

CENTENNIAL REVIEW

African trypanosomiasis

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Trypanosomiasis remains one of the most serious constraints to economic development in sub-Saharan Africa and, as a consequence, related research has been subject to strong social and political as well as scientific influences. The epidemics of sleeping sickness that occurred at the turn of the 20th Century focussed research efforts on what became known as 'the colonial disease'. This focus is thought to have produced 'vertical' health services aimed at this one disease, while neglecting other important health issues. Given the scale of these epidemics, and the fact that the disease is fatal if left untreated, it is unsurprising that sleeping sickness dominated colonial medicine. Indeed, recent evidence indicates that, if anything, the colonial authorities greatly under-estimated the mortality attributable to sleeping sickness.

Differences in approach to disease control between Francophone and Anglophone Africa, which in the past have been considered ideological, on examination prove to be logical, reflecting the underlying epidemiological divergence of East and West Africa. These epidemiological differences are ancient in origin, pre-dating the colonial period, and continue to the present day.

Recent research has produced control solutions, for the African trypanosomiasis of humans and livestock, that are effective, affordable and sustainable by small-holder farmers. Whether these simple solutions are allowed to fulfil their promise and become fully integrated into agricultural practice remains to be seen. After more than 100 years of effort, trypanosomiasis control remains a controversial topic, subject to the tides of fashion and politics.

The trypanosomiasis have been and remain a serious constraint to economic development in sub-Saharan Africa, impacting on the health of the people as well as their domestic livestock (Shaw, 2004). As with most of the diseases threatening the developing world, much of the necessary research funding has been underpinned by external agencies, in the first instance provided by colonial regimes and, in the present day, by development agencies and charitable foundations in their various guises. Because of its economic significance, the research agenda for trypanosomiasis has often been subject to strong social and political as well as scientific influences. This review will seek to shed light on the drivers of change that have influenced research aimed directly at control

of the diseases in humans and their domestic livestock, and how such changes have impacted on the lives of those in the affected countries of Africa.

Attempts to understand and control trypanosomiasis are intimately bound up with the history of African development. Why trypanosomiasis should have taken such a central role in development is not difficult to understand, for without trypanosomiasis the whole of the sub-Saharan continent would, like Latin America, have been readily conquered by European forces long before the 19th Century. The Conquistadors made rapid inroads into Latin America from the 16th Century onwards (Diamond, 1999) but, by contrast, European explorers such as Livingstone were still trekking across Africa on foot in the middle of the 19th Century; without horses progress was painfully slow.

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Livingstone used oxen to carry goods on his expeditions but he was well aware that tsetse flies were a serious problem, even for oxen, in the hinterland. Moreover, oxen cannot be readily used as machines of war, as horses had been by the Conquistadors in Latin America. That the conquest of Latin America was not repeated in Africa in the 16th Century may simply be ascribed to the fact that, as the Portuguese had found in the 15th Century, 'a horse's lifespan in West Africa was short' (Reader, 1997). Even up to the period of the First World War (1914–1918), allied forces were still losing thousands of horses to trypanosome infections in East Africa (Hornby, 1952). Horses are highly susceptible to trypanosomiasis, in particular to what is now recognised as *Trypanosoma brucei brucei*, which 'more than any other trypanosome, has protected African people from invasion and African wildlife from destruction' (Ford, 1971).

Apart from its impact on transportation in sub-Saharan Africa, trypanosomiasis also had a very serious human-health impact. The disease now referred to as 'sleeping sickness' had long been recognised in West Africa but the first accounts of the disease were by a naval surgeon, John Atkins, in 1721. In 1792, Thomas Winterbottom, Physician to the Colony of Sierra Leone, described a disease he found there as 'negro lethargy'. Slave shippers rejected those with swelling of the posterior cervical lymph nodes — a manifestation, commonly associated with African trypanosomiasis, that is still known as Winterbottom's sign (www.gpnotebook.co.uk). Another century would elapse before any further progress was made in our understanding of the disease but, in 1901, an Englishman working on the River Gambia was treated for malaria without success; when his blood was examined, trypanosomes were found and named *Trypanosoma gambiense* by Dutton (1902), who was then working for the Liverpool School of Tropical Medicine. The Liverpool School had been established in 1899 and Everett Dutton and his

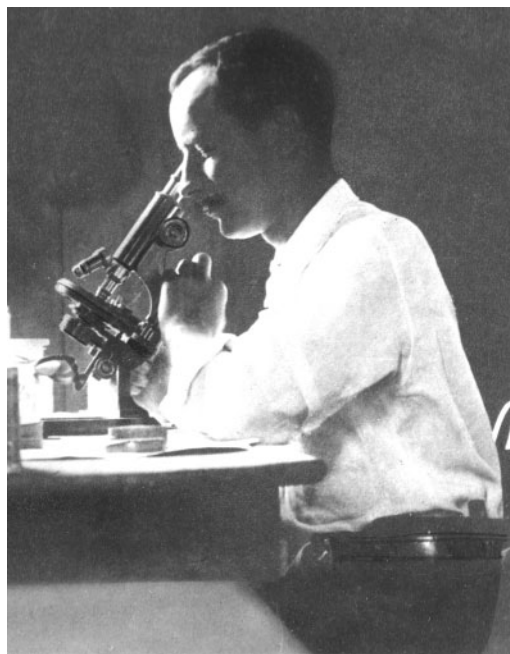


FIG. Everett Dutton, from the Liverpool School of Tropical Medicine, who died on an expedition to the Congo at the age of 29 years.

colleagues published extensively on trypanosomiasis in West Africa in the *Memoirs of the Liverpool School*. Dutton (see Figure) died a tragically premature death in the Congo at the age of 29 years. The Liverpool School continued to publish 'memoirs' until 1906 when it was decided that its output should appear in a journal, the *Annals of Tropical Medicine and Parasitology*, whose centenary is now being celebrated.

While Dutton was working in West Africa, Castellani had been researching the same problem in Uganda and had isolated trypanosomes from patients infected in the course of an epidemic of sleeping sickness in Busoga. Prophetically, Castellani (1903) named the organism *Trypanosoma ugandense*. The link between the transmission of sleeping sickness and an insect vector was made by Bruce, who had already shown that a trypanosome disease of cattle, recognised as nagana in South Africa, was spread between animals by the bite of infected tsetse flies (Bruce, 1895). Because of his

recognised expertise, Bruce was asked by the British Government to join the Sleeping Sickness Commission to investigate the epidemic in Uganda. Bruce arrived in Uganda on 16 March 1903 and left on 28 August of the same year. Amazingly by today's standards, he was able to draw fundamental conclusions about the epidemiology of this disease within 2 months of his arrival. On 29 May 1903, the Commission sent a report to the Royal Society (Bruce *et al.*, 1903) which concluded that: (1) '*sleeping sickness is caused by...a species of trypanosome*'; (2) '*this species is probably that described by Dutton from the West Coast of Africa and called by him Trypanosoma gambiense*'; and (3) '*trypanosomes are transmitted by Glossina palpalis, and it alone*'. Bruce's conclusions about the vector were correct but the identity of the trypanosome involved in Busoga, in which he was clearly at odds with Castellani, has been the subject of much, sometimes heated, debate ever since.

A COLONIAL DISEASE?

The European powers made what even today would be considered enormous investments in their African colonies. The British, for example, wanted a railway to run from Mombasa to Kampala; the railway reached Kisumu in 1901 and finally Kampala in 1931. This huge investment in the infrastructure of the region was made for the purposes of trade but the railway suffered from cost over-runs. To meet the costs of operating the railway, the colonial authorities encouraged the growing of cash crops, especially cotton, which became very profitable and central to the economy of the colony. The investment in the railway was not wasted, as it reduced the cost of transporting each tonne of cotton to the coast from £220 to £2.40 (Reader, 1997). It must therefore have come as a terrible shock to the British authorities, at the turn of the 20th Century, to realise that the farmers of

Uganda, who with their cash crops were the mainstay of the economy, were dying in alarming numbers following the onset of an apparently unstoppable epidemic of sleeping sickness. Deaths reached such numbers (with an estimated total of 300,000) that the then Governor, Hesketh Bell, decided to act, and in 1908 the local population was removed from the shores of Lake Victoria; infected people were isolated in sleeping-sickness camps. This drastic action was effective and was adopted, in modified form, by King Leopold, for dealing with the same problem in the Congo Free State; here the disease was so wide-spread that evacuation was not an option but infected people were placed in sleeping-sickness camps (*lazarets*). These interventions reflected the prevailing epidemiological view that the disease was spread by the movement of infected people. As discussed below, unbeknown to them, Governor Bell and King Leopold were, in fact, dealing with two distinct diseases with very different epidemiologies and for which different strategies were required.

Apart from these Draconian interventions, the colonial authorities also realised that there were questions that required scientific analysis — hence the Sleeping Sickness Commission on which Bruce served. Apart from their scientific interest, the reports of the Commission reflect the magnitude and urgency of the situation in Uganda, with hundreds of thousands of people suffering from a fatal disease. Perhaps more than any other event, the '1901 epidemic' in Busoga proved a turning point in tropical medicine, which was transformed from a rather esoteric pursuit on the fringes of medical interests into a serious subject, with institutes of tropical medicine all over Europe attracting resources. In hindsight, this investment in tropical medicine, or 'colonial' medicine as some historians view it (Lyons, 1992), may be seen as part of a damage-limitation exercise. The European powers were at this time becoming concerned not simply with the direct effects of such epidemics on the

health of their African subjects but also with the negative images their colonial exploits were presenting to the European public. The 'scramble for Africa' was a race with very high stakes, political as well as economic (Packenham, 1991), and sleeping sickness was not just a disease; it had become **the** colonial disease (Lyons, 1992). Indeed Lyons (1992) takes the view that epidemics of sleeping sickness allowed the colonial authorities to increase their political hegemony through public-health measures, originating in response to this single disease. Lyons (1992) implies that this concentration on sleeping sickness resulted in the development of 'vertical' health services aimed at this one disease, while neglecting other, vital, public-health issues.

There is, however, no doubting the fact that hundreds of thousands of cases of sleeping sickness were diagnosed between 1900 and 1940. This is a disease that, if left untreated, is fatal, and Africans do not acquire protective immunity to trypanosomiasis, as they do to malaria (Hviid, 2005). It is hardly surprising, therefore, that sleeping sickness continued to dominate colonial medical attention for many years. Moreover, it is now apparent that the colonial authorities were probably under-estimating the death toll from this disease. Even in present-day Busoga, it has been estimated that for every reported death caused by sleeping sickness, 12 go undetected (Odiit *et al.*, 2005). MacKichan (1944) noted that people affected by the second great epidemic in Uganda, in the 1940s, were '*distrustful of hospitals*' and such avoidance would have led to under-estimates of the fatalities. One can also be sure, given the limits of the diagnostics then available, that the rates of detection in the colonial era were poor. Estimates of the deaths from sleeping sickness during this period have therefore probably been greatly under-estimated and may have run into millions across the continent. Rather than neglecting other important health issues, the colonial

authorities were dealing with a pandemic which, in terms of urgency, may be better compared to the current HIV/AIDS situation in Africa.

'EAST IS EAST AND WEST IS WEST...'

When Kipling wrote *The Ballad of East and West* in 1901, he was describing social differences between the orient and occident but he could as readily have been referring to east and west sub-Saharan Africa. This divide is reflected most strikingly in the nature of 'sleeping sickness', which is now recognised as two discrete diseases, one, in East Africa, caused by *Trypanosoma brucei rhodesiense*, and the other, in West Africa, caused by *T. b. gambiense*. The two parasites have distinct clinical manifestations: *T. b. rhodesiense* is an acute infection, the condition of the patient deteriorating rapidly as the parasite moves from the blood and lymphatic systems (early-stage infection) to the central nervous system; *T. b. gambiense* is usually a chronic infection, often with a long symptomless stage of some years, and a chronic meningo-encephalitic condition during the late stage (Apted, 1970).

The responses of the Anglophone and Francophone colonial powers to trypanosomiasis differed and this was reflected in their research agendas. Francophone countries chose to concentrate directly on the medical problems presented by the disease in humans. The Anglophone countries, while shocked by the rapidity and extent of the 1901 Busoga epidemic, were also concerned with the more wide-spread problem of disease in domestic livestock; this was also a problem in the drier regions of West Africa (e.g. in northern Nigeria) but was more politically significant in East Africa. To promote cash-crop agriculture and hence productivity, the British had encouraged large-scale settlement of a huge area of East Africa, where trypanosomiasis of livestock threatened the livelihoods of the settlers. The Anglo-French differences in

focus did not then, as is commonly thought, simply reflect competing science bases but were largely the product of logical economic drivers. This becomes clearer when the contrasting ecologies and economies of West and East Africa are considered. The Francophone colonies were located only in West Africa, where animal trypanosomiasis, while a problem, did not represent an overwhelming economic threat to the well-being of France and Belgium's colonial investments, particularly in the Congo, which was forested and largely unsuitable for cattle rearing. The spread of Gambian sleeping sickness did, however, threaten the supply of agricultural labour, and this threat was taken very seriously by the authorities in the Belgian Congo, where half a million people are estimated to have been killed by the disease in 1901 alone.

'Catch 22'

Following the invention of the pneumatic tyre in the 1880s, there was an increasing demand for rubber, and Belgium's riches were largely dependent on the harvest of wild rubber in the Congo. For the Congolese people, however, sleeping sickness presented a dilemma that has been described, in painful detail, by Lyons (1992). People forced into the forests of the Congo to collect wild rubber to pay the imposed colonial taxes were at greater risk of contracting sleeping sickness, as they would spend up to 24 days/month in forest. On contracting sleeping sickness they would be incarcerated in 'hospitals' or *lazarets*; here they were isolated in an attempt to halt the spread of disease and, as there were no curative drugs, would simply die. Those who failed to collect sufficient rubber to meet their tax bills were, however, risking extreme and even macabre punishments (Hochschild, 1999).

The Drug Culture

The dyestuff industry formed an important part of the industrial revolution in Europe,

and Britain dominated this sector until the 1870s. By the end of the 1880s, however, it was the German organic-chemical industry that reigned supreme. It is no surprise that, in the search for trypanocidal drugs in the later 19th and early 20th Centuries, the dyestuffs industry was at the 'cutting edge'. Atoxyl, the first effective trypanocide, was a synthetic dye containing arsenic. Although it was discovered by Paul Ehrlich when searching for cures for syphilis, Wolferstan Thomas, working at the Liverpool School of Tropical Medicine, subsequently showed that atoxyl was effective against *T. b. gambiense* (Riethmiller, 2005). The Nobel Laureate Robert Koch was the first to use atoxyl as a treatment for sleeping sickness, in Uganda in 1906, but the drug proved disappointing because of its serious side-effects. The first really useful drugs became available in the 1920s: suramin, for the first stage of the disease, and tryparsamide, an organo-arsenic compound, for the second stage, when there was central-nervous-system (CNS) involvement. The Francophone countries were quick to adopt the wide-spread use of both these drugs to treat Gambian sleeping sickness. This policy was promoted vigorously by Eugene Jamot who, between 1925 and 1935, treated hundreds of thousands of cases in Cameroon and Upper Volta in a campaign of 'atoxylisation'. Underpinning this process of mass chemotherapy lay 'Jamot's doctrine', which was also adopted by the Belgian authorities in the Congo. Jamot decreed that passive screening would not solve the problem; rather, infected people should not move but should be treated, wherever they were found, by specialised mobile medical teams sent to search for such cases (Stanghellini, 1999). Jamot was held in such esteem for his achievements that he was nominated for the Nobel Prize in 1931 by a grateful French government. After the Second World War, chemoprophylactic treatments based on 6-monthly injections with pentamidine (a highly effective drug, for the first stage of the disease,

that did not contain arsenic) were developed. The efforts made in the subsequent 'pentamidinisation' campaigns are difficult to imagine today; in the 1950s, for example, some 2 million people in the Belgian Congo each received two to four pentamidine injections at 6-month intervals. Such mass chemotherapy was also adopted in the British colonies in West Africa, as they faced similar threatening epidemics of Gambian sleeping sickness; between 1931 and 1945, for example, around half a million people were treated in Nigeria. The logic of mass chemoprophylaxis seems impeccable from the viewpoint of control; the aim was to control the disease by protecting a high proportion of the community and so eliminate the human reservoir of trypanosomes. What is not in doubt is that Jamot's doctrine was highly effective; while not eliminating the disease, incidence could be reduced to an apparent zero. This undoubtedly efficient strategy was, however, very unpopular with the communities involved and, quite naturally, led to 'concealment', which, in turn, made the long-term goal of elimination by chemotherapy difficult, if not impossible (Waddy, 1970).

...and Never The Twain Shall Meet?

There are fundamental biological reasons why trypanosomiasis-related health risks differ between East and West Africa, and these differences have acted historically as differential drivers for Francophone and Anglophone researchers. The human disease in West Africa, referred to as Gambian sleeping sickness, is chronic in form, and many years may elapse before it becomes fatal. The human disease in East and southern Africa was first recognised [if the work of Castellani (1903) in Uganda is, for the time being, ignored] as a distinct entity in what is now Zambia, and was, unlike the Gambian disease, resistant to atoxyl (Stephens and Fantham, 1910). This form, still referred to as Rhodesian sleeping sickness, is usually fatal within 3 months of

infection (Odiit *et al.*, 1997; Fèvre *et al.*, 2004). A simple north-south line can be drawn through present-day Africa to delimit the distributions of Gambian and Rhodesian sleeping sicknesses (Welburn *et al.*, 2001a). This line also largely separates the Francophone and Anglophone spheres of interest in the colonial era (although Ghana and Nigeria become included in the Francophone region) and delimits their distinctive responses to disease control.

Significantly and, as it turned out, quite correctly, British scientists suspected almost immediately that they were dealing with a zoonosis in Uganda; Bruce *et al.* (1903) and later Duke (1913) tried to provide evidence of this, by fly-transmission experiments involving antelopes. That the disease in East Africa was zoonotic was proven beyond doubt in the 1950s, in colonial Kenya, by the expedient method of taking blood from an infected bushbuck and injecting it into human 'volunteers' (Heisch *et al.*, 1958). Incidentally, the fact that a bushbuck was used in this initial experiment led to the erroneous idea that this rather rare animal is a major reservoir of human disease — nothing could be further from the truth in, for example, modern-day Uganda (Picozzi *et al.*, 2005).

Long before there was definitive proof, the zoonotic nature of Rhodesian sleeping sickness had been assumed, as a result of various observations. The Tinde experiment in Tanzania, for example, showed that trypanosomes isolated from humans could be serially transmitted, by tsetse, between laboratory animals for over 20 years and yet remain human-infective (Ashcroft, 1959). The (assumed) zoonotic nature of Rhodesian sleeping sickness gave rise to the idea of a special relationship between vector and host — flies found in savannah areas with abundant wildlife (i.e. flies of the *morsitans* group) were the exclusive vectors of the parasites causing Rhodesian sleeping sickness whereas riverine flies (i.e. flies of the *palpalis* group) were the vectors of the causative agents of the Gambian disease. A

'human-fly-human' cycle was used to describe the transmission of the parasites causing the Gambian disease whereas a 'game-fly-human' cycle was linked to the Rhodesian form (Apted, 1970). This special relationship between fly and trypanosome was apparently confirmed by the outbreak of a serious epidemic in Busoga in the 1940s, which, all agreed at the time, was of Rhodesian and not, as in 1901, Gambian sleeping sickness. The vector involved this time was not apparently *G. palpalis* (held by Bruce to be exclusively responsible for the 1901 epidemic) but a fly of the *morsitans* group: *G. pallidipes* (MacKichan, 1944). This apparent change in vector **and** trypanosome species in Busoga between 1900 and 1940 was rationalized thus: the parasites causing Rhodesian sleeping sickness must have been introduced into Uganda, possibly by the movement of infected people from southern Africa, and then transmitted by a savannah species of tsetse (*G. pallidipes*) that had been invading the area, spreading and, as the disease was a zoonosis, feeding preferentially on a wild animal reservoir. The tracking of the assumed movement of the 'Rhodesian-type' trypanosomes between 1911 and 1940, northwards from Zambia through Tanzania to Kenya and Uganda, has been described elsewhere, in some detail (Apted, 1970). The trypanosomes circulating in Busoga today, however, are known to be closely related to those circulating, in the same area, in the 1960s but are genetically distinct from those found in Zambia (Hide *et al.*, 1994, 1996). Moreover, despite the wide spectrum of clinical manifestations observed in patients in present-day Busoga (Smith and Bailey, 1997), there is no evidence of 'Gambian-type' trypanosomes circulating there today (Hide *et al.*, 1994). The results of a recent analysis of the original case records from the 1901 epidemic in Uganda (Fèvre *et al.*, 2004) show that the patients examined by Bruce and his colleagues on the Sleeping Sickness Commission were, in fact, not suffering from Gambian sleeping sickness, as long

assumed, but from the acute form of Rhodesian sleeping sickness, caused by *T. b. rhodesiense*. Castellani (1903) was therefore correct in claiming the discovery in Uganda of a new trypanosome, which should, by rights, still be called *T. ugandense* in his honour (Koerner *et al.*, 1995). Moreover, there is now no doubt that riverine flies can transmit the parasites that cause Rhodesian sleeping sickness just as well as savannah species, with *G. f. fuscipes* identified as the vector involved in the most recent epidemic of sleeping sickness in Busoga, which broke out in the 1980s (Okoth and Kapaata, 1986). The existence of a 'game-fly-human' cycle had, in any case, been challenged by the post-colonial researchers who firstly suggested that cattle were a reservoir for *T. b. rhodesiense* (Wilde and French, 1945) and then demonstrated definitively that domestic animals were involved in the cycle of disease in Kenya, by infecting 'volunteers' with blood from cattle (Onyango *et al.*, 1966). In present-day Uganda, cattle form a major reservoir of Rhodesian sleeping sickness, and spread of the disease has been linked to the cattle movements associated with restocking campaigns (Fèvre *et al.*, 2001).

The question of the involvement of a significant animal reservoir for Gambian sleeping sickness remains unresolved. Molecular studies have demonstrated the presence of *T. b. gambiense* in domestic animals, particularly pigs, in the Democratic Republic of Congo (DRC) and Cameroon (Schares and Mehltz, 1996; Nikinin *et al.*, 2001; Simo *et al.*, 2006), and in a range of wild hosts in Cameroon (Herder *et al.*, 2002; Njiokou *et al.*, 2006). Monkeys infected experimentally with *T. b. gambiense* display chronic symptoms very similar to those seen in human cases of Gambian sleeping sickness (Ouwe-Missi-Oukem-Boyer *et al.*, 2006). Moreover, Rogers (1988) calculated that an animal reservoir is required to maintain this disease in the population. There remain lingering doubts, however, about the importance of an animal

reservoir in the epidemiology of this disease, especially as the chronicity of the disease in humans ensures that untreated infected people can themselves act as a reservoir over many years. It is also doubtful that the 'Jamot doctrine' (treating only the human reservoir) would continue to be as effective as it is against epidemics of Gambian sleeping sickness (Jannin and Cattand, 2004) were an animal reservoir to play a similar role in the Gambian disease as in epidemics of the Rhodesian disease (Welburn *et al.*, 2001*b*, 2006). Mathematical modelling indicates that, in the absence of a significant animal reservoir, it should be possible to resolve epidemics of human trypanosomiasis simply by removing human cases whereas, in the presence of a significant animal reservoir, it is necessary to deal with the vector and/or the animal reservoir (Welburn *et al.*, 2001*b*). In the recent epidemics in Sudan, north-western Uganda, the DRC and Angola, it has become clear that, although the failures in medical services resulting from civil disruption can quickly lead to epidemics of Gambian sleeping sickness, the restoration of these systems, no matter how inefficient they may be (Robays *et al.*, 2004), can bring the situation under control (Abel *et al.*, 2004; Jannin, 2005; Lutumba, 2005), **without** the need for tsetse control. In contrast, as seen in Busoga, action other than the treatment of infected humans is necessary to control epidemics of Rhodesian sleeping sickness. In the 1901 epidemic in Busoga, Draconian measures (i.e. the removal of the entire population at risk) were taken; in the most recent epidemic, extensive tsetse control (aerial spraying combined with ground spraying and trapping) was required to resolve the outbreak. As predicted using a mathematical model (Welburn *et al.*, 2001*a*), in the presence of a significant animal reservoir, there is no option but to attack the tsetse vector vigorously (Welburn *et al.*, 2006).

There remains the historical puzzle that scientists in colonial Francophone Africa

apparently did not repeat the definitive experiments with human 'volunteers' of Heisch *et al.* (1958). Ford (1971) has suggested that such experiments would have taken too long with Gambian sleeping sickness and would have been dangerous. Such considerations did not deter scientists in colonial Kenya, however, and it is doubtful that such niceties would have acted as a deterrent to the authorities in Francophone Africa, given their otherwise robust attitude to the human rights of their colonial subjects (Hochschild, 1999). While it is clear that animals, both domestic and wild, may be infected with 'Gambian' trypanosomes, the centrality of an animal reservoir in the epidemiology of Gambian sleeping sickness remains uncertain.

There is a footnote to the east-west story. Uganda is the only country that hosts both forms of sleeping sickness: Rhodesian in the south-east and Gambian in the north-west. Although these two foci of disease have remained apart since records began, there are disturbing signs that they have been moving gradually towards each other in recent years. Although the second line of *The Ballad of East and West* is '*...and never the twain shall meet*', it appears that, in Uganda, the distributions of the two forms of sleeping sickness will, in time, coalesce. Unless preventive measures are taken, millennia of isolation of these two very different diseases could be brought to an end, with worrying consequences for diagnosis, treatment and control (Picozzi *et al.*, 2005).

THE TSETSE FLY — PUBLIC ENEMY NUMBER ONE

While the work of the Sleeping Sickness Commission in Uganda provided impetus for trypanosome studies, it was not long before vector control became a priority for British researchers. They reasoned that the simplest way of dealing with the problem would be to remove the vector, but to do so would require detailed knowledge of the

flies involved. This feeling was already reflected in the early work of the Sleeping Sickness Commission, when Muriel Robertson (Robertson, 1913) detailed the life-cycle of the trypanosome in the fly. Much trypanosomiasis research funded by successive British governments up to the present day has been applied to the control or elimination of the tsetse vector, reflecting the priorities of a sphere of influence very different from that of Francophone countries. A century ago, the British had made little attempt to 'settle' their possessions in West Africa, which were, for a variety of political and economic constraints, viewed as suitable for trade rather than expatriate farmers. In contrast, the Europeans settling in eastern and southern Africa were mostly farmers who were not overly concerned with the threat of contracting sleeping sickness. In any case, the nature of their activities made it unlikely that they would be bitten by infected flies on a daily basis, unlike the African labourers they employed. The settlers were far more concerned with the threat that trypanosomiasis posed to their livestock, which they knew, from the early work of Bruce (1895), was linked to the presence of tsetse. They were therefore keen to see tsetse flies eliminated from their farms; as a result of this political pressure, British researchers, almost from the start, tended to concentrate on entomological solutions to the problems posed by trypanosomiasis. Removing the tsetse fly would also have dealt with the problem of Rhodesian sleeping sickness, which, as its main reservoir was in wild animals, would not bend to the 'Jamot doctrine'. The culling of wild animals in Anglophone Africa was, however, simply directed at removing the source of food on which tsetse populations were reliant and not on the removal of any vertebrate host of the parasites.

Differences in the Anglophone and Francophone approaches to disease control also had ecological drivers. Anyone familiar with eastern and southern Africa will have

been impressed with the huge uninhabited areas described evocatively by Ford (1971) as 'no-man's-land' or '*grenzwildnis*'. Even in present-day Africa, with its burgeoning human population, tourists are struck by the vastness of these wilderness areas, which are still largely untouched by the plough and home to all kinds of wildlife. Such environments also lend themselves to the untrammelled expansion of tsetse populations, and the unwary tourist may be attacked mercilessly by tsetse flies; a few such tourists are unlucky enough to contract sleeping sickness (Jelinek *et al.*, 2003). By contrast, tourists in West Africa are highly unlikely ever to encounter a tsetse fly, reflecting the very different ecology, demography and economic development pathways of this region.

Vast populations of savannah tsetse species, feeding largely on a diet of wildlife, especially threatened the livelihoods of colonial farmers attempting to graze livestock on the fringes of such areas. British scientists and their colonial masters developed what can only be described as an obsession to exterminate the tsetse fly, best illustrated by an unpublished speech given by William Ormsby-Gore, Undersecretary of State for the Colonies, at a meeting of the Royal Colonial Institute on 24 March 1925:

I do not think that people in this country, or even Africa, have yet realised the importance of the problem of the tsetse fly. The tsetse fly really tends to depopulate some of the richest countries in Africa. People think that the chief danger of the tsetse fly is sleeping sickness. It is true that many hundreds of thousands of Africans have been killed by sleeping sickness, caused by the tsetse fly, but that is only one incident in the problem. Where the tsetse fly exists there can be at present no animal transport. There can be, above all, no cattle; and it is, with rare exceptions, impossible to get an African to live without cattle. The result is that where the tsetse fly advances — and it is advancing — you get a country given

over to the bush. And here the vicious circle begins, because the tsetse fly can only exist if there is bush. Hitherto science has devoted, in my opinion, too much of its attention to the attempt to deal with the disease carried by the tsetse fly, particularly sleeping sickness. That is, of course, important, but it is of minor importance. The real problem before the practical African, east and west, is the extermination of the tsetse fly. That is the root problem which should face not only the British governments in Africa, but the Belgian, French and Portuguese governments as well. Let us strike at the root of the problem and endeavour to eliminate altogether the tsetse fly in Africa. Nothing short of it will in the long run prevent periodic outbreaks of sleeping sickness and the destruction of cattle and animal transport which is so essential to the economic development of these vast territories.'

How was the extermination of the tsetse fly to be achieved? The first plan was simply to remove vegetation conducive to the biology of the tsetse fly (Swynnerton, 1925) and this was done with some vigour; for example, some 16,500 ha were cleared in Kenya between 1952 and 1959. This method has its drawbacks, however, as it was labour-intensive (i.e. costly) and the bush regenerated in time. The second plan was to remove the host animals on which tsetse fed and which acted as reservoirs of trypanosomiasis — in other words 'game destruction'; enormous numbers of animals were shot in Zimbabwe, Zambia, Mozambique, Botswana and Uganda as a result of this policy. Ford (1970), a master of litotes, remarked that destruction of the larger fauna '*...may provoke powerful opposition that may become politically embarrassing*'.

Chemical Warfare

Following the Second World War residual insecticides burst on to the world market and immediately changed the face of tsetse control. DDT [1,1-bis(p-chlorophenyl)-2,2,2-trichloro-ethane] became available in

1945 and the ground spraying of vegetation with this compound was embraced with great enthusiasm in the Anglophone countries of Africa. These insecticide campaigns were driven by the availability of affordable chemicals and the biology of the tsetse fly — tsetse were found to be much more susceptible to insecticides than most other common insect pests (Burnett, 1963). The first large-scale success was in South Africa, where tsetse were removed from Zululand by a combination of aerial spraying with the gamma isomer of benzene hexachloride (γ -BHC) and the ground spraying of otherwise inaccessible areas with DDT (Du Toit, 1954). This was a military-style operation carried out using the aircraft, pilots and ground crew of the South African Air Force, conveniently recently returned from active service in the Second World War (Kappmeier *et al.*, 1998). Grander schemes followed in East and West Africa, some of which, such as the drive to remove tsetse from the whole of the north of Nigeria by ground spraying with DDT and dieldrin, were extremely successful (Jordan, 1986). Some control schemes were, however, not sustainable, for a variety of reasons. Although environmentally harsh conditions favoured tsetse control in northern Nigeria, where the fly was in, any case, on the limits of its distribution, high humidity in the middle belt of Nigeria favoured year-round tsetse survival and also negated insecticide treatments (Jordan, 1986). Successful or not, these insecticide-based control schemes eventually drew the attention of environmentalists, and in the post-colonial era, despite evidence that the environmental damage directly linked to tsetse-control schemes was quite limited (Grant, 2001), such programmes became increasingly difficult to justify.

The Greening of Tsetse Control

Scientists are 'children of their times' and subject to the same pressures associated with 'movements' as artists. Movements are

driven by the 'market', which, in the case of most science, means research funding. Trypanosomiasis researchers have not been immune to these forces and, indeed, are often held up by social historians as being simply the tools of colonial authorities — hence the sobriquet 'the colonial disease' (Lyons, 1992). Colonialism has not been the only driver of trypanosomiasis research, however, and this is best illustrated by considering the moves made to develop more environmentally-friendly methods of tsetse control. The origins of this movement lie in public distaste for the large-scale campaigns that were mounted to obliterate the tsetse fly from the face of Africa, whether by destruction of the environment or indiscriminate use of insecticides. The response of researchers and their funding agencies to this political impasse was to explore more environmentally-friendly means of removing tsetse, which had often already been developed in various parts of Africa but had never taken off on a commercial scale. A bewildering array of devices had been developed in the colonial era to trap tsetse, some of which verged on the bizarre. Take, for example, the Blunt land-sailing trap, designed to take advantage of the flies' known preference for a moving host. Designed by Commander Blunt (ex British Royal Navy), the trap was blown by the wind across a clearing and then tacked back against the wind, trapping flies *en route* (Swynnerton, 1933). What all of these original devices had in common was a lack of efficacy over time, and their sheer size and complexity often ruled out their use on a large scale. The shape of things to come had been anticipated by Morris (1950), whose DDT-impregnated traps killed flies very successfully, although the effect wore off too quickly to have long-term effects. Into the fray in the 1970s stepped a group of British scientists determined to improve trap efficiency to the point that traps would be commercially viable. In order to make such improvements, some measure was needed to record the behaviour of flies around trapping devices; the breakthrough came with

the development of the electric net, which tsetse did not see but which collected unsuspecting flies approaching a trap (Vale, 1974 *a, b*). With this wonderfully innovative tool, 'trap efficiency' became a metric and the components of fly attractants, which involved both visual and odour cues, could be quantified. Specific colours, notably at the blue end of the spectrum (Green, 1986), and odours (Vale *et al.*, 1986) that greatly improved trap catches were identified. The power of video recording was also brought to bear on fly movements around traps (Gibson *et al.*, 1991). Traps were redesigned to improve their portability, manufacturing simplicity and cost. Very simple traps or targets — pieces of cloth impregnated with insecticides — proved efficient for controlling flies, and were shown to be effective on a large scale in savannah environments (Vale and Torr, 2004). 'Bait technology' had come of age and was a serious option for control.

The Francophone countries were initially uninterested in tsetse trapping, as the prevailing wisdom was that the Jamot system was sufficient to control trypanosomiasis. Although trapping was generally considered impractical in the forest foci of West Africa, French scientists eventually developed excellent traps adapted to the more humid environments of western Africa (Challier and Laveissière, 1973; Lancien and Gouteux, 1987). Strangely, given the analytical nature of the French scientific heritage, these trap designs were developed in what might be considered a truly British, empirical manner, often ignoring the quantitative methodologies for discriminating movement (Vale, 1974*a*), colour (Green, 1986) or odour (Vale *et al.*, 1986) that had been so painstakingly developed by scientists in the Anglophone world. Unfortunately, research on odour attractants for riverine species of tsetse, which might have greatly improved trap efficiency, proved unproductive. There is evidence that *G. tachinoides* is attracted by natural odours (Merot *et al.*, 1988; Spath, 1997) but *G. palpalis palpalis*, *G. p.*

gambiensis and *G. f. fuscipes* are not as responsive to odours as flies of the *morsitans* group (Green, 1994; Mwangelwa *et al.*, 1995). As flies of the *palpalis* group are generally found in riverine or highly fragmented habitats, there might be evolutionary reasons for them not developing/expressing the repertoire of behaviours that permits flies of the *morsitans* group to locate hosts, over great distances, in savannah habitats.

DISEASE AND SOCIETY

Pax v. Bellum

Colonial epidemiologists considered the shocking epidemics of sleeping sickness, which they witnessed between 1900 and 1940, the result of the so-called '*pax Britannica*'. Colonisation, it was posited, prevented inter-tribal conflicts and made it possible for people to leave the safety of town walls, develop farms in the bush, and open up trade further afield. The downside to this new-found freedom of movement was increased 'human-fly' contact in the bush, and trade that brought with it carriers of trypanosomes and the risk of epidemics (Davey, 1948). The epidemics of sleeping sickness that had swept across the African continent were initially related to movements of people, which were catalogued with great, apparent precision. Over 80 years ago, Murray (1921) suggested that sleeping sickness had originally been confined to the coast of West Africa and the lower regions of the Congo but had spread across the Congo, after 1892, as a result of military movements. He also suggested that the disease was then introduced into Uganda by Emin Pasha's followers, and subsequently spread rapidly throughout East Africa, reaching Malawi and Zimbabwe by 1908 (Murray, 1921). Several decades later, however, an alternative view, which saw the parasite maintained in ancient 'endemic' foci from which, occasionally, epidemics developed, was put

forward. This approach considered the interaction between the parasite, the host and the social, political and economic environments as crucial (Kegels, 1997). Among the first to perceive trypanosomiasis as a societal rather than a technical issue was John Ford, who, in his seminal work (Ford, 1971), saw African trypanosomiasis as a problem that, before European expansion in the region, would have had limited impact. Ford argued that the continent and its peoples had been, in the ecological sense, at ease with each other and their environment prior to the European invasion. The 'scramble for Africa' exacerbated the problem, as demonstrated by the epidemics of sleeping sickness seen across the continent following the European conquest. The so-called '*pax Britannica*', aimed at preventing inter-tribal conflicts and viewed as wholly beneficial by the conquering powers, was, in Ford's view, better seen as *bellum* than *pax*. By introducing intensive systems of agriculture, colonial regimes had dramatically altered the environment in sub-Saharan Africa, an environment that millennia had settled in balance.

The '*pax*' analysis of the epidemiology of sleeping sickness can be seen as flawed in the light of the results of recent molecular studies. *Trypanosoma b. rhodesiense* was clearly not introduced into Uganda by migrant workers from Zambia following the '*pax*' (Hide *et al.*, 1996). Rather, this parasite is native to the region and has probably affected the peoples of Busoga for centuries (Koerner *et al.*, 1995). It seems more likely that, as suggested by (Ford, 1971), most epidemics arise in ancient foci and are triggered by some form of societal disruption that upsets the ecological balance, resulting in 'epidemiological disorder'. Ford (1971) went so far as to pinpoint the village (Wakoli's) that he considered the endemic focus of both the 1900 and 1940 epidemics in Uganda. In making this connection between these two outbreaks of disease, Ford was forced to gloss over the fact that, at the time he was writing, these

two epidemics were assumed to have been caused by different parasite species.

People, Cattle and Disease

Much has been made of the effects of the rinderpest epizootic (which ravaged sub-Saharan Africa between 1896 and 1898) on the incidence and distribution of trypanosomiasis. This epizootic spread with lightning speed, resulted in the collapse of practically all cattle stock and wildlife, and, in consequence, may have led to a fall in the density of the human populations in the affected areas between 1890 and 1920. The loss of grazing animals was thought to have led to the replacement of grasslands by bush that was ideal for tsetse flies. Maps were drawn detailing the 'spread' through East Africa of tsetse (particularly the savannah species) between 1900 and 1960, and the consequent expansion in the distribution of trypanosomiasis, that appeared to result from the rinderpest epidemic (Ford, 1971). There are problems, however, in quantifying the perceived 'spread' of tsetse populations and, as Ford (1971) admits, even the evidence for a decline in the human population after the rinderpest epidemic is not quantitative. In the period when the 'spread' of tsetse populations was supposed to have occurred, there were no good tools available for assessing the limits and size of tsetse populations. Carpenter (1924), in a valiant effort to get to grips with the epidemiology of sleeping sickness around the shores of Lake Victoria, simply estimated the human population by hut counts, the tsetse density by 'fly rounds' (conducted by 'fly boys', the quantum becoming 'number of flies caught per boy hour'), and the prevalence of sleeping sickness in humans by gland palpation. None of these measurements will have been accurate, least of all tsetse density and distribution, which are very difficult to measure from the ground; even using the latest techniques, only 'apparent densities' of tsetse can be measured.

Movements of tsetse are now, however, well understood, and the 'spread' of a tsetse population, in the absence of a barrier (natural or artificial), can be predicted rather accurately. Hargrove (1981, 2000) has shown that, under these circumstances, tsetse move diffusively, rather like gas molecules, with a daily root-mean-square displacement (λ) of 0.2–1.0 km, and that their populations can grow by no more than 1.5%/day. Invasion fronts move as the product of growth rate (r) and λ . If the growth rate is 0.75%/day, an invasion front will advance at about 2.5 km/year for each 100-m increment in λ . Approximately 30% of a tsetse population could travel 10 km in a year, and >3% could travel this distance in 3 months. It is clear from these estimates that tsetse populations can rapidly become a serious problem, with or without rinderpest, if left unchecked (Hargrove, 2003). Nowadays, the regional distribution of tsetse populations can be estimated more accurately by satellite imagery (Rogers, 2000) than by mapping based on 'fly rounds'. Recent improvements in diagnostics and, thanks to global positioning systems (GPS), in mapping have simplified the task of estimating the prevalence and movement of the trypanosomiasis. Even with the latest molecular technology, however, errors may still occur. Using such technology, Picozzi *et al.* (2005), for example, recently found that point estimates of the prevalences of trypanosome infections in domestic livestock could be inadequate when compared with the results of longitudinal studies using the same technology.

Use of a combination of molecular diagnostics and GPS has recently provided much more information about the movements of livestock and the spread of disease in East Africa (Fèvre *et al.*, 2001, 2006). In consequence, it is tempting to propose that it is movements of domestic livestock, rather than of people, that have historically been responsible for the apparent spread of Rhodesian sleeping sickness and subsequent epidemics. If it is accepted that movements

of livestock can be critical, then the defining event in the history of epidemics of Rhodesian sleeping sickness is likely to have been the Bantu migrations from 1000 BC onwards, when Bantu speakers spread south to the savannah lands of Angola and east to the Lake-Victoria region. Over the next 1500 years, Bantu peoples scattered throughout central and southern Africa, from their home in what is now Nigeria and Cameroon, taking with them, most importantly, their cattle (McEvedy, 1995). During this migration, Bantu cattle would have been brought into contact with the wild animal reservoir of Rhodesian sleeping sickness and this could well have upset a pre-existing stable relationship, developed over long periods of time, between trypanosomes, wild hosts and aboriginal human populations — Ford's 'epidemiological disorder' (Ford, 1971). It has been suggested that the pygmy peoples of the Congo are trypanotolerant in comparison with the Bantu population (Vincendeau *et al.*, 1999). For Bantu immigrants, who would have been familiar with the chronic Gambian form of sleeping sickness in their homelands, exposure to the acute, zoonotic, Rhodesian form could have been devastating. Importation of their cattle may well have set off a chain of epidemics of sleeping sickness in East Africa, probably starting from a primordial focus in the Lake-Victoria basin.

The social history of trypanosomiasis control in colonial Africa has been dominated by two main questions (Grischow, 2004): (1) did colonialism itself trigger the spread of human trypanosomiasis across the continent in the early 20th Century; and (2) were colonial officials correct in their remedies? Science has shown that, whatever other horrendous outcomes occurred as the result of the colonisation of Africa by the European powers, it seems unlikely that blame for the spread of sleeping sickness across Africa should be laid at the colonialists' doors. Scientists and historians should be less than sanguine, however, when

considering the colonial response to the epidemics they faced.

Ford (1971) attributed the sleeping-sickness outbreaks of colonial times to 'ecological catastrophe' brought about by the arrival of the Europeans and the subsequent 'spread' of tsetse populations. The epidemics of equal seriousness that have recently sprung up in both West and East Africa appear, however, to be totally unrelated to the 'spread' of tsetse populations. Failures in the medical and veterinary services consequent on civil disruption are the likely cause of recent outbreaks in quiescent foci of Gambian sleeping sickness (WHO, 2006). Outbreaks of Rhodesian sleeping sickness may result from changes in the animal reservoir (domestic livestock populations) that are also consequent upon civil upheaval.

Community-based Disease Control

In his classic paper, Winslow (1951) suggested that poverty, and particularly inadequate food supply, might be a cause of disease and that a more integrated approach was therefore needed for disease control. Interestingly, he took sleeping sickness as an example of a disease preventing agricultural development in sub-Saharan Africa; hence controlling the disease would, he reasoned, lead to increased agricultural outputs. In other words, fertile land lay idle because of disease. Today, 55 years later, this phenomenon can still be seen over vast tracts of land where trypanosomiasis impacts on both human and animal health. Interestingly, Nash and Morris, both entomologists working in West Africa, anticipated the ideas of Winslow (1951). In what would be regarded nowadays as an holistic approach, these colonial scientists saw the problem of trypanosomiasis as not simply tsetse-related but rather as an issue of rural development. The Anchau scheme for rural development and resettlement was planned in response to the very high incidence (>30%) of sleeping sickness in some villages near Zaria in

Nigeria in the 1940s. Riverine tsetse were firstly removed from the 'Anchau corridor' by bush clearing, and then people were resettled in the centre of the corridor. Anchau town was enlarged, to relieve overcrowding, and spacious suburbs were built to improve sanitation as well as to remove the threat of tsetse (Nash, 1948). Morris (1946) adopted a similar developmental approach in Ghana. Firstly vegetation was 'selectively' cleared from 320 km of linear tsetse habitat, which removed the fly and hence the sleeping-sickness problem; this was followed up with a planned programme of resettlement and development, including roads and water supplies. While these plans did not extend to the building of complete towns, Morris, like Nash, envisaged planned development designed to reduce food insecurity for thousands of people (Grischow, 2004).

In recent times there has been much debate about the most sustainable approach to tsetse control, and, inevitably, this has raised social and economic as well as technical issues. The development of GPS-based tracking systems has made it feasible to spray very large areas with insecticide from the air in the confidence that the entire designated area has been covered; untreated pockets of tsetse, the bane of earlier control projects, are no longer a problem. As recently seen in the Okavango delta of Botswana (Allsopp and Phillemon-Motsu, 2002), aircraft equipped with the latest satellite-navigation equipment and spraying very low doses of deltamethrin (0.26 g/ha) can successfully eliminate tsetse from a relatively large area (7180 km²). Note that the word 'elimination' is chosen advisedly, as re-invasion is a constant threat to any non-isolated population of tsetse (Hargrove, 2003). [It is helpful to follow the definitions proposed by Dowdle (1998), in which 'control' is a reduction in the incidence, prevalence, morbidity or mortality of an infectious disease to a locally acceptable level, 'elimination' is a reduction to zero of the incidence of disease or infection in a

defined geographical area, and 'eradication' is the permanent reduction to zero of the world-wide incidence of infection.] Tsetse-control schemes involving aircraft can be effective (given caveats about isolation) but are expensive; the aircraft hire and insecticide for the spraying operation in the Okavango cost U.S.\$1,907,319 (Allsopp and Phillemon-Motsu, 2002). Such operations are way beyond the means not only of the individual farmer but also of most of the governments of the poorer affected countries of sub-Saharan Africa and, of necessity, they must be treated as a public good (in the economic sense).

The advent of efficient traps and targets to remove tsetse had promised a much cheaper and possibly sustainable approach to tsetse control. The question then arose as to who would take up these new technologies. Community-based systems had been shown to be highly effective in the field of human health, and it was hoped that, by adopting a community approach, people would work together to deploy and, more importantly, maintain sufficient traps/targets in the environs of their villages to impact on disease transmission. Sadly, experience was to show that community-based trapping schemes were rarely sustainable, not only for a variety of social reasons but also technically, because of problems of re-invasion; tsetse are not, after all, 'community-based' but rather given to roving (Hargrove, 1981, 2000).

Tsetse researchers were clearly out of their depth in trying to solve problems of sustainability but into the breach stepped social scientists. Their analysis of community-based programmes of tsetse control produced mixed advice which roughly can be summed up as 'we would never have started from here'; insufficient care had gone into preparing the communities involved for the undertaking expected of them (Dransfield and Brightwell, 2004). More importantly, it appeared that, in the absence of a sleeping-sickness epidemic, which would present a compelling driver

for control, controlling tsetse flies to prevent animal trypanosomiasis alone did not present an urgent enough problem for the efforts expected from these poor communities (Barret and Okali, 1998). Socio-economists have also reflected on the fact that the provision of such a public good is hedged with difficulty (Swallow and Woudyalew, 1994). The problem of sustaining a public resource that everybody is free to over-use emerges in many social dilemmas, and can result in a 'tragedy of the commons' (Hardin, 1968).

'WIND OF CHANGE'

In a speech in Cape Town in 1960, the British Prime Minister, Harold Macmillan, spoke of a '*wind of change*' blowing through the continent of Africa, as more and more majority black populations claimed the right to rule themselves. So began the British and French withdrawal from their African 'possessions', and from then on the funding of trypanosomiasis research ceased to be the exclusive domain of European science. National institutes [e.g. the Nigerian Institute for Trypanosomiasis Research (NITR), the Kenya Trypanosomiasis Research Institute (KETRI), and the Uganda Trypanosomiasis Research Organisation (UTRO)] were established in the affected countries of East and West Africa, joined, in the 1970s, by internationally funded institutes, dedicated wholly or partly to trypanosomiasis research [e.g. the International Laboratory for Research on Animal Diseases (ILRAD) in Kenya, the International Centre of Insect Physiology and Ecology (ICIPE) in Kenya, and the International Trypanotolerance Centre (ITC) in The Gambia]. The planned repatriation of the trypanosomiasis-research agenda to African centres was, however, blown off course in the 1980s as a result of the Structural Adjustment Programs. These schemes to balance national budgets, which were promoted by the World Bank and

International Monetary Fund, resulted in the downsizing of public-sector workforces and services (Brown, 1995). In this climate it was inevitable that institutes devoted to a single disease, carrying considerable transaction costs, became difficult to sustain. KETRI became absorbed into KARI (the Kenya Agricultural Research Institute), UTRO was absorbed by LIRI (the Livestock Health Research Institute, Uganda) and the International Livestock Research Institute (ILRI) took over ILRAD, with a much broader research remit.

As a result of these economic pressures, the drivers of trypanosomiasis research and control have also changed significantly. In a reversion to what might be viewed as the 'post-colonial' arrangements, funding for research and control has become largely dependent on agencies in the developed world. The Regional Tsetse and Trypanosomiasis Control Programme (RTTCP) that was set up in 1986, for example, was funded by the European Commission (Van den Bossche and Doran, 2002). More recently the research agenda has been set by the Millennium Development Goals (MDG) agreed by the world's leading development institutions (www.un.org/millenniumgoals). The first of these MDG — to eradicate extreme poverty and hunger — clearly underlines the importance of agricultural research and development. Development agencies are not now concerned so much with narrow sectoral problems in agriculture, among which trypanosomiasis continues to play a major role, but rather with the broader benefits that may accrue to poor people from effective interventions. This implies the empowering of poor farmers with appropriate and sustainable approaches to disease control (Sachs, 2005).

Fortunately, an innovative and appropriate tool for poor farmers to control tsetse has emerged from research on bait technology. Ironically, the odour attractants, so painstakingly identified, turned out to be

components of cattle odour and, in a leap of logic, it was suggested that it might be better to 'cut out the middle man' and simply treat cattle directly with insecticide. This approach had been tried before using DDT but, due to formulation problems, had not been effective (Whiteside, 1949). New formulations of synthetic pyrethroids (SP) proved much more effective (Thomson, 1987; Thompson *et al.*, 1991) and recent research has shown that costs can be cut by treating only the larger cattle within a herd (Torr and Mangwiro, 2000) and only the parts of the cattle on which tsetse preferentially feed — the legs and belly (Torr *et al.*, 2001). This 'restricted-application' methodology also reduces the attendant risks of environmental damage normally associated with indiscriminate use of insecticides (Vale and Grant, 2001; Torr *et al.*, 2005). As a result of this research, there is no longer any need to see the control of tsetse at the community level as being necessarily a tragedy in the making; by using insecticide-treated cattle as the bait for tsetse, the 'public-good' problem is avoided, as benefits are perceived to be individual. With insecticide-treated cattle, the African farmer can now choose to get to grips with the problem of trypanosomiasis of his own volition. At a cost of around U.S.\$1/animal-year, the restricted-application methods are well within the reach of poor farmers (Torr *et al.*, 2005) who — as witnessed by the size of the market in trypanocidal drugs — are willing to spend considerable proportions of their incomes on effective trypanosomiasis control (Holmes *et al.*, 2004). Using live bait, tsetse control becomes an individual exercise providing individual benefits, including, as a beneficial side-effect, a reduction in the problems posed by tick-borne diseases (Eisler *et al.*, 2003). This approach also avoids the difficulties of 'free-riding' associated with the community-based control of tsetse. Along the way, Rhodesian sleeping sickness may also be held in check (Welburn *et al.*, 2006). It must be emphasised that, to achieve these

benefits, farmers in affected areas will have to be incentivised to treat their cattle, perhaps by engaging with the private sector to (1) improve insecticide-delivery networks, (2) ensure that farmers know that cheap solutions are available, and (3) encourage the continued use of appropriate trypanocidal drugs. As Hargrove (2003) indicated, live-bait techniques can only be effective in controlling tsetse populations where there is a sufficient density of treated livestock.

As with drugs for the treatment of human African trypanosomiasis, drugs for the treatment of livestock rest on a very old legacy. Because of the relatively limited market in Africa and the high costs of developing and licensing new drugs, pharmaceutical companies have little interest in the development of new trypanocides for use in livestock. The three trypanocides currently used to control tsetse-transmitted trypanosomiasis in domestic animals in Africa have been in use for over 40 years and, not surprisingly, drug resistance is now a problem; the current challenge is to achieve optimal use of these relatively old drugs (Geerts *et al.*, 2001). The introduction of live-bait technology can reduce the demand for trypanocides and the problems of drug resistance in a ranch setting (Fox *et al.*, 1993). The effects of treating cattle with an SP are not limited to tsetse but also include reductions in tick and nuisance-fly burdens. Intriguingly, such treatments can lead to animal-health benefits even when they have little effect on the size of the local tsetse population (Baylis and Stevenson, 1998). The wide-spread and uncontrolled use of SP is not, however, without risks, such as acaricide resistance, detrimental effects on the invertebrate fauna associated with the breakdown of cattle dung, and increased susceptibility to tick-borne diseases (Eisler *et al.*, 2003).

An alternative to farmer-based trypanosomiasis control, proposed by the Pan African Tsetse and Trypanosomiasis Eradication Campaign (Anon., 2001), is to

adopt 'area-wide' tsetse-control programmes; a successful model for this approach has been provided by the programme of aerial spraying in Botswana discussed above (Allsopp and Phillemon-Motsu, 2002). The sterile-insect technique (SIT), involving the release of artificially reared sterile males, appears, on the surface, to offer an environmentally friendly option for tsetse control and has been used successfully to eliminate tsetse from Unguja Island, Zanzibar (Vreysen *et al.*, 2000). Such top-down control schemes are extremely expensive to carry out, however, and do not necessarily fit with the MDG of developing countries; indeed they are, almost by definition, the preserves of affluent societies. SIT has, for example, been used most effectively to deal with the problems of screwworm fly in the Americas (Galvin and Wyss, 1996). The use of SIT in African settings has been severely criticised on ecological, logistical and financial grounds (Molyneux, 2001; Rogers and Randolph, 2002; Hargrove, 2003; Bourn *et al.*, 2005) and by agencies interested in supporting sustainable development (Short, 2002).

At present, much research that falls under the banner of African trypanosomiasis is devoted to the fundamental biology of the parasite for, as Cross (1996) has so elegantly put it, this parasite has many striking 'aberrations' associated with its metabolism and genetics that stem from the trypanosome's very early divergence in the eukaryotic-cell lineage. This fundamental research has the strategic aim of prospecting for designer drugs; so far, success has proved elusive but hope springs eternal in the (scientific) human breast. Recently, Landfear (2006) optimistically stated: '*These results raise the intriguing possibility of developing drugs that act selectively against the trypanosome...*'. Research on the molecular biology of trypanosomes has proven extremely useful for the development of diagnostics (Hutchinson *et al.*, 2004; Chappuis *et al.*, 2005) and improving our

understanding of the epidemiology of sleeping sickness (Welburn *et al.*, 2001b; Welburn and Odiit, 2002). Satellite imagery has also revealed itself as a very powerful tool for understanding and even predicting epidemics of trypanosomiasis (Hendrickx *et al.*, 2000; Rogers, 2000; Fèvre *et al.*, 2006).

To this day, the control of epidemics of Gambian sleeping sickness in West Africa is reliant on active case finding and chemotherapy (Jannin and Cattand, 2004) and, despite its apparent simplicity, this approach remains remarkably effective. With the interruption of civil strife in Angola, Central African Republic, the DRC, Sudan and Uganda, active case finding has been re-instated, leading to substantial declines in the number of new cases (WHO, 2006). For this strategy to be successful over the longer term, early detection (i.e. before parasites start to destroy the CNS) is paramount if the use of the existing arsenic-based drugs, such as melarsoprol, is to be avoided (Jannin, 2005). Effective treatment of Gambian sleeping sickness is, however, threatened by problems associated with drug resistance (Van Nieuwenhove, 2000), and it is imperative that new drugs are developed; given the enormous costs now associated with drug discovery, this can only succeed on a collaborative basis.

Public-private partnerships (PPP) are increasingly seen as the model to finance drug discovery, as it is unlikely that significant private-sector investment will be forthcoming for diseases, such as sleeping sickness, that have no global market. To ensure sustainable development of, and equitable access to, drugs for tropical diseases, the public sector must play a much greater part (Zumla, 2002). Fortunately, with the guidance of the WHO, PPP have been established to address both the chemotherapy (Banerji, 2003; Jannin *et al.*, 2003; McKerrow, 2005) and diagnosis of sleeping sickness (www.finddiagnostics.org). In the case of Rhodesian sleeping sickness, control of the animal reservoir

remains a priority (Jannin, 2005), especially in Uganda, where spread of this disease could, for the first time, result in an overlap of the Gambian and Rhodesian foci of infection, with its attendant diagnostic and treatment problems (Picozzi *et al.*, 2005).

Human African trypanosomiasis, unless treated, is a fatal disease; control of this disease on humanitarian grounds alone has to be viewed as a public good, and the response of non-governmental organizations and aid agencies in recent years has been encouraging. There is, however, a strange echo of the debate over the blinkered colonial response to sleeping-sickness epidemics in current discussions of the concentration of humanitarian resources on the 'big three' (i.e. HIV/AIDS, malaria and tuberculosis). It is argued that focus on the 'big three' has led to the neglect of diseases that exclusively affect the poor and the powerless in rural and impoverished urban areas of developing countries — the 'neglected tropical diseases' that include human African trypanosomiasis (Hotez *et al.*, 2006).

Attitudes to disease control in Africa have evolved since colonial times and are no longer centred on the mechanical doctrine of controlling parasites. Health care now implies doing what is necessary to assist communities and individuals to manage their own problems (Kegels, 1997). For the poor keeper of livestock in sub-Saharan Africa, researchers have provided 'cheap and safe' tools (Bourn *et al.*, 2005) to deal with trypanosomiasis within the community (Torr *et al.*, 2005; Welburn *et al.*, 2006). In the much longer term, even in the absence of interventions, the problem of tsetse may resolve itself, as demography transforms the landscape of sub-Saharan Africa. The population of Kenya, which was a mere 8.6 million at independence, is around 34 million at present and is projected to rise to 65 million by 2050; this sort of demographic pressure will afford little room for the vectors of trypanosomiasis (Bourn *et al.*, 2001).

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