Human African trypanosomiasis: an emerging public health crisis

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There is a dramatic resurgence of human African trypanosomiasis (HAT) in sub-Saharan Africa. *T. b. gambiense* is spreading epidemically in large areas of Central Africa, especially the Southern Sudan, Congo-Zaïre, Angola, Uganda and the Central African Republic. Devastating epidemics of *T. b. rhodesiense* have occurred in south-eastern Uganda.

The causes of the re-emergence of sleeping sickness as a public health problem include widespread civil disturbance and war, declining economies, reduced health financing and the dismantling of disease control programmes. Despite the inevitably fatal outcome without treatment, HAT is often given low priority by donors and national governments. The advances made in diagnosis, treatment and vector control have not been sufficiently implemented.

To limit the human impact in some of the poorest communities in Africa, endemic countries will require external support to implement strategies for disease control. Donor agencies, NGOs and mission organisations could play an important role in supporting control efforts. National authorities will need to control and co-ordinate these efforts with assistance from WHO and the international community.

Human African trypanosomiasis (HAT) is caused by subspecies of *Trypanosoma brucei*, transmitted by tsetse flies (*Glossina* spp) and confined to sub-Saharan Africa in defined geographical foci in some 36 countries. Only 20–25 000 cases are notified to WHO each year, but the true figure may now exceed 300 000. Even this figure may be an underestimate. Given the often chronic progressive nature of infection, the fatal outcome with meningo-encephalitis and the therapeutic and diagnostic difficulties, Africa is facing a human crisis of substantial proportions to which most aid organisations and national governments are either ignorant of or unable to respond.

Resurgence and epidemics of African trypanosomiasis are associated with economic decline, civil disturbance, war, population movements and refugees. Foci of high endemicity occur in remote rural areas and are
often accorded low priority by politicians and health officials. In addition, vertical disease control programmes have been progressively dismantled in preference to integrated, community-based, health care. While sleeping sickness has declined in a number of West African countries such as Ghana, Nigeria and The Gambia, vast areas of central Africa from the southern Sudan and Uganda, through Congo-Zaire south to Angola are experiencing progressive epidemic spread. This paper outlines the history and epidemiology of HAT, describes the situation in Central Africa, especially in Congo-Zaire and Angola where there is resurgence and epidemic spread of *T.b. gambiense*, and Uganda where devastating epidemics of *T.b. rhodesiense* occurred in settled agricultural areas during a period of civil unrest.

A century after the description of the parasite, its transmission through tsetse flies and recognition of early epidemics which caused some three quarters of a million deaths in central Africa in the early 1900s, it is timely to review the recent resurgence of human African trypanosomiasis and assess the possibilities for control of this vector-borne disease which is currently attracting little international attention.

**An historical perspective**

*Trypanosoma brucei* and the role of tsetse flies (*Glossina*) as vectors was identified in game animals in Zululand by David Bruce a century ago. Later, morphologically identical trypanosomes were identified in the blood of a European from The Gambia, West Africa, and transmission by riverine tsetse (*Glossina palpalis*) confirmed. Subsequent studies revealed the extensive, often focal distribution of the disease, the substantial endemicity and the chronic progressive nature of human infection in West and Central Africa. The disease was called Gambian Trypanosomiasis and the parasite, *T. gambiense* (later *T. brucei gambiense*). In 1908, a severe, rapidly fatal, trypanosomal infection was identified in the Luangwa valley (Zambia). Further investigation confirmed its clinical severity, the distinct epidemiology with transmission via savannah tsetse and the zoonotic nature of infection from game animals harbouring *T. brucei*. This led to the description of Rhodesian Trypanosomiasis due to *T. rhodesiense* (*T.b. rhodesiense*). Other members of the *T. brucei* group that were non infective to humans and occurred in game animals and domestic animals were designated *T. brucei* (subsequently *T.b. brucei*).

**The parasite**

Trypanosomes (genus: *Trypanosoma*) occur in the blood of man and animals as the trypomastigote. They are motile and possess a kinetoplast
with extranuclear DNA enclosed in a mitochondrial envelope and associated with the basal body of the flagellum. They range in length from 15–35 μm. All members of the *T. brucei* group are morphologically identical. *T. brucei* parasites have evolved mechanisms for evading host immune responses by regular switching of the variant surface antigen glycoproteins\(^4\). The zoonotic nature of *T.b. rhodesiense* was initially established by ‘volunteer’ inoculation with parasites from a Bushbuck (*Tragelaphus scriptus*)\(^5\) and later, domestic cattle. Subsequently, the blood incubation infectivity test (BIIT) was developed to assess the human infective potential of parasites from a range of wild and domestic animals. More recently, a number of molecular techniques, especially isoenzyme analysis\(^6\) and restriction fragment length polymorphism (RFLP)\(^7\), have been used as markers for parasite strains to explore the molecular epidemiology of this complex group of infections. These techniques allow *T.b. gambiense* to be distinguished from *T.b. rhodesiense*. *T.b. gambiense* comprises six zymodemes from West and Central Africa and the Bouaffle group also identified in domestic and wild animal stocks and possibly of low human virulence. *T.b. rhodesiense* comprises two main zymodeme groups, Zambezi which occurs in the southern range of disease and Busoga, prevalent in the region around Lake Victoria, especially in south-eastern Uganda, where it co-exists with Zambezi zymodemes. Both Busoga and Zambezi zymodemes have been isolated from a range of wild and domestic animals.

**Vectors and animal reservoirs**

In West and Central Africa, HAT is transmitted by riverine species of tsetse fly (*Palpalis* group) which require sustained levels of humidity and prefer dense riverine habitats. They feed preferentially on man especially where man–fly contact is high, such as water collection and bathing points, river crossings and sacred groves. Riverine species include *Glossina palpalis*, *G. tachinoides* and *G. fuscipes*. Man provides the reservoir of infection, although both wild and domestic animals may play a minor role in particular foci. Throughout most of the range, *T.b. rhodesiense* transmission is effected by savannah species of tsetse (*Morsitans* group). *G. morsitans*, *G. pallidipes* and *G. swynnertoni* survive in drier, more open areas of woodland, savannah and Acacia thicket. They prefer to feed on game animals and domestic stock. Human infection occurs sporadically in individuals coming into contact with the zoonotic cycle, for example poachers, hunters, honey gatherers, firewood collectors and tourists. A wide spectrum of animals, notably game animals and domestic cattle, provide a reservoir of infection. In
East Africa the epidemiology is different, leading to epidemic potential, where *T. b. rhodesiense* is transmitted by a riverine species of tsetse – *G. fuscipes* – and domestic cattle are the main reservoir.

**The clinical disease**

*T. b. gambiense*, in most endemic areas, causes a protracted, often initially unrecognised, illness with episodes of fever, headache and malaise, accompanied by progressive lymphadenopathy and followed later by the development of a progressive, fatal, meningo-encephalitis. This contrasts with the acute, severe, febrile disease observed with *T. b. rhodesiense*, with rapid progression to meningo-encephalitis. There is a relentless deterioration to a stuporous state, with cachexia, wasting and progressive malnutrition, deepening coma and death, within a few months in *T. b. rhodesiense* and extending for months or even years in *T. b. gambiense*.

**The diagnosis**

In *T. b. rhodesiense* HAT, parasitaemia is readily detected in the peripheral blood, especially in early infections. Examination of thick blood films is often adequate for initial screening. In *T. b. gambiense* HAT, where lymphadenopathy is common, lymph node aspiration is the traditional diagnostic technique but parasitaemia is more variable and commonly too low for regular diagnostic use of blood films to be reliable. However, parasitaemia varies between foci and disease stage. In northern Uganda, careful thick blood film examination was positive in 75% of card agglutination tests for trypanosomiasis (CATT) positive cases and, in combination with lymph node aspiration, may detect a substantial proportion of infections in situations where further investigation is not possible.

Blood concentration techniques are required when simple blood film examination and gland aspiration are negative. They include the haematocrit centrifugation technique (HCT) with the examination of the area above the buffy coat in from 4–8 micro-haematocrit tubes. This technique increases the sensitivity but requires experienced technical support. The quantitative buffy coat (QBC) technique, developed for the diagnosis of malaria, has been evaluated in Uganda. It provides a highly sensitive method, which in a series of studies proved superior to a combination of other diagnostic techniques. QBC is a modification of HCT. The upper layer of the expanded buffy coat, stained with acridine
orange, is examined in a fluorescent system and motile stained trypanosomes are readily identified. The mini-anion exchange column technique (mAECT) has been used in specialist centres with good sensitivity but, under other circumstances, has proved technically difficult and less effective. Examination of the cerebrospinal fluid, including concentration by centrifugation, may provide the first evidence of trypanosomes. The role of antigen detection systems such as CIATT and the polymerase chain reaction (PCR) remains to be determined.

In areas of T.b. gambiense HAT, where the early features of trypanosomiasis may be few, the CATT provides a serodiagnostic technique for the detection of antibodies. Plasma dilution increases the specificity of the test. CATT on whole blood and plasma dilutions is based on agglutination of freeze dried coloured trypanosomes which agglutinate in the presence of a variant specific antibody (Litat 1.4) used as an antigen. The sensitivity varies in different geographical areas, but CATT may double the number of cases found with conventional techniques. A liquid medium has been developed for culturing trypanosomes (KTVI) but has not proved robust enough for field diagnosis. Diagnostic tests have been refined to provide greater sensitivity and specificity. The use of CATT for screening populations for T.b. gambiense has greatly improved the potential for community diagnosis. Despite these advances, newer techniques, especially CATT, have rarely been put into practice in endemic areas except as part of an externally funded programme. This relates in part to cost but, even in highly endemic situations, simple diagnostic tests are often not employed.

**Therapeutics**

Despite poor funding, advances have been made recently in the treatment of T.b. gambiense HAT whereas treatment of T.b. rhodesiense-infected patients has remained unchanged for 40 years. Eflornithine became the first new drug for African trypanosomes since the late 1940s. Its trypanocidal action was discovered by accident. This drug and many other polyamine synthesis inhibitors were developed in a quest for new strategies against cancer, but a better understanding of the importance of polyamines in trypanosomes led to animal and, rapidly, human trials. Eflornithine is slightly less effective than melarsoprol in late-stage new cases of Gambian HAT at the currently recommended dosage (10% relapse rate versus 6% with melarsoprol) but it is far less toxic. Most fatalities during eflornithine treatment occurred in patients who were in a desperate condition before receiving the drug and probably had more to do with advanced sleeping sickness than drug toxicity. 100 mg/kg i.v. 6 hourly for 14 days is recommended.
by the manufacturers. It probably would be possible to increase to 125 mg/kg and reduce the failure rate without significant toxicity but this cannot be recommended within a mass treatment approach, if only because of the added cost. Unfortunately, eflorenthine cannot be used as first-line treatment of late-stage *gambiense* trypanosomiasis because it costs US$ 300 per patient, about 5 times more than melarsoprol. The results of a multicentre trial comparing 7 to 14 days of eflorenthine, at 100 mg/kg 6 hourly, should be available by mid-1998. This trial has already shown a much higher relapse rate in *gambiense* patients from northwest Uganda than from West and Central Africa, the causes of which will have to be explored.

For the 6% of Gambian HAT patients who relapse following melarsoprol therapy, eflorenthine is remarkably effective and is their only chance of survival. A recent study showed that, in relapsing cases, a 7 day regimen, at 100 mg/kg 6 hourly, is as effective as the 14 day course \(^{14}\), presumably because of better CSF penetration by eflorenthine due to an impaired blood-brain barrier in patients who have had a meningoencephalitis for months or years. This reduces the cost of treating such relapses. Even those who can afford eflorenthine may not be able to obtain it. It is uncertain whether Hoechst-Marion-Roussel or another manufacturer will continue to produce eflorenthine.

Another advance in the treatment of late-stage Gambian HAT has been the demonstration that prednisolone, at 1 mg/kg/day (up to 40 mg), reduces by two-thirds the risk of melarsoprol-induced encephalopathy and by half the mortality during melarsoprol treatment \(^{15,16}\), without increasing the failure rate. There is no reason why late-stage Gambian HAT patients treated with melarsoprol should not be given concomitant prednisolone: its total cost is currently US$ 2, approximately 3% of the cost of melarsoprol, which is mainly covered by the savings from the lower frequency of encephalopathy, the treatment of which is expensive (i.v. steroids, anticonvulsants, epinephrine [adrenaline] and i.v. fluids). For the first time in 50 years of use, there is now some understanding of the pharmacokinetics of melarsoprol \(^{17}\). More rational regimens have been proposed and could one day replace the weird ones currently in use, but only if proper clinical trials were to prove that they resulted in a better balance between efficacy and toxicity and reduced cost. For patients with early-stage Gambian HAT, a better understanding of the pharmacokinetics of pentamidine may soon lead to more rational regimens \(^{18}\).

Chemotherapy of *T.b. rhodesiense* HAT has not advanced. Suramin remains the standard drug in the early stage, but a better delineation of its pharmacokinetics in AIDS and cancer patients has not affected HAT. For late-stage cases, eflorenthine is ineffective, even at 800 mg/kg/day: even though it has been tried in only a dozen of melarsoprol-resistant
patients, the results were so poor that further studies are unlikely. Melarsoprol remains the only effective drug for late-stage patients. Prednisolone has not been evaluated in the prevention of reactive encephalopathy in such patients, although the underlying mechanisms must be the same as in Gambian HAT.

Research priorities are clinical trials of new regimens of melarsoprol \((gambiense\) and \(rhodesiense\)) and combinations of eflornithine and melarsoprol \((gambiense)\) whose synergism has been well documented in the murine model\(^{19}\). Melarsoprol binds to trypanothione, a spermidine-glutathione conjugate whose production is impaired by eflornithine\(^{20}\). This combination should be tried in relapsing cases (specially patients who relapse after melarsoprol and eflornithine) and eventually in new cases. A few days of eflornithine followed by 1–2 injections of melarsoprol is cheaper than melarsoprol monotherapy but has not yet been proved to be as effective.

**Current epidemiology**

Human African trypanosomiasis is a public health problem in large tracts of country in central Africa. \(T.b.\) \(gambiense\) is endemic, often at high levels and largely undocumented in the early period of transmission because early symptoms are mild and \(T.b.\) \(rhodesiense\) is an acute epidemic disease when transmitted close to human populations, especially by a riverine species of tsetse.

**The epidemic in Congo-Zaire**

Over 19 000 cases were reported annually in 1994, 1995 and 1996 in Zaire, now the Democratic Republic of Congo. In 1994, the true incidence was probably twice the reported one\(^{21}\). Control programmes were interrupted again during the 1996–97 civil war. Their future status depends on the attitude of donors towards the new regime, security problems, and the degree of priority given to HAT compared to other urgent public health problems. Because of this new breakdown in control activities, there is no doubt that the annual incidence will soon reach 100 000 cases per year. Most of the victims will die without any treatment. Congo-Zaire already bears 80% of the global burden of HAT. The situation is most dramatic in the Equateur (northwest, specially in Karawa and Gemena districts) and Bandundu (center of the country, mostly in Kenge and Masi-Manimba districts) regions, where 85% of the country’s caseload is seen and where several communities have had annual incidences over 200 per 1000. Other endemic regions
are, in decreasing order of importance, Kasai, Bas-Zaïre and Maniema. In Kimbanzi village, Bandundu region, a case-finding survey in 1994 showed that 72% of the population had HAT: this suggests that more isolated communities may have been completely wiped out by sleeping sickness in recent years. Sleeping sickness will progress especially rapidly in the Equateur region where the epidemic is relatively recent and the population is non-immune. It will also spread to new areas that have a sufficient vectorial capacity.

This suffering results from a 2–3 years’ slowdown in control activities (1991–93), following a political dispute with the previous regime. Control efforts from 1965 to 1990, funded by Belgian aid, had stabilized the incidence at 5–10 000 cases per year. Why 25 mobile teams working over a quarter of a century failed substantially to reduce HAT incidence in Zaïre is a complex question. The disintegration of Zaïre during that period is a major part of the answer: ridiculous salaries, poorly motivated staff, dismal road conditions, recurrent petrol shortages and widespread corruption all damaged the efficacy of mobile teams. These teams persisted in using traditional methods from the colonial era. Better control would have been achieved if CATT had been implemented earlier in very active foci. Its cost would have been compensated, over a few years, by savings on trypanocidal drugs. The resources available were never sufficient: given the size and ‘at-risk’ population of Zaïre, 25 mobile teams are the equivalent of one or two teams in neighbouring countries. So much of the budget had to be spent on trypanocidal drugs that little was left to maintain the mobile teams and to set up additional teams.

The epidemic in Angola

Gambian HAT was first recognised in northern Angola in the late 19th century. The Portuguese Colonial Government put emphasis on control and created a national programme in 1949, called Missão de Combate as Tripanosomiase (MCT), with mobile teams cruising the country and logistical back-up by the colonial army. Each village was visited at least once a year so that the whole population of endemic areas had regular access to diagnosis and treatment. More recently, the basic screening procedure has been the CATT test, followed by puncture of enlarged cervical lymph nodes and CSF examination. The colonial control programme was effective in reducing the incidence of HAT and its mortality. In the 1950s, some 5000 cases were reported and treated each year, while in 1974, only three new cases had been recorded country-wide. In 1976, Angola became independent and the country was thrown into a cruel civil war for two decades. Tension between the warring factions continues to the present day. One of the many dreadful
consequences was the complete collapse of the health system and the discontinuation of the control programme. Sleeping sickness returned with a steady increase in incidence, although data for the period between the late 1970s and 1995 are incomplete.

Today, Angola is one of the countries most affected by HAT. From north to south there is a sharp decrease in seroprevalence. A recent national CATT survey showed a decline from 15% in the north to almost 0% in the south. In some northern districts, sleeping sickness is now the major cause of adult mortality. The sight of abandoned villages along the river valleys or of numerous patients lying ‘sleepy’ along the roadside in glaring sun is depressing considering the achievements of the past. The epidemic will cause an incalculable amount of hardship and suffering among the rural population in the north of the country. Four provinces are severely affected: Uige, Zaire, Cuanza Norte and Bengo. Others are reporting many patients and may harbour unknown foci of transmission. The vector, *Glossina palpalis*, is recorded in 10 more provinces highlighting the potential for further spread of the disease once the population starts to migrate as a result of the end of the war. At least one-third of the overall population of 12 million are directly exposed to the risk of infection.

Most of the national health structures in rural areas are not operating because of lack of resources. Non-governmental organisations (NGOs) are trying to bridge the gap but their efforts can never fill the needs on a country-wide level. Presently six NGOs are involved in activities directed against HAT. They have different philosophies and implementation strategies and work independently from each other. The National Trypanosomiasis Control Programme (NTCP), under the Angolan Ministry of Health, tries to co-ordinate the different NGO efforts. There are now national treatment guidelines and common registration forms\(^2^2\). In the future, this process of co-ordination, boosted by bilateral aid to the national authorities, might put the NTCP into a position to develop and implement an effective and comprehensive control strategy. Staff are available, but are presently unmotivated because of insufficient salaries, mismanagement and bad working conditions. Access to endemic areas is difficult because of the continuing political instability and the division of the country into areas controlled either by the government or the UNITA. Any success in the fight against HAT in Angola remains dependent on the contribution of NGOs and church groups.

Most NGO activities focus on the establishment of treatment centres, either as additional wings in district or provincial hospitals or as specialised structures (*hipnoserías*). Patients come on their own initiative to receive treatment (‘passive case-finding’). This activity, although necessary from a humanitarian point of view, remains ineffective for
control of transmission. In the last two years more than 5000 patients have been treated, predominantly in units supported by Caritas. More than 90% were late stage and were recruited by passive surveillance. Preliminary community surveys in endemic areas in the north, indicate a CATT positivity rate of up to 60%.

Comprehensive control programmes require a co-ordinated approach; treatment of infected individuals, active case-finding by global and regular screening of the population, health education and vector control measures, usually by trapping at the sites of man–fly contact. These efforts almost invariably overwhelm the capacities of individual NGOs, especially on a country-wide scale. Apart from increased efforts of each party, which means a strong and lasting commitment of the respective donors, a better harmonisation and co-ordination in the field is required, as already initiated by the NTCP. However, all efforts will be in vain if Angola does not succeed in ending the war. Priorities for the well-being of people are not set by medical teams but by the political powers.

The epidemic of T.b. rhodesiense in Uganda

From 1901 onwards, massive epidemics of sleeping sickness erupted around the shores of Lake Victoria, in southern Uganda and subsequently western Kenya which continued for the next 15 years leading to an estimated 250 000 deaths. Thereafter, HAT persisted in a number of discrete foci. Partly because of the 'G. palpalis group' vector and the chronicity of late stage infections, this was considered to be T.b. gambiense although it has recently been suggested that the early epidemics were due to T.b. rhodesiense. Epidemics of a more acute, severe, disease were first observed in the 1940s in the southern forested areas of Busoga on the shores of Lake Victoria, in a persistent focus in the Llambwe Valley and in Tanzania.

The recent epidemic occurred at a time when war, insecurity, civil unrest and deteriorating economic circumstances led to a breakdown of health services and disease control. Agricultural practices also changed; cash crop cultivation, especially cotton, declined and large tracts of previously intensively cultivated land fell into disuse. In these areas, agricultural land was replaced by extensive thickets of Lantana camara, close to human habitation, which provided excellent habitats for G. fuscipes fuscipes. Transmission became peridomestic, resulting in a dramatic epidemic which affected all age groups and both sexes and often clustering in individual homesteads. Despite the absence of diagnostic facilities for much of the time, between 1976 and 1990 more than 40 000 parasitologically confirmed cases were identified in Busoga.
District and a further 6000 notifications from neighbouring districts. The monthly incidence of new cases peaked at 1000 new cases in 1987. A brief period of external assistance was provided in the late 1970s by GTZ and between 1985 and 1993 ODA (now DfID) provided technical assistance, equipment and training.

Before the introduction of control activities, the virtual absence of effective health care facilities led to a situation where there were large numbers of severe, late-stage, comatose patients, presumably contributing to the reservoir of infection, and a very high mortality, much of which occurred within 3 months of infection. The control interventions established in 1985 consisted of equipping rural health centres for diagnosis and management, establishing a surveillance system utilising staff previously used for vector control and providing training for health service staff teams in diagnosis and management. The surveillance system comprised blood film diagnosis of acute febrile cases and referral of blood film negative suspects to static units. This led to an increase in reporting and a rapid decline in late stage and comatose hospital admissions. Surveillance also increased the accuracy in defining epidemic areas. The epicentre of the epidemic was in central wooded areas between lakes Victoria and Kyoga, in Kigulu and Luuka counties, in densely populated areas. There was marked seasonality with peaks of transmission occurring in the warmer months from late December until the onset of the long rains in March. The epidemic spread to neighbouring counties and then into Tororo District and western Kenya. More than 90% of cases were treated in rural health centres. Training programmes were carried out for health centre staff teams (medical assistants, nurses and laboratory technicians) and 10 centres equipped for diagnosis and treatment using standard protocols. With active surveillance and standardised treatment, the proportion of patients presenting in late stage HAT declined from over 80% to about 25%. The outcome of treatment was studied in 400 individuals, 30% of whom were late-stage. The overall mortality was 6.3%. 75% of the deaths occurred soon after admission or during treatment. The causes of death included irreversible coma, cardiac failure and overwhelming secondary infections. 15–20% of deaths were attributed to reactive encephalopathy. The mortality in early infections was 2.5% rising progressively to 25% in severe, comatose, late-stage patients. The early detection of infection reduced the mortality and the potential for permanent neurological, behavioural or cognitive disorders. The epidemic placed enormous burdens on the limited resources available to health centres which sometimes had more than 100 patients being treated at any one time. In some villages more than 25% of the population contracted trypanosomiasis over a 5 year period. Active surveillance had the added benefit of identifying cases early in the course of infection, leading to simpler treatment and lower mortality.
The epidemic was characterised by a wide diversity of disease patterns, ranging from severe febrile illness, often with an initial chancre, progressing rapidly to meningo-encephalitis, to a chronic infection continuing for many months with slower development of meningo-encephalitis. This led to an examination of isoenzyme characteristics of parasite isolates. 49 isolates were obtained during the epidemic period from which 12 zymodemes were identified belonging to both Zambezi and Busoga zymodeme groups. The busoga group isolates were from a predominant single zymodeme B17 which was associated with an acute, severe disease, usually presenting early in the infection and often accompanied by a chancre but progressing within weeks to meningo-encephalitis. This zymodeme was consistently observed in epidemics in the central, densely populated areas, distant from the lake shores, remote from the established endemic areas. Other zymodemes mostly of the Zambezi group occurred more frequently in lake shore and riverine situations. These were associated with a more chronic infection, indistinguishable at times from *T.b. gambiense*. The prolonged course extending beyond a year in some instances and the clinical features, including fever, weight loss and lymphadenopathy, led to frequent confusion with HIV/AIDS.

Vector control measures were introduced after the main epidemic had occurred. Aerial spraying with endosulphan and impregnated pyramidal traps were subsequently introduced in selected subcounties. Lancien achieved a 95% reduction in fly populations within 3–4 months using 10 traps per km² at an estimated cost of US$ 0.9 per person per year. Postepidemic surveillance has been at a reduced level, but suggests that whilst cases are continuing to occur, endemicity remains low with less than 20 notifications per month in south eastern Uganda.

**Future strategies for control**

Despite the improved understanding of the epidemiology of HAT and advances in diagnosis, treatment and control as well as in molecular biology, HAT has returned in epidemic proportions to many countries in the region, creating a public health crisis. This resurgence has not been accompanied by sustained or effective control interventions. Some of the important reasons for this include the civil disturbance and insecurity in many affected areas, the severe budgetary constraints of health ministries and the difficulty of initiating and sustaining control strategies against a background of health service decentralisation. The first prerequisites are, therefore, a stronger and more sustained commitment from donors and national health authorities, and improved definition of
endemicity. The success of HAT control in the first half of this century has resulted in sleeping sickness being given a low priority by health planners. Its comeback should lead, hopefully, to better funding which, in terms of cost effectiveness in dollars per DALY saved, would probably be competitive with many other health interventions. Decision-making officials need to be made aware of the changing epidemiological picture of HAT and of the potential savings generated by effective HAT control on the cost of trypanocidal drugs, which are less toxic and much cheaper when patients are identified in the early stage.

In most areas of *T. b. rhodesiense*, passive surveillance gives adequate information on the endemicity provided diagnostic facilities are adequate. The sporadic nature of infection does not require active public health programmes, except in epidemic prone areas, especially where transmission is from ‘palpalis’ group flies, and domestic animals provide an important reservoir. Under epidemic circumstances, active surveillance becomes increasingly more cost effective.

What would be the best way of spending the limited resources available in areas of *T. b. gambiense* HAT? Active case-finding remains the cornerstone of HAT control. Integration within primary health care structures modestly improves passive case-finding, but is insufficient to break the epidemiological chain of transmission, since individuals infected with *T. b. gambiense* can be parasitaemic and infectious for months, maybe years, before symptoms lead them to the health centre. The traditional method of active case-finding, lymph node palpation and aspiration, worked reasonably well in the colonial era when coercive compliance was close to 100% but is clearly insufficient when only half of the population attend case-finding sessions. Examination of blood, through wet smears or thick smears, increases the sensitivity of case-finding but is time-consuming and needs to be limited to subgroups, for instance febrile individuals or those with palpable lymph nodes whose aspirate is negative. The CATT has been grossly underused by control programmes. This relatively cheap, field-adapted assay, is very sensitive and allows microscopists to concentrate their efforts on the seropositive population.

However, trypanosomes are often found in less than half of CATT-positive individuals. While some of these are false positives, a variable proportion are genuinely infected but the low sensitivity of most parasite detection assays used in field activities means that they are not parasitologically confirmed. Control programmes have been reluctant to treat these serological suspects since the standard 7-injection course of pentamidine will lead to the death of 1% of its recipients, a risk unacceptable for asymptomatic individuals who may or may not be infected. However, it seems possible that treatment of such individuals with a single injection of pentamidine may cure most with very low
toxicity. Thus a strategy of ‘targeted early chemotherapy’ could provide a more effective control tool. TDR is considering a trial which would evaluate efficacy and acceptability. In any event, control programmes should systematically use the CATT in high-incidence communities, for example, those with an annual incidence of 1% or more.

The variable epidemiology, the need for intersectoral collaboration and the limited health resources available in most endemic areas, complicate attempts to develop effective and sustainable disease control. National statistics grossly underestimate the true incidence and whilst NGOs have, in recent years, increased their programme support, especially in emergency situations, other forms of external support have declined. At the national level, a targeted strategy is required which identifies appropriate and sustainable action based on data regarding distribution of HAT and the health resources available. Where resources are very limited, suitable health facilities need to provide passive case-finding, staging of disease and standardised treatment of confirmed infections: target 1 requires laboratory facilities, trained staff and availability of drugs; target 2 extends activities with the introduction of strategies to increase treatment seeking behaviour of symptomatic individuals and requires additional health education, publicity and CATT testing; target 3 further extends activities aimed at identifying asymptomatic infections in the community and includes population surveys and CATT testing of communities and the identification of high risk groups; and target 4 provides all the previous activities and incorporates vector control strategies, including the strategic deployment of impregnated tsetse traps at major transmission sites.

External funding will be essential for control programmes in most high-incidence countries. It is likely that assistance will be provided mostly through NGOs rather than through bilateral agreements. Mission organisations, although previously not involved in HAT, could play a more important role in future strategies. National authorities, assisted by WHO, will need to co-ordinate the efforts of these NGOs, ensure that their efforts are technically sound and that national standards, for example for treatment, are respected. They will also need to collect and disseminate reliable surveillance data, essential to motivate donors, the NGO community, mobile teams staff and primary health care institutions.

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