as the parasite population found in buffaloes is extremely diverse genetically. Furthermore, the very low parasite load found in cattle infected with buffalo-derived parasites means large numbers of cattle would be required in the production process, quite possibly making it economically unviable.

The scaling up of ITM has been hampered by high production and delivery costs, although in recent years there has been renewed interest in administering the vaccine to prevent outbreaks of the disease. For example, since 2016 ILRI has been scaling up ITM use, especially in non-traditional dairy areas in Kenya where the high prevalence of ECF previously discouraged adoption of improved dairy breeds. The project has worked with private sector distributors through a subsidy programme to stimulate demand among pre-commercial dairy farmers. This also involves the training of vaccinators to increase local expertise. These efforts have attracted additional support from donors and local governments as demand has increased.
IN SEARCH OF ALTERNATIVE SOLUTIONS

Most pastoralists and dairy farmers in the regions affected by ECF have had to find ways of coping with the disease without the vaccine. Their main line of chemical defence has involved the use of acaricides, which also help to control other cattle diseases, but these have their drawbacks. They must be frequently applied, they are costly, and their continual use has led to resistance in the tick population. Although ECF can be treated with drugs, these are only effective if they are used at the early stage of infection and require constant monitoring of cattle, which can be challenging in remote pastoral situations. The drugs are also expensive. Many pastoralists and dairy farmers choose to stick with indigenous cattle, which are less susceptible to the disease, but less productive than exotic or crossbreeds.

Little wonder, then, that the development of a cheap and efficacious subunit vaccine – in other words, a non-live vaccine which uses synthetically generated parts of the parasite antigen – has for many years been a major focus of research for ILRI and its partners. This is no easy task, not least because of the complex nature of the parasite: *Theileria spp* have approximately 4000 genes, compared to less than 20 for an RNA virus like SARS-CoV-2.

The development of a vaccine is greatly helped by understanding the factors through which individuals develop immunity to an infection. In the case of ECF, this means identifying which *T. parva* antigens stimulate a protective immune response in cattle. Research at the International Laboratory for Research on Animal Diseases (ILRAD) in the late 1970s and early 1980s demonstrated that antigens on the *T. parva* sporozoites could stimulate an antibody response that could neutralize sporozoite infectivity in an *in vitro* assay. This led to the identification of the p67 sporozoite antigen, which in immunization experiments provided immunity to ECF. Other sporozoite antigens have subsequently been discovered but these have yet to be tested in cattle. The quest to develop a subunit vaccine is described in greater detail in the innovation brief ‘Developing a subunit vaccine for East Coast fever’ (https://hdl.handle.net/10568/119496).

Other ways of tackling the disease are also being explored. Recent research in Western Kenya has found that animals infected with ECF are less likely to die when they have been co-infected with one of *T. parva*’s less virulent cousins. The project, whose findings were published in 2015, looked at what happened to 500 indigenous East African shorthorn zebu calves when they were infected by both *T. parva* and the relatively innocuous *T. mutans*. Left untreated, the former kills some 80% or more of the animals infected: in contrast, the latter leads to a mild infection and infected animals often show no clinical symptoms. The researchers found that when animals were infected with both parasites there was an 89% reduction in mortality associated with *T. parva* infection. These findings could lead to an effective way of preventing the disease by pitting one form of parasite against another.

Researchers at ILRI have embarked on a new project to develop an attenuated live parasite vaccine. This involves removing some of the parasite’s genes to create a vaccine which, if successful, will stimulate an immune response without requiring a dose of antibiotics. This is the subject of another innovation brief ‘A genetic approach to tackling East Coast fever’ (https://hdl.handle.net/10568/118005).

In another potentially ground-breaking development, scientists at ILRI recently demonstrated that cattle derived from a single indigenous bull were resistant to ECF. In partnership with the University of Edinburgh’s Roslin Institute, the group combined the clinical data from the cattle with knowledge of their genetic background to identify a marker which is closely associated with resistance. This genetic marker could be used to spread the resistance trait more widely, either by using it in traditional breeding programmes or through gene-editing technology (discussed in another technical brief) – and it could thus become a key weapon in the armoury to defeat ECF.
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Publications


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