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3 Tsetse and Trypanosomiasis Control in West Africa, Uganda and Ethiopia: ILRI's Role in the Field

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Introduction

African animal trypanosomiasis (AAT) occurs where the tsetse fly vector exists in sub-Saharan Africa, between the latitudes 15°N and 29°S (Randolph *et al.*, 2003). It affects ruminants, camels, horses and pigs, and constrains cattle production over an area variously estimated to be between 8 and 10 million km[2] in Africa. Around 67 million cattle live in tsetse-infested areas out of a total of 253 million in Africa[1]. In some situations, around one in 20 of the cattle at risk die each year, and the productivity of the survivors in terms of draught power, milk production, growth and birth rate are lowered by 10–40% (Swallow, 2000). Estimated total losses due to trypanosomiasis range widely depending on the methods used, assumptions made and types of losses estimated (ILRAD, 1994; Budd, 1999; Kristjanson *et al.*, 1999; Swallow, 2000). The upper range of published estimates would make annual losses from trypanosomiasis equal to one-third of the estimated livestock gross domestic product in sub-Saharan Africa.

The disease is complex, involving three species of parasite, namely *Trypanosoma congolense*, *T. vivax* and *T. brucei*. *T. vivax* can also be transmitted mechanically by biting flies, and thus is also found in parts of Africa free or cleared of tsetse and in parts of Central and South America.

Two related parasites, *T. brucei* subsp. *gambiense* and *T. brucei rhodesiense*, cause human African trypanosomiasis (HAT), also known as sleeping sickness. While HAT is generally considered a disease of people, livestock and wildlife act as reservoirs for *T. b. rhodienense* and possibly for *T. b. gambiense*, complicating the control of HAT. Knowledge of the biology of tsetse and trypanosomiasis was greatly advanced by Mulligan and Potts (1970) and by Maudlin *et al.* (2004).

Trypanosomes have the ability to undergo antigenic variation (Cross, 1975), enabling host invasion and allowing them to establish persistent infections. In addition, each species comprises an unknown number of strains, all capable of elaborating a different repertoire of variable antigen types. Hence, no vaccine is currently available (the problem of antigenic variation and the history of vaccine development are discussed in Chapter 2, this volume).

The initial mission of the International Laboratory for Research on Animal Disease (ILRAD) was to tackle AAT and East Coast fever, two of the most serious intractable African livestock diseases. As a result, a large body of research on AAT was conducted over 30 years: genetics, breeding and immunology research are discussed in Chapters 1, 2 and 4 of this volume, respectively. This chapter reviews the earlier field work of ILRAD followed by that of International Livestock Research Institute (ILRI) after 1994 in East and West Africa, including the engagement of those institutions with regional and global initiatives.

Field Work on African Animal Trypanosomiasis

AAT has long been regarded as the single most important cattle disease in Africa, and between 1905 and 1960 it commanded the attention of five imperial powers, dedicated government services, and national, regional and international research institutions. It has been estimated that 25% of colonial research spending went to trypanosomiasis (Rogers and Randolph, 2002). However, the final decade of the last century saw practical control of trypanosomiasis. With the onset of the Great African Depression in the 1980s (Leonard and Straus, 2003), tsetse programmes, like other government services, became increasingly underfunded and dysfunctional, and donors were less willing to pay for large-scale, long-term control. Moreover, control efforts before the 1980s usually relied on ground and aerial spraying of insecticide, which was increasingly seen as expensive in economic and environmental terms. One study (Meyer *et al.*, 2016) argues that tsetse control operations covered barely 1.3% of the estimated infested area in sub-Saharan Africa.

As a result of this decline in the funding available for control, an upsurge of AAT cases occurred during the post-independence period. In some countries, this was exacerbated by the movement of people and livestock into formerly sparsely inhabited tsetse-infested areas. AAT incidence increased rapidly in the 1980s and 1990s, and cattle herds almost disappeared in some areas, such as the Ghibe Valley of Ethiopia and the Yale agropastoral zone of Burkina Faso. The 1980s also saw a major epidemic of HAT in Sudan and Uganda, which spread into Kenya. As a result of these upsurges in human and animal disease, there was renewed interest in the field control of AAT, several new initiatives were established involving ILRAD and the International Livestock Centre for Africa (ILCA).

Apart from efforts to understand and manage AAT, ILRI focused on three major areas: (i) the promotion of trypanotolerant cattle; (ii) community-based control of tsetse in Ethiopia and later Burkina Faso; and (iii) managing resistance to trypanocides. ILRI did not engage with the attempt to eradicate tsetse from Africa, which scientists believed was infeasible. The areas of ILRI activity are first briefly outlined, and the rest of the chapter focuses on the work done and the impacts achieved in different countries. Table 3.1 summarizes ILCA/ILRI research since about 1990 on field aspects of trypanosomiasis control.

Trypanotolerance

The challenges of tsetse control and the ongoing cost of trypanosomiasis control by veterinary drugs were recognized early in the history of ILRI. One option that gained attention early on was to exploit the genetic tolerance to trypanosomiasis infection found in several African cattle breeds, such as the taurine N'Dama and West African

Table 3.1. Research on tsetse and trypanosomiasis control in West Africa and East Africa since 1990 by ILRI and partners. (Data from ILCA and ILRI annual reports, various years.)

Institution	Location	Period	Objectives	Interventions	Tsetse reduction from baseline	Reduction of AAT prevalence	Difficulties	Sustainability
ILCA	Ghibe River Valley, Ethiopia	1990–1992	Vector control	ITC, ITT, TRY	74–81% depending on species	85%	Theft of traps, socio-political disturbances	Unsustained. Tsetse reinvasion, second phase from 1993 mixed results
ILCA	Ghibe River Valley, Ethiopia	1991–1993	Vector control	ITC, TRY	0–93% depending on species	60%	Slow decline in tsetse densities	Sustained in the short-term. Control was in place 5 years later. Full cost recovery from farmers
ILRI evaluation on CIRDES projects	Burkina Faso	1990–2000	Vector control	ITC, ITT	98.4%	80%	Farmers could not meet costs to continue control	Epidemics controlled; however, tsetse reinvasion and return of AAT after campaign
ILRI evaluation of ICIPE project	Kenya	2002–2006	Vector control	ITC	Not measured	22%	Low effectiveness	No business case for innovation
ILRI	Burkina Faso, Mali, Guinea	2002–2006	Integrated control	ITC, ITT, TRY, TTC	Significant	Significant	Communal action difficult; disabling policy	Only TRY proved sustainable

CIRDES, Centre International de Recherche-Développement sur l'Elevage en zone Subhumide; ICIPE, International Centre of Insect Physiology and Ecology; ITC, insecticide-treated cattle; ITT, insecticide-treated traps and targets; TRY, trypanocidal drugs; TTC, trypanotolerant cattle.

Shorthorn breeds of West and Central Africa. These breeds had evolved over millennia to acquire a significant degree of innate resistance to trypanosomiasis. Trypanotolerant cattle were therefore identified as a promising approach to livestock keeping in tsetse-infested areas (Murray *et al.*, 1982).

There is evidence that cross-breeding occurs between bos indicus and bos taurus in West and Central Africa and that this may enhance resistance to trypanosomiasis (Traoré *et al.*, 2017 for southern Mali). The African Trypanotolerant Livestock Network (ATLN) was established in 1977 as a joint venture between ILRAD and ILCA. ILRAD was to investigate animal health, infection status and vector behaviour, while ILCA was responsible for animal production, nutrition and data processing. This research fell into four areas: (i) the epidemiology of AAT; (ii) the criteria of trypanotolerance; (iii) the genetics of trypanotolerance; and (iv) the health and productivity benefits of interventions. Field sites were located in Côte d'Ivoire, Ethiopia, Gabon, Zaire, The Gambia and Senegal. Along with the Food and Agriculture Organization of the United Nations (FAO), ILCA surveyed the number and distribution of trypanotolerant cattle in 1977 and updated those figures in 1985.

Two ILCA/ILRAD monographs established the state of scientific knowledge at the outset of the ATLN (Trail *et al.*, 1979a,b). A long compendium (ILCA/ILRAD, 1988) summarized the work of the first decade of the ATLN, findings that were extended by Rowlands and Teale (1994) and Itty (1992). The work of the ATLN included the following:

- Establishment of a research network to improve livestock production by ensuring optimal application of existing knowledge and recent research.
- Understanding the vectorial potential of tsetse.
- Supporting multiplication of herds of trypanotolerant animals.
- Maintaining experimental cattle and small ruminant herds.
- Evaluating the performance of livestock under AAT risk.

Community-based tsetse control

Tsetse (*Glossina* spp.) are unusual flies. The females do not lay eggs but instead produce a single, large larva and have only up to 12 offspring in a typical lifetime. Their low reproductive rate makes them vulnerable to interventions that cause even small increases in mortality. Historically, area-wide and aerial spraying was successfully used to control tsetse. However, the flies reinvaded after control, and repeated campaigns proved expensive and raised environmental concerns.

A more targeted approach is the use of cloth traps or targets that are soaked with insecticide, with or without baits. In the early 1900s, sticky traps worn by plantation workers were successfully deployed on the Island of Principe to eradicate *Glossina palpalis*. In the mid-20th century, great advances were made in the design of traps and targets, making them highly effective at reducing tsetse. The live-bait technique involves treating cattle with appropriate insecticide formulations, usually by means of cattle dips, or as pour-on, spot-on or spray-on veterinary formulations. These are highly effective against tsetse and have the additional advantage of controlling other flies and cattle ticks. The availability of these simple, cheap and effective technologies led to interest in community-based approaches to tsetse control.

Trypanocide resistance

In the absence of a vaccine (Chapter 2, this volume), the principal control strategies are reducing or eliminating the tsetse vector, applying trypanocides and keeping trypanotolerant stock. Less than 1% of the infested area is under vector control and fewer than 20% of the cattle at risk are trypanotolerant, but around the majority of cattle at risk receive trypanocidal drugs making this the most popular control option and one that is both effective at scale and sustainable without continued external support. Current trypanocides have been in use for over 40 years and new drugs have not been developed because drug development is expensive. One older survey of drug research and development costs derived an estimate of 'nearly' US$900 million per new compound across a range of human drugs (DiMasi *et al.*, 2003). The market for trypanocides in smaller African markets is estimated to be US$20 million per year (Sones, 2001). Hence, it will probably be unprofitable for private firms to develop new trypanocides for the African market. Given this context, threats to the efficacy of

the older trypanocides undermine the most widely used strategy for control.

Drug resistance is the heritable loss of sensitivity of a microorganism to an antimicrobial to which it had been sensitive. Modern cattle trypanocides were introduced in the 1950s, and the first cases of resistance were reported in the next decade. The emergence of resistance further complicated the breakdown in testse control that had led to reinvasions of tsetse.

ILRAD scientists had a major role in this emerging research area. Much of this work was laboratory based, focused on understanding the mechanisms of resistance and developing tests and assays for resistance. In addition, drug-resistant strains isolated from the field were characterized at ILRAD. However, ILRAD and ILCA scientists were also involved in some of the early studies on field resistance and were among the first to assess resistance in Ethiopia, Uganda, Kenya, Guinea, Mali, Ghana and other countries.

ILRI scientists were also instrumental in developing field tests for trypanocide resistance. These involved testing cattle for the presence of trypanosomes, treating them with trypanocides and then examining blood at intervals over 98 days to see if the trypanosomes were still present despite treatment (an indication of resistance). These methods were widely applied by other researchers and subsequently refined by shortening the follow-up period to 28 days. This abbreviated methodology for evaluating the presence of resistance lowers the cost significantly so that it can be used more readily by national agencies as an initial protocol for screening (Mungube *et al.*, 2012). The abbreviated trypanocide resistance tool has subsequently been used by other researchers.

ILRI impacts on AAT in Kenya

Given that ILRAD's mandate focused on vaccine development, there was relatively little field epidemiology in Kenya. Moreover, East Coast fever was seen by most stakeholders as of higher priority in Kenya. Small studies addressed aspects of control resulting in useful recommendations, although it is not clear to what extent recommendations were taken up or what impact they had.

An early study, conducted between 1982 and 1986 in coastal Kenya, evaluated the efficacy and subsequently cost–benefit of using prophylactic versus curative control. (Prophylactic drugs are given to prevent the animals from becoming sick; curative drugs are given to animals when they become sick.) Prophylactic treatment was more expensive but more profitable, mainly because lactation loss was avoided. When disease fell below a certain level, prophylaxis was less profitable (Itty *et al.*, 1988).

For example, ILRI research did contribute to the growing interest in using pour-ons for control of tsetse. A study in Kwale found incidence rates of trypanosomiasis in the biweekly-treated (28.2%) and monthly-treated (38.6%) animals were statistically lower than in the bimonthly (63.9%) and control (72.6%) groups (Muraguri *et al.*, 2003). Similarly, a study in a trypanosomiasis endemic area in Teso District, western Kenya, found that when the tsetse density was very low, control of trypanosomiasis in the Orma-Teso Zebu offspring in western Kenya required targeting of individual affected animals in the dry seasons (Gachohi *et al.*, 2009).

One of the most important studies in Kenya was a combined epidemiological and economic investigation into a promising novel technology: a synthetic tsetse repellent (Bett *et al.*, 2010). The evaluation involved 2000 cattle: 1000 head in a control group and another 1000 animals treated with tsetse-repellent dispensers suspended from neck collars. The effectiveness of the repellent was monitored for 16 months. The trial results showed that the treatment reduced trypanosomiasis infection rates by between 18% and 23% compared with the control levels, indicating that the repellent was not 'a viable alternative to existing control techniques' (Irungu *et al.*, 2007).

ILRI impacts in Ethiopia

In the 1970s and 1980s in Ethiopia, there were substantial movements of people and their livestock from the densely populated northern highlands to the scarcely populated, tsetse-infested south-western region. These livestock were vulnerable to AAT, and losses were originally high. Concern over the situation in Ghibe Valley, south-west Ethiopia, prompted ILCA to select it as the Ethiopia study site for the ATLN. This network comprised a set of 11 research sites located

in different trypanosomiasis-risk areas throughout tropical Africa in order to study the complex interactions that affect trypanotolerance, to provide baseline data for livestock development in tsetse-affected areas and to evaluate different methods for controlling trypanosomiasis (see Map 4, p. xx).

Studies on the prevalence of trypanosome infections in East African Zebu cattle and the tsetse challenge that such animals are exposed to started in January 1986. An average of 840 East African Zebu cattle (non-trypanotolerant) from around ten herds in the Ghibe Valley were monitored from January 1986 to April 1990. The studies provided information on the epidemiology and transmission dynamics of AAT, which were subsequently used in disease models and in planning control. Moreover, they resulted in the detection of drug resistance for the first time in Ethiopia (Rowlands *et al.*, 1993). Although sick animals were treated with trypanocides, the prevalence of AAT increased yearly, raising the suspicion of drug resistance, which was confirmed by laboratory analysis of trypanosome isolates collected in 1989.

It was decided to test an intervention based on tsetse control using cloth screens impregnated with insecticides. This approach had been first used in 1914, when tsetse was eradicated from the Island of Principe, in the Gulf of Guinea, by killing the flies using 'sticky traps' – wooden boards coated with sticky material strapped to the backs of plantation workers. Serious interest in the use of vector capture was revived in the 1970s with the development of more effective cloth traps and screens and the discovery that particular colours and odours attract tsetse flies. Much of the foundational research was conducted in Zimbabwe, with another focus in West Africa.

Both traps and targets (cloths or screens) were developed and successfully piloted in South, East and West Africa, but had not been used for the control of trypanosomiasis in cattle in situations where resistance to trypanocides occurs. The trial found that use of targets reduced vector populations and infections, even in the presence of drug resistance, but did not appear to be sustainable due to widespread thefts of targets (Leak *et al.*, 1996).

Another approach to tsetse control is to turn cattle into mobile targets. The animals are dipped or sprayed with insecticide or the compound is poured on them. This method was first tried with limited success in the 1940s using dichlorodiphenyltrichloroethane (DDT). However, development of pour-on formulations using pyrethroids, a safe and biodegradable insecticide, led to successful control of tsetse in trials in Zambia and elsewhere. In 1991, a control scheme was started in Ghibe Valley using insecticides poured directly on to cattle. This was considered to be more sustainable, as farmers directly benefited and the transaction costs in maintaining screens or traps were avoided. For the first 2 years, insecticides were given free of charge. The control was very effective and promoted widely by ILCA, and as a result, many families migrated into the area.

An economic assessment quantified the benefits (Omamo *et al.*, 2002). Following control, the apparent density of tsetse and biting flies in the region fell by 95%. This reduction in tsetse challenge led to a decrease in trypanosome prevalence in cattle of over 61%, despite a high level of resistance to trypanocides. The number of curative drug treatments per animal fell by 50%. Mean calf growth rate increased by 20%, while mean calf mortality and abortion decreased by 57%. Average cow body weight was boosted by 4%, the cow:calf ratio increased by 49% and adult male body weight increased by 8%. Between 1995 and 1997, expenditure on trypanocidal drugs fell by US$39,000, which more than offset the US$16,000 cost of the pour-on. The value of increased output of meat (40%) and milk (30%) implied a benefit:cost ratio of 11.6 over 2 years and of 9.3 over 10 years, with increases in annual household income between 10% and 34%.

After 2 years of free treatments, a more sustainable model was investigated with the imposition of a charge of US$0.6 per treatment. An economic study found that, while many farmers continued to pay for treatments, there was a reduction in demand (from 97% of farmers to around 60%) and that poorer farmers dropped out disproportionately (Swallow and Woudyalew, 1994). There were also efforts to hand management of the scheme over to the community. By 2000, ILRI was no longer able to continue supporting the scheme; it appears that the treatments stopped and the tsetse increased (Wilson, 2003). In a subsequent project from 2008 to 2011, ILRI helped to establish 13 trypanosomiasis cooperatives to link private

veterinary drug suppliers to the remote communities to ensure a supply of trypanocides to and to reduce dependence on the public supply system. This promising delivery approach has not been systematically evaluated.

An analysis of land-use change by ILRI in 2003 revealed huge increases in human and animal populations, as well as land cultivated in the Ghibe Valley (Wilson, 2003). This analysis concluded that the control of tsetse had a role in attracting migrants, but this was difficult to quantify because other climatic and demographic factors influenced population movements.

ILRI impacts in Uganda

Trypanosomiasis has long been a concern in Uganda. Both the Gambian and Rhodesian forms of HAT are found in Uganda, and one of the largest recorded human epidemics occurred in the early 19th century, when over 500,000 people are estimated to have died. After the political unrest of the 1980s, tsetse invaded new areas of Uganda, and various control campaigns were implemented (Okello-Onen et al., 1994; Okoth, 1999).

ILRI was a partner in one of the research projects, which aimed to better understand the infection dynamics and drug sensitivities of the trypanosome parasites prevalent in dairy systems in peri-urban Mukono District, Uganda, between 1995 and 1999. This demonstrated a low prevalence and a low pathogenicity of trypanosome infections in cattle. An economic study by ILRI found that, while trypanocides constituted up to 7.2% of health costs, they decreased profitability on farms only by 1%. The dairy farms were profitable, and the authors suggested trypanosomiasis was less important than previously thought, demonstrating the importance of economic analysis to justify interventions (Thornton and Odero, 1998).

As a result, the research consortium decided that the methodologies developed in the project should be applied to other areas of Africa where the disease was thought to have a significant detrimental effect on livestock production, particularly in areas where drug resistance was suspected to occur, and Burkina Faso was selected for the next phase.

ILRI contributed to research on the control of HAT in South-east Uganda from 2000 to 2003 (see Chapter 8, this volume). Surveys found that reporting was strongly biased to areas near health centres with good capacity, and models suggested that the major impact of sleeping sickness was deaths in people who were never treated or reported. A livestock survey helped identify hotspots. It linked cattle movement to the introduction of sleeping sickness to new areas and suggested that mass treatment of cattle might prevent the spread of sleeping sickness. The treatment of 30,000 cattle in Kamuli was highly effective at removing human-infective HAT parasites from the cattle reservoir and contributed to a significant decrease in human HAT cases (Fyfe et al., 2016). This work noted relatively little interest in trypanosomiasis as a stand-alone issue and concluded that community approaches would need external support.

In 2002, ILRI undertook research in Uganda to develop decision-support tools for improving trypanosomiasis control. This objective was to enable technicians working with tsetse and sleeping sickness in Uganda to learn techniques for conducting geographical information system (GIS) analysis to provide decision makers with information to facilitate targeting for control of the disease. The project successfully established GIS capacity within Uganda.

ILRI impacts in West Africa

Field work in West Africa initially started under ATLN. These conducted ground-breaking research into understanding the presence, prevalence and impacts of tsetse and HAT. For example, herds were monitored monthly for several years to understand production economics under the risk of trypanosomiasis. The ATLN work concluded, in seven papers in the Democratic Republic of the Congo (formerly Zaire), Togo, Ethiopia and The Gambia (summarized by Thornton and Odero, 1998, pp. 8–11), that trypanotolerant cattle were 'economically justifiable' in a variety of situations with respect to tsetse challenge, control methods and experience with trypanotolerance.

Following the Ugandan and ATLN work, ILRI collaborated and later led a research programme on trypanocide resistance in West Africa. The recommended control strategy was an integrated approach. This comprised vector

suppression in epidemiological hot spots, disease management at the herd level and strategic use of trypanocides, combined with keeping local tolerant breeds. The first activity, from 1998 to 1999, was to assess AAT prevalence, tsetse challenge and drug use. Resistance of trypanosomes to isometamidium and diminazene was also demonstrated by both *in vivo* and *in vitro* methods (McDermott *et al.*, 2003; Knoppe *et al.*, 2006).

This led to a more ambitious programme that sought to ensure the efficacy of trypanocides as a component of integrated control of trypanosomiasis in the cotton zone of West Africa. The first objective was to assess the presence and level of resistance across three countries (Burkina Faso, Mali and Guinea) in the cotton zone of West Africa. This entailed an enormous survey, eventually covering more than 30,000 cattle. The results showed a marked gradient in land cover, tsetse species, cattle breed, resistance and productivity, from more extensive, low-input, low-output, low-disease systems in east Guinea to more intensive, productive and high-disease systems in west Burkina Faso. The pattern of tsetse distribution, trypanosomiasis prevalence and trypanosomiasis risk varied predictably, with intensified agriculture apparently driving change from a situation of low disease and little resistance to one of high disease and high resistance. Tailored recommendations were made for optimal control across the region (Clausen *et al.*, 2010).

An epidemiological model describing the transmission dynamics of trypanosomiasis was developed and used to explain the trends identified in the spatial analysis for West Africa (Grace, 2006). The model suggested that a change in cattle breed is driving the emergence of resistance through the increase in drug use by farmers to maintain trypanosusceptible Zebu – the main driver is hence the change in preferred cattle breed rather than drug use. Moreover, the situation in West Africa appears to be on the accelerating portion of the sigmoidal resistance curve, implying that prevalence, morbidity and mortality, and resistance are likely to deteriorate considerably from the present levels (Grace, 2006). The optimistic conclusion from modelling is that vector control, even if only resulting in small increases in tsetse mortality, may rapidly reverse the trend of emerging resistance.

In the next stage, four 'best-bet' strategies were evaluated: (i) trypanotolerant cattle; (ii) community-based trypanosomiasis control; (iii) training farmers and paravets in integrated AAT control; and (iv) rational drug use information for farmers and service providers. Community-based control using insecticide-treated targets and insecticidal spraying decreased cattle mortality (71%), decreased abortion (66%), increased traction (95%) and decreased farmer expenditures on drugs (50%), while milk production increased by 10%. The intervention was deployed in a highly participative way, testing the hypothesis that previous attempts at community-based control had failed because they were top down and insufficiently participatory (Meyer *et al.*, 2016). (A review of previous vector-control projects in Burkina Faso showed that community-based control was in all cases effective and in no case continued after the project withdrew; Grace, 2003). However, while efforts were more sustainable than attained previously, most of the activities were eventually abandoned. Researchers concluded that community tsetse control does work but does not continue without external support because of high transaction costs of setting up and maintaining the community-level institutional innovations needed to sustain control efforts (Box 3.1). This substantiated earlier theoretical work that also argued that community-based control was not sustainable because of its 'prisoners dilemma' nature (McCarthy *et al.*, 2003).

As part of the capacity building, several appropriate technologies were developed, adapted and tested. Anaemia is an important sign of trypanosomiasis and one that farmers were poor at detecting. Researchers tested two field devices: a colour chart developed for diagnosing anaemia in sheep and a blood prick test designed for diagnosing anaemia in pregnant women. Both were effective, but the colour chart system was simpler and cheaper (Grace *et al.*, 2007). The project also calibrated a weight band for the cattle population in the cotton zone. This is a tape measure that converts girth into body weight and hence allows more appropriate dosing. Several decision-support tools to aid differential diagnosis were also tested with varying success.

Trypanotolerant cattle keeping was evaluated and it was found that, while farmers regard

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Box 3.1. Community-based trypanosomiasis control.

An ILRI initiative to improve control of AAT in Burkina Faso started with an evaluation of previous projects (Grace, 2003). Research projects are rarely revisited after initial implementation, and this threw light on the 'life after project' scenario by looking at eight completed projects in Burkina Faso, six of which had a major participatory component. The projects took place over 25 years and encompassed a wide range of farming systems, institutions, partners and social conditions. They incorporated community participation and used low-cost and effective strategies that resulted in the rapid and total resolution of trypanosomiasis problems in all project areas. Participation and long-term viability issues (including cost recovery) were incorporated from the onset, and benefits to farmers were major, obvious and acknowledged. Yet, despite these substantial successes, none of the communities has continued with the strategies; tsetse reinvasion has occurred in all cases, and after years of investment in participative trypanosomiasis control, farmers are once more 'on their own' and experiencing substantial losses from trypanosomiasis. The review identified some factors that blocked sustainability. While farmers learned technical skills for tsetse control, they did not learn management or business skills in implementing these. Although control was relatively cheap, the small financial requirements were a barrier. Farmers showed much more hypothetical willingness to pay than actual. None of the projects used delivery systems that were capable of delivering control after the withdrawal of the project. The systems used were either of known low sustainability (e.g. government, project or existing village groups) or new institutions whose sustainability and appropriateness for village conditions was unproven (e.g. private vets*). Communities encountered unexpectedly high transaction costs in avoiding free riders.

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the productivity (and disease resistance) of trypanotolerant cattle quite highly, they also cite their undesirable features: unpredictable temperament, low working speed, short legs rendering them liable to damage the crop while weeding, slow growth and slow weight gain, smaller overall size, and low sale price and slower sale. The project confirmed other findings that trypanotolerant cattle were gradually being replaced as farmers switched to more productive breeds, and concluded that encouraging trypanotolerant cattle was not a viable strategy, at least while development, wealth and market integration were on an upwards trend.

The second intervention combined training on vector control, diagnosis and treatment of trypanosomiasis, and diagnosis and treatment of other common diseases, as well as use of traditional medicines and nutrition. Scientists found large and significant differences in knowledge and skill both in farmers (in Burkina Faso) and in paravets (in Guinea) before and after training, and between those trained and their peers who had not been trained (Grace *et al.*, 2008). Ten months after training, there was no significant decrease in the level of knowledge and skill. Moreover, there was a clear synergistic effect between training and vector control. For example, in the villages with intervention, the annual expenditure on trypanocides per farm household

was reduced substantially. In villages with paravets, the expenditure was reduced by 36%, while in villages with both vector control and paravets, expenditure was reduced by 58%. Integration of trypanosomiasis control strategies is often advised, both because each strategy has limitations and because perverse effects are possible (successful vector control in the absence of training and information on drug use, for example, has resulted in paradoxical increased use of trypanocides; Kamuanga, 2001a,b). Researchers concluded that the intervention was successful but the cost of training farmers and paravets was a barrier to widespread use. Moreover, in some situations, paravets are not allowed to operate.

The project was the first to explore rational drug use in a context of 'harm reduction' as an option for trypanosomiasis control. This was a concept borrowed from human health work with prostitutes and drug users. It assumes that if people are highly motivated to do things that are not recommended by authorities, punishing them will lead to worse outcomes and they should instead be supported to undertake the activities as safety as possible. Although official policy is that veterinary treatments should only be given by veterinarians or paraprofessionals under their direct supervision, the project had shown that most veterinary treatments were given by farmers and that it was neither feasible

nor economically viable for treatments to be given by veterinarians. In this context, the project set out to see whether farmers who were going to treat their animals anyway could be persuaded to treat them more rationally.

Much effort was spent in developing messages that could be understood by illiterate farmers. These addressed the problems identified as being most likely to lead to treatment failure, specifically misdiagnosis, underdosage and poor injection technique. The intervention was evaluated through a large cluster-randomized, double-blinded, controlled trial, which at the time was one of the most rigorous evaluations conducted by ILRI. It found that rational drug information improves farmer practice and reduces drug underdosage: the improvement in dosage was particularly encouraging, given the highly significant relationship between underdosage and treatment failure. In the medium term, there was a 35% increase in farmers giving the correct dosage and an 8% increase in the appropriate use of isometamidium as a prophylaxis in the test group versus the control. In addition, there were better clinical outcomes and fewer treatment complications with rational drug use information: improvements in clinical parameters were significant only for a decrease in animal temperature (indicating less fever). The simple hygiene information that was provided resulted in an important decrease in side effects. High levels of complications are associated with unhygienic administration. The researchers conclude this was an effective, cheap, sustainable and scalable option. The main challenge was the reluctance of national authorities to countenance farmers giving treatments.

The researchers saw the need for additional action to promote the uptake of successful strategies. Customized informational brochures and training materials were designed to support 'Rational drug use' (Fig. 3.1). Prototype materials, including a visually appealing, cartoon-style booklet with an engaging storyline were designed for targeting adult literacy programmes and primary-school children. A communication strategy for dissemination of rational drug use messages, including using radio messages, was also formulated. The project formulated recommendations for how drug companies could improve the quality of the information provided with their products that would promote 'Rational drug use'. While company representatives were in favour of the suggestions, they felt that the current low returns to investment in the trypanocide market did not merit the added cost of adopting the recommendations.

Fig. 3.1. An example of extension material to promote rational drug use.

A subsequent study assessed farmers' knowledge and management of trypanosomiasis. In the absence of a clear control group, propensity score matching was used (Liebenehm *et al.*, 2009). Using three different matching algorithms, significant and robust differences between matched participants and non-participants regarding cattle farmers' knowledge were identified. Hence, it can be concluded that the gain in farmers' knowledge is attributable directly to participation in the research intervention. The strongest effect of the research intervention is on the curative knowledge of AAT and subsequent adequate control decisions. Moreover, significant advancements in preventative strategies were also observed. Overall, the research project was effective in increasing farmers' knowledge of good practices and contributed significantly to improved livestock and farm productivity (Affognon *et al.*, 2009).

ILRI found widespread concern among farmers and market agents about a proliferation of fake and substandard trypanocide drugs. However, market studies using 'dummy customer' or 'secret shopper' methods found no evidence of counterfeit drugs, and the results of drug quality tests conducted in 2005 on samples of drugs taken from both formal (veterinary pharmacies) and informal (black markets) sources revealed no major difference in quality of the products.

Economic and policy analysis was undertaken in parallel with the epidemiological studies. Affognon (2007) investigated the short-term productivity effect of drugs in controlling AAT under increasing drug resistance. For the first time, a damage-control framework was applied to animal disease control in Africa. The results showed that the marginal value product (MVP) of isometamidium in all epidemiological conditions and the MVP of diminazene in conditions of high disease prevalence and high drug resistance revealed a suboptimal (underuse) of these two major trypanocide molecules, not taking into account the externality of resistance. This means that, even in the face of increasing drug resistance, trypanocidal drugs remain economically attractive. Moreover, at the current suboptimal level of isometamidium use for the epidemiological conditions, investing in more drug use would be more than compensated for by avoided production losses. For decades, the veterinary experts had promoted reduced use of trypanocides in response to resistance and these economic findings suggest why the messages might not have high uptake.

AAT economic and environmental studies

A methodological innovation at ILRI was combining economic analysis with herd simulation models. Von Kaufmann *et al.* (1990) developed a bioeconomic herd model (called here the ATLN model) that was used to quantify the costs of AAT, to assess control strategies and to evaluate the benefits of trypanotolerant livestock (Itty, 1992; Itty and Swallow, 1994). Some estimates of these costs are as follows:

- The Gambia: 37% of the national herd in The Gambia were at risk annually from trypanosomiasis (ILRAD, 1993). The annual economic costs of trypanosomiasis were estimated to be less than 1 % of the annual value of the total cattle herd and nearly all of the costs of trypanosomiasis were attributed to production losses.
- Zimbabwe: due to extensive tsetse control campaigns, only 4% of Zimbabwe's cattle population were at risk in the late 1980s and early 1990s (ILRAD, 1993). The annual cost of trypanosomiasis control in Zimbabwe was largely attributable to tsetse control by spraying, not to production losses, which were small as a percentage of the value of the national cattle herd.
- Côte d'Ivoire: the annual cost of trypanosomiasis was estimated to be 90% from production losses and 10% from control costs.
- Cameroon: in Adamawa Province, tsetse control led to substantial reductions in mortality rather than to significant increases in cattle numbers. Changes in land use involved a shift to mixed farming among previously pure pastoralists.

Subsequent economic analyses estimated that AAT in West Africa (Burkina Faso, Mali and Ghana) was estimated to cause annual losses of US$450 million in the 1990s (Itty, 1992). The use of trypanocides in those three countries was thought to protect some 17 million head of cattle from the disease. However, the general use of trypanocides was inducing resistance to trypanocides

and though the older studies mentioned the cost of resistance they did not quantify it.

The economics of trypanosomiasis control using trypanotolerant cattle were investigated under the auspices of ATLN in Kenya, Ethiopia, The Gambia, the Democratic Republic of the Congo, Togo and Côte d'Ivoire (Itty, 1992). Itty and Swallow (1994) showed that tsetse control appeared appropriate in situations with higher disease risk and that imports of trypanotolerant stock (in the Democratic Republic of the Congo and Togo) were not necessarily profitable. Studies were undertaken to determine farmers' willingness to participate in vector-control programmes. These so-called 'contingent valuation surveys' have been conducted in Burkina Faso, Ethiopia and Kenya to assess willingness to contribute labour and money to vector control (Thornton and Odero, 1998, pp. 69–71, summarizing three studies). Contingent valuation methods suggested that farmers were willing to pay around US$0.5–1 per treatment. In several countries, this was compared with the revealed willingness to pay during campaigns: in general, the observed willingness to pay correlated with the estimates derived from contingent valuation studies but was less and, in at least one country, declined with time (Kamuanga *et al.*, 2000, 2001b).

The most recent work on the economic benefits of intervening against AAT is a study of Ethiopia, Kenya, Somalia, South Sudan, Sudan and Uganda. Using a map of cattle production systems, herd models for each system were developed for scenarios with or without AAT. The herd models were based on estimated parameters of cattle productivity (fertility, mortality, yields, sales) from which growth of cattle populations and income were estimated over a 20-year period. A spatial expansion model was adapted to estimate how cattle populations might migrate to new areas when maximum stocking rates are exceeded in older production areas. Last, differences in income between the with and without scenarios were mapped, giving a measure of the potential benefits that could be obtained from intervening against tsetse and trypanosomiasis (Shaw *et al.*, 2014). The estimated net present value of benefits to livestock keepers for the entire study area is nearly US$2.5 billion, at a discount rate of 10% over 20 years – is approximately US$3300/km^2 of tsetse-infested area – varying from from less than US$500/km^2 to more than US$10,000/km^2. The greatest potential benefits are to Ethiopia, because of its high livestock densities and the historical importance of animal traction, followed by regions of Kenya and Uganda (Shaw *et al.*, 2014).

A related study built on these findings to evaluate the cost:benefit ratios as profitability measures for various control methods (Shaw *et al.*, 2015). Trypanocide prophylaxis is the only profitable approach at low cattle density. Where cattle densities are higher, the use of insecticide-treated cattle is the most consistently profitable method, with benefit:cost ratios greater than 5. In areas of high potential for mixed farming using oxen in Western Ethiopia, the fertile areas north of Lake Victoria and the dairying areas of western and central Kenya, all control methods achieve benefit:cost ratios from 2 to over 15, and for elimination strategies, ratios from 5 to over 20. The costs of interventions against tsetse exceed benefits where cattle densities are less than 20/km^2.

McCarthy *et al.* (2003) developed a theoretical model to explain why farmers might use different methods of trypanosomiasis control. They argued that the public goods nature of traps and targets, combined with an underlying incentive structure that may resemble a prisoner's dilemma, explained the well-documented failure of community-based control with traps and targets, a failure that was most commonly attributed to a lack of community participation.

ILRI also developed guidelines on methods and tools for conducting impact assessments of tsetse/trypanosomiasis interventions on the environmental, social and economic systems and on approaches for the integrated impact assessment of the interventions (Maitima *et al.*, 2007)[2].

Other AAT research and impacts

ILRI examined possible changes in distribution of the three groups of tsetse in relation to changing climate, human population density and expected disease control activities (Reid *et al.*, 2000; Coleman *et al.*, 2001; Grace, 2014). The key findings of these studies were that climate change is indeed likely to change the distributional potential of tsetse but that anthropogenic

changes resulting directly from population expansion would be more important in determining actual changes in tsetse distributions. With respect to population density, it was estimated that human population growth after 2000 would reduce tsetse-infested areas from roughly 8 million km^2 to between 5 and 6.5 million km^2 in 2040 (Reid *et al.*, 2000, p. 231).

In the early 2000s ILRI developed a deterministic mathematical model for trypanosomiasis transmission. This was initially used to compare the effectiveness of different control strategies (McDermott and Coleman, 2001). The relative rankings of the effect of control strategies on reducing disease prevalence were vector control, vaccination and drug use, in that order. Epidemiological modelling was used in several other projects, mainly to inform design and research questions.

Conclusions and the Future

AAT has long been regarded as the single most important disease of the single most important livestock species in Africa. Early research at ILRI focused on developing a vaccine. As it became clear that this was no easy endeavour, and as AAT worsened or became more obvious in many African countries, ILRI stepped up to address our understanding and control of AAT in advance of a vaccine.

Work started in East Africa and then extended to West Africa. There was emphasis on understanding the disease and its impacts and on testing solutions. Over four decades of field research on AAT, an evolution is evident: researchers went from publishing in proceedings to publishing in high-impact-factor journals, from focusing on the efficacy of solutions to their uptake, and from forthright advocates of favoured strategies to more nuanced critiques of the challenges of AAT control.

ILRI participated in important networks, most notably ATLN, and did not participate in important failed attempts to control AAT. It investigated all three of the major strategies for controlling AAT and found two of them wanting, at least without continued external support.

Trypanotolerant cattle have many advantages in terms of disease resistance, but they are not preferred by farmers who are increasingly focused on productivity. However, trypanotolerant cattle populations have been declining for decades relative to Zebu crosses, which are preferred for their production characteristics. One study (Agyemang and Rege, 2004) found that the shares of trypanotolerant stock in all cattle in west and central Africa were falling in the late 1990s 2004).

Trypanotolerant stock are likely to persist, without the need for much external support, in areas where, because of poor market access and other constraints, low-input, low-output systems remain attractive. In other areas, trypanotolerant cattle will probably continue to be replaced by higher value and more productive Zebu crosses. Control of tsetse flies by insecticides has been much promoted and has generated many scientific innovations and successful pilots. However, the high cost and high level of coordination and management needed means it has never proven sustainable outside ranches and externally supported projects. The use of trypanocidal drugs, in contrast, is both sustainable and scalable. Farmers are willing to buy and use curative and, although to a considerably less extent, preventative drugs. Drugs are on the whole wisely used, but the lack of information on correct treatment certainly leads to some irrational use and hastens the development of resistance. ILRI research showed how providing simple information to farmers can slow this.

Looking to the future, AAT is likely to remain a priority constraint for African livestock. We now have approaches that are highly effective at reducing the impact of AAT, either singly or in combination. We also understand better the challenges of adoption of even economically attractive strategies and how the changing dynamics of AAT may lead to future opportunities for optimized control.

Acknowledgements

Notes

[1] William Wint, personal communication, April 2019.
[2] See Introduction, Box I.1 on 'Aspects of the Economic Burden of Trypanosomiasis' for mention of *ex-ante* modelling of a hypothetical trypanosomiasis vaccine.

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