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The control of East Coast fever of cattle by live parasite vaccination: A science-to-impact narrative

B.D. Perry

Jenner Institute, Nuffield Department of Medicine, University of Oxford, UK
P.O. Box 437, Gilgil 20116, Kenya

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ABSTRACT

There is an increasing interest in determining the impact of vaccine technologies developed using public funding targeted at international development, and understanding the factors and ingredients which contribute to the success and impacts of such vaccines. This paper chronicles the development of a live vaccine against East Coast fever, a tick-borne disease of cattle caused by *Theileria parva*. The paper describes the technological innovation, commonly known as infection-and-treatment, which was developed some 40 years ago, explores the institutional settings in which the vaccine was developed and refined, and discusses the political dynamics of both during the decades from first development to field deployment and impacts. The paper also analyses the direct and indirect indicators of success of ITM and the many qualifiers of these, the impacts that the emerging technology has had, both in positive and negative terms, and maps the key contributors and milestones on the research-to-impact pathway.

1. Introduction

Cattle are highly valued in Africa, and in the eastern, central and southern regions of the continent, they play diverse roles in the livelihoods and economies of peoples and countries. So when a highly fatal disease of cattle appears to be interfering with the exploitation of this diverse livestock resource, the call for a sustainable solution is loud. So it has been with the call for a vaccine to protect cattle against East Coast fever (ECF).

ECF is tick-borne and indigenous to the region, probably originally a parasite of the Cape buffalo (*Syncerus caffer*). It was first described in eastern Africa as *Amakebe* by Bruce et al. (1910) [1], where it had been endemic and apparently recognised for centuries as a relatively mild disease of calves. Surprisingly, it was only when tick-infested cattle were exported by boat from eastern to southern Africa in 1901 and 1902, and the disease appeared in what is now Zimbabwe, that the disease became widely recognised [2]. Rinderpest had earlier swept down through southern Africa, wiping out over 2.5 million cattle in South Africa alone, before it was eradicated from that country in 1899. As a result of rinderpest and of the effects of the Boer war (1899–1902), the cattle populations of southern Africa had become depleted, and were inadequate to meet the multiple needs of the region [2]. As a result, cattle were imported from many sources, including Kenya and Tanzania, where ECF, in its milder form in the resistant indigenous animals of the region, had been existing almost unnoticed for generations. It was only when the early European settlers started to arrive in eastern Africa, importing exotic cattle breeds, that the disease was recognised there, and it was not until 1911 that the endemic disease in eastern Africa and the epidemic highly fatal disease in southern Africa were found to be one and the same [3].

This narrative describes the story behind the development of a live vaccine against ECF, probing the technological achievements which laid the groundwork for the innovation, the institutional settings in which this occurred, and the political dynamic of both over the last 50 years. It also analyses the indicators of success and the many qualifiers of these, the impacts that the emerging technology has had, both in positive and negative terms, and maps the key contributors and milestones on the research to impact pathway.

2. Livestock disease priorities in Eastern Africa in the evolving social and political landscape

2.1. The legacy of colonial livestock systems and accompanying research imperatives

Somewhat surprisingly in the context of 2016, the fundamental and widespread belief in Kenya in the late 1960s and early 1970s was that the priority disease of cattle in eastern Africa was ECF. While this disease undoubtedly continues to feature in any livestock disease-ranking in Kenya and indeed in other countries of the eastern and southern African region, in today's context we would likely ask the questions: "priorities to whom?"…and…. "on what evidence?" The evidence that was available at the time to answer these unasked questions was derived almost entirely from the more commercially orientated livestock enterprises of the European settler community and the priorities of the former colonial government and its veterinary services and diagnostic

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laboratories. The changes and development in livestock systems, particularly in Kenya, have been phenomenal over the past 35 years, and especially over the past 15 years or so; the trend in the highland regions has been a progressive intensification[1] of smallholder mixed farming systems in which livestock are central (see for example Van de Steeg et al., 2005) [4]. In these systems tick-borne disease control has moved from a broad public sector responsibility, administered through community cattle dips, to farmer operated backpack application, spray race systems and private dips, depending on the scale of the enterprise. This devolution of responsibility has provided much more effective control of ECF, even in the absence of a vaccine.

But it is not only the livestock production systems that have changed; the animal disease research environment has had its own dynamic. Looking back at the veterinary research landscape in Kenya during the late 1960s and early 1970s, the period immediately following independence, the already existing and competent disease research infrastructure which had existed was replaced, at least for a decade or so, by a wave of new technical assistance attempting to provide continued veterinary service and research support to post-colonial livestock enterprises, and to train the new generation of African scientists. But the story was not that simple.

2.2. The changing institutional framework

During the latter part of the colonial era in eastern Africa, the main centre of research on ECF and other tick-borne diseases (TBDs) was at the East African Veterinary Research Organization (EAVRO). EAVRO was one of five research organizations responsible to the East African Agricultural and Fisheries Research Council, under the East African High Commission (EAHC). The EAHC operated from 1948 to 1961, then became the East African Common Services Organization (EACSO) from 1961 to 1967, and finally the East African Community (EAC) from 1967 to 1977. The EAC collapsed in 1977, (but was revived in 2000). The 1956/57 Annual Report of EAVRO stated that their laboratories at Muguga North were completed towards the end of 1954 and opened by the Governor of Kenya Sir Evelyn Baring on 21st February 1957. The staff listing contained some notable names, such as Walter Plowright, who was to go on to receive the World Food Prize for his work on rinderpest tissue culture vaccine development,[2] which contributed significantly to the ultimate global eradication of rinderpest in 2011.

The tick-borne disease research group at the time was led by Steve Barnett, with colleagues David Brocklesby and Peter Bailey, among several others in the team. ECF was a major focus of their work, principally studying the transmission and chemotherapy of the infection; some research on immunisation of cattle had started which involved a 28-day therapy regimen of the antibiotic aureomycin following their infestation with ECF-infected ticks, which was perhaps the first successful exploitation of an ITM approach undertaken at EAVRO.

In December 1963, just five years after the opening of EAVRO at Muguga, Kenya gained its independence from the UK, and the UK government continued its support to livestock disease research. In 1967 the United Nations Development Programme (UNDP) initiated the funding of a 10-year research programme on tick-borne disease research under the auspices of the Food and Agriculture Organisation (FAO), based at EAVRO, Muguga.[3] It was this FAO-administered research programme which was ultimately responsible for developing the ITM live vaccination against ECF.

While having as its objective the study of controlling ticks and tick-borne diseases in general, the project placed special emphasis on immunological work designed to control ECF by means of a vaccine. The project started operations in May 1967 at the laboratories of EAVRO, originally a project of three years duration but as a result of two extensions it continued until the end of 1976, just prior to the collapse of the EAC. With the collapse of the EAC in 1977, EAVRO was absorbed into the Ministry of Agriculture and renamed the Veterinary Research Department (VRD) and in 1986 it was brought under the Kenya Agricultural Research Institute (KARI) as the National Veterinary Research Centre (NVRC). Research on ECF continued at Muguga at the renamed NVRC. Importantly, despite the end of FAO's important contributions to EAVRO, the organisation continued to be heavily committed to supporting research on ECF and other TBDs in eastern and southern Africa for several decades to come, and many of the subsequent regional discussion forums held were co-financed by FAO.

2.3. The birth of the CGIAR and ILRAD

There was substantial international interest in providing technical support to the newly independent countries of eastern Africa and elsewhere during the years immediately following Kenya's independence in 1963. The Ford and Rockefeller Foundations had helped launch the International Rice Research Institute (IRRI) in the Philippines, and two years later the two Foundations began discussing the possibilities of a centre concerned with improving the yield and quality of tropical food crops other than rice; the International Institute of Tropical Agriculture (IITA) was opened in 1967 near Ibadan, Nigeria [5]. This process gained momentum and in 1970 the Rockefeller Foundation proposed a worldwide network of agricultural research centres under a permanent secretariat. Notably, this was coincident with the early years of the FAO programme at EAVRO in Muguga. The concept was further supported and developed by the World Bank, FAO and UNDP, and the Consultative Group for International Agricultural Research (CGIAR) was established on May 19, 1971 to coordinate international agricultural research efforts aimed at reducing poverty and achieving food security in developing countries.

A study had been commissioned by the Rockefeller Foundation to explore the creation of a livestock disease research centre (McKelvey and Pino, 1971) [6]. The CGIAR created an "African Livestock Subcommittee", which asked the Rockefeller Foundation to act as executing agency in negotiations with the EAC for the establishment of an animal disease research laboratory, to be known as the International Laboratory for Research on Animal Diseases (ILRAD) and to be located at EAVRO, Muguga. At a meeting of the EAC Council on July 20th 1972 a decision was taken that the EAC could not host an autonomous institution as had been proposed, and the invitation to establish ILRAD within the EAC was withdrawn. The subcommittee then agreed to pursue an alternative option of establishing ILRAD at Kabete outside Nairobi. The first step was to reopen negotiations with the Kenya Government, through a letter from the then President of the World Bank, Robert McNamara, to President Jomo Kenyatta. In the letter, reference was made to earlier correspondence in which President Kenyatta had expressed his interest in research on animal diseases in eastern Africa, and had offered facilities and support of the Kenya Government. The letter mentioned that if and when a comprehensive animal production and health centre should be established for tropical Africa (referring to parallel negotiations going on at the time with the Imperial Ethiopian government on the establishment of the International Livestock Centre for Africa -ILCA), there would be the possibility of a link between *or even the integration of* these two centres. Ironically in January 1995 the two CGIAR institutes of ILRAD, based in Nairobi, Kenya, and ILCA, based in Addis Ababa, Ethiopia, were united as the International Livestock Research Institute (ILRI).

[1] FAO (2004) defined intensification as an increase in agricultural production per unit of inputs (which may be labour, land, time, fertilizer, seed, feed or cash). For practical purposes, intensification occurs when there is an increase in the total volume of agricultural production that results from a higher productivity of inputs, or agricultural production is maintained while certain inputs are decreased (such as by more effective delivery of smaller amounts of fertilizer, better targeting of plant or animal protection, and mixed or relay cropping on smaller fields). The ethics of sustainable agricultural intensification, FAO, Rome. http://www.fao.org/docrep/007/j0902e/j0902e00.htm#Contents.

[2] http://www.worldfoodprize.org/en/laureates/19871999_laureates/1999_plowright/.

[3] http://www.fao.org/docrep/003/x6519e/x6519e00.htm.