3. LITERATURE REVIEW

3.1 The economic impact of African animal trypanosomosis and its control

African animal trypanosomosis (AAT) is a very important disease of domestic livestock in sub-Saharan Africa. According to the Food and Agriculture Organization of the United Nations (FAO), it is probably the only disease which has profoundly affected the settlement and economic development of a major part of a continent. Animal trypanosomosis affects the health and productivity of livestock. It occurs in 37 sub-Saharan countries covering about 9 million km^2, an area which corresponds approximately to one-third of the Africa's total land area (Mattioli *et al*., 2004). An estimated 45 to 60 million cattle and tens of millions of small ruminants are at risk from trypanosomosis (Chadenga, 1994; Gilbert *et al.,* 2001). FAO estimates that about three million cattle die each year due to AAT (FAO, 2000). Other valuable livestock, such as camels, also suffer from trypanosomosis (ICIPE, 2006).

Direct costs due to AAT involve decreased livestock productivity (mortality, fertility, milk yield, ability to work as traction animals) to which can be added expenditure on controlling the disease (Shaw, 2004). Thirty five millions doses of trypanocides are administered each year to protect livestock in tsetse infected areas (Sones, 2001). Direct losses due to trypanosomiasis are estimated to amount to between US$ 1-1.2 billion each year whereas the indirect impact of AAT on agriculture in sub-Saharan Africa exceeds this amount. A pondered evaluation extrapolated for the total tsetse-infested lands values the total losses, in terms of agricultural Gross Domestic Product, at US$ 4.75 billion per year (FAO, 2004).

The overall impact extends to the restricted access to fertile and cultivable areas, imbalances in land use and exploitation of natural resources and compromised growth and diversification of crop-livestock production systems (Mattioli *et al*., 2004). The presence of tsetse flies and animal trypanosomosis in much of Africa south of the Sahara also had a major influence on the agricultural systems. Large areas of tropical Africa are unsuitable for livestock production due to presence of tsetse flies (Murray and Gray, 1984). In some Central African countries like the Republic of Gabon, the Republic of Congo, the Democratic Republic of Congo and southern Cameroon there are still extensive areas of relatively undeveloped land. Only trypanotolerant breeds of domestic livestock can be kept here without chemoprophylaxis.

3.2 The epidemiology of African animal trypanosomosis

The epidemiology of vector-borne diseases is complex due to variability in the ecology of the different actors involved, i.e. parasites, vectors and hosts. Tsetse-borne trypanosomosis is a widespread protozoal disease-complex affecting wildlife, livestock and people in sub-Saharan Africa, with a range of pathologies, from chronic and long lasting to acute and rapidly fatal, depending on circumstances (Bourn *et al.,* 2001). The epidemiology of AAT in tsetse infected areas of Africa is determined by four biological factors, namely: trypanosomes, tsetse flies, reservoir hosts and livestock. However, cattle are the domestic species in which the disease is most frequently diagnosed and treated. When dealing with the tsetse-transmitted trypanosomosis, much depends on the distribution and the vectorial capacity of *Glossina* species responsible for transmission. Of the three groups of *Glossina*, the savannah and riverine are the most important since they inhabit areas suitable for grazing and watering. Biting flies may act as mechanical vectors, but their significance in Africa is still undefined. However, in Central and South America, *T. vivax* is thought to be transmitted readily by such flies (Urquhart *et al.,* 1987).

3.2.1 Pathogen

African Animal Trypanosomosis is a parasitic infection caused by an extracellular flagellate. Trypanosomes are unicellular protozoan parasites of the phylum Sarcomastigophora, order Kinetoplastida, family Trypanosomatidae, and genus *Trypanosoma* (Hoare, 1972). The *Trypanosoma brucei* complex comprises three morphological identical subspecies: *T. brucei brucei*, *T. b. rhodesiense*, and *T. b gambiense*. Only *T. b. brucei* is pathogenic to cattle, the other subspecies cause acute sleeping sickness in East Africa and chronic sleeping sickness in West Africa. Recent studies have resulted in a subdivision of the *T. congolense* species in several types which can be distinguished by isoenzymatic differences and molecular techniques. These are designated as *T. congolense* savannah type, *T. congolense* Tsavo type, *T. congolense* forest type, *T. congolense* Kilifi type (Majiwa *et al.,* 1985; 1993). *T. congolense*, *T. vivax* and, to a lesser extent *T. b. brucei*, are the major pathogenic species of African cattle (Morrison *et al*., 1981). *T. congolense* is considered the most important cause of AAT in East Africa, and *T. vivax* in West Africa (Stephen, 1986). However, mixed infections that involve two or three species are frequent in areas of medium to high tsetse challenge (Taylor and Authie, 2004). Trypanosomes are able to infect a wide variety of domestic animals and more than 30 species in the wild (OIE, 2005). *T. vivax* and *T. b. brucei* have spread beyond the tsetse fly belt by transmission through mechanical vectors.

In cattle, the pathogenesis is dominated by three features: anaemia, tissue lesions and immunosuppression. The cause of anaemia is complex and involves a variety of mechanisms. Although haemolysins are released by trypanosomes, intravascular haemolysis is not a prominent feature, and anaemia is rather attributed to erythrophagocytosis by cells of the mononuclear phagocytic system in the spleen, bone marrow, lungs and lymph nodes; these cells are stimulated by the formation of complexes between immunoglobulin specific for trypanosomes and antigen or complement attached to red cells. Pathology in tissues is associated with the ability of the parasites to invade extravascular spaces and organs. Whereas *T. congolense* remains confined to the vascular system, *T. b. brucei* is distributed in both the circulation and in the tissues; *T. vivax* although primarily a vascular parasite, has also been found in extravascular locations (Taylor and Authie, 2004).

3.2.2 Vector

Tsetse flies (*Glossina* spp.) are found only in Africa. They are the biological and/or mechanical vector of trypanosomes and constitute a potent and constant threat to humans and livestock over much of sub-Saharan Africa (Gooding and Krafsur, 2004). Thirty-one species and subspecies of these tsetse flies have been identified. Only a few species are vectors of human sleeping sickness but all are potential vectors of animal trypanosomosis. The historical classification of tsetse, based on morphological criteria, divides the species into three groups (Newstead *et al*., 1924). The fusca group flies (subgenus *Austenina*) tend to occur in the lowland rainforests of West and Central Africa. The palpalis group (subgenus *Nemorhina*) is found in the riverine galleries of West and Central Africa but can extend into savannah regions between river systems; *G. palpalis* and *G. tachinoides* are important AAT vectors in this group. The morsitans group (subgenus *Glossina)* occurs in a variety of savannah habitats lying between the forest edges and desert and includes several important vectors of AAT including *Glossina morsitans* spp., *G. pallidipes* and *G. austeni.*

Tsetse feed exclusively on blood; they are holometaboulos insects with females giving birth to full-grown larvae which rapidly pupate in the soil. Their longevity, mobility and frequent feeding make these flies highly efficient vectors, but the low rate of population growth means even small increases in mortality rate can result in population decline and even extinction (Hargrove, 2003a). Tsetse flies can fly at speeds of up to 25 km per hour, but they usually fly more slowly and only for short periods of time, e.g. up to 50 minutes and usually rest more than 23 hours per day in trees to avoid desiccation. The tsetse fly is very sensitive to environmental conditions - it will not survive in areas that are too hot, too dry, or too high.

When the tsetse flies suck blood, development of trypanosomes in them depends on the species of *Trypanosoma*. *T. vivax* only colonizes the proboscis, *T. congolense* and *T. simiae* the midgut and the proboscis, whereas *T. b. gambiense*, *T. b. rhodesiense* and *T. b. brucei* develop in different regions of the intestine. The metacyclic infectious forms are found in the salivary glands of the tsetse fly.

3.2.3 Host

Wildlife, i.e. warthog, bush pig, duiker, bush buck, kudu, buffalo and monitor lizard are the natural hosts of tsetse and may acquire prolonged, symptomless trypanosome infections. Livestock exhibit a range of susceptibilities to infection, from refractory to highly vulnerable (Bourn *et al.,* 2001). However, the wildlife in Africa generally tolerates infection and often serves as a reservoir for human and livestock-infective trypanosomes (Taylor and Authie, 2004). Monkeys, rats, mice, guinea pigs and rabbits can also be infected by trypanosomes; ruminants, wild equidae, lions, leopards and wild pigs can serve as carriers (OIE, 2005).

Susceptibility of cattle to trypanosomosis depends on breed, age, behaviour, previous exposure and health status (Murray *et al.,* 1984). The indigenous zebus are trypanosusceptible and West African *Bos taurus* breeds are trypanotolerant, i.e. they can survive and be productive without treatment under trypanosomosis risk. Exotic imported ruminants (e.g. improved dairy cattle) are more severely affected than local genotypes (Taylor and Authie, 2004).

The diurnal tsetse flies are induced by breath and urine components of the host to fly upwind, near the host they orientate visually, responding more strongly to moving than stationary hosts. Colours are discriminated, blue being particularly attractive and the different species prefer different regions of the body of the host for bloodsucking. Recent studies have shown that brown and fawn coloured cattle were more likely to be infected than cattle of other colours (Carty, 2002).

3.2.4 Environment

A broad view of the whole environment (place, time, interface between host and vector) is necessary to understand the variety of situations that can be encountered in an epidemiological system (De la Rocque *et al.,* 2001). With continued demographic pressure and ever widening human impacts on the environment, the further retreat of some tsetse species and reduction in the wildlife reservoir can be anticipated. Human population growth, agricultural expansion and economic development have brought profound changes in

vegetation and land use in sub-Saharan Africa (Bourn *et al.*, 2001). The habitat of tsetse is changing due to these human activities.

Analysis using Geographical Information System (GIS) technology has deepened the understanding of the spatial and temporal epidemiology of trypanosomosis (Rogers and Randolph, 1993). GIS is the powerful technology that has been used mainly in map-making and an enormous amount of knowledge can be gained simply by geographical data projection (De la Rocque *et al.,* 2001). This approach has been used to predict probabilities of tsetse distributions. The relationship can then be applied to areas which have not been sampled, or where data are out-of-date; to provide a predicted probability of presence for areas outside the original training data set and to generate information which can be used for planning and *post hoc* evaluation of control.

3.3 Drug treatment

Over most of sub-Saharan Africa, bovine trypanosomosis continues to be controlled primarily by trypanocides (Holmes *et al*., 2004). Trypanocidal drugs remain widely available and also affordable for farmers (at approximately US$1 per treatment). They are often the first drugs tried by farmers when their cattle develop (any) symptoms of the disease (Geerts *et al.,* 2001). Consequently treatment given by livestock owners is not without serious drawbacks because most farmers do not have adequate knowledge on diagnosis and the appropriate drug to use even in areas of high prevalence of trypanosomosis; and because trypanocides are frequently used in the absence of diagnosis or used to treat conditions for which they are not effective (Holmes *et al.,* 2004). However, used properly, veterinary drugs permit higher levels of production, improve animal welfare and safeguard the livelihood assets on which 700 millions poor farmers in developing countries rely. Used improperly, veterinary drugs waste scarce resources, occasion avoidable sickness and death, mask poor production and promote drug resistance leading to exacerbated disease in animals and humans (Grace, 2005).

Trypanocidal drugs are the most widely applied method that farmers use to treat and prevent trypanosomosis in sub-Saharan Africa. It has been estimated that about 35 million doses of trypanocides are administered each year to an approximately 45 - 60 million cattle at-risk of trypanosomosis (Kristjanson *et al.*, 1999; Sones, 2001). Trypanocides are popular because farmers can directly treat and, if successful, cure their own animals without relying on the efforts of others. Despite livestock keepers' dependence on trypanocides only three compounds namely isometamidium chloride, homidium (bromide and chloride) and

diminazene aceturate, are currently available for treating cattle. All these drugs have been on the market for over 40 years and several generic forms of them from a wide range of companies have become available on the African market (Holmes *et al.*, 2004). Isometamidium is principally used as a prophylactic drug and can provide up to 6 months protection against trypanosomosis. Whilst homidium has limited prophylactic properties, it is primarily used as a therapeutic agent. Although it has been shown that diminazene provides also a short term protection of 2 to 3 weeks, it is mainly used for therapeutic purposes.

Although there is a continuous demand for trypanocides by livestock keepers, the African market of trypanocides estimated at about US$ 30 millions (Borne, 1996), is not considered sufficient to justify investment by large pharmaceutical companies in the development and licensing of new animal trypanocides; the cost of which is estimated from 200 to 800 millions dollars (Di Masi *et al*., 2003). Manufacturers of drugs do not consider treatment of trypanosomosis to offer profitable potential (Veeken and Pecoul, 2000) and thus investment in drugs against these diseases is low. Therefore, the control of trypanosomosis in livestock will continue to depend on the use of currently available compounds, because it is unlikely that new trypanocides will be developed and be released in the near future. The challenge, therefore, remains to make optimal use of the three relatively old compounds until new methods of treatments emerge (Holmes *et al*., 2004). Thus, trypanocidal drug treatment will probably remain the mainstay of control of African bovine trypanosomosis for the foreseeable future, and the development of resistance to the small number of available compounds would generally be a cause of considerable concern (Geerts and Holmes, 1998).

3.4 Drug resistance

Drug resistance is the heritable loss of sensitivity of a micro-organism to a drug to which it was before sensitive. Information on the extent and significance of the problem of drug resistance is still scant (Sinyangwe *et al.,* 2004). The exposure of trypanosomes to sub-therapeutic concentrations of trypanocidal drugs, the treatment frequency and the degree of drug exposure of the parasite population are important factors influencing the development of drug resistance (Geerts and Holmes 1998). Furthermore, some trypanocidal drugs such as ethidium are well-known mutagenic compounds and might induce mutations, the most resistant of which might be selected under drug pressure (Holmes *et al.,* 2004). The phenomenon of cross-resistance has now been clearly demonstrated. Quinapyramine usage has been shown to induce resistance to isometamidium, homidium and diminazene

(Ndoutamia *et al*., 1993). Research on drug resistance in *Plasmodium* has shown also that the genetic structure of a parasite population (clonal or panmictic) is an important parameter influenced by the transmission intensity, and this in turn might influence the rate of development of drug resistance (Holmes *et al.,* 2004).

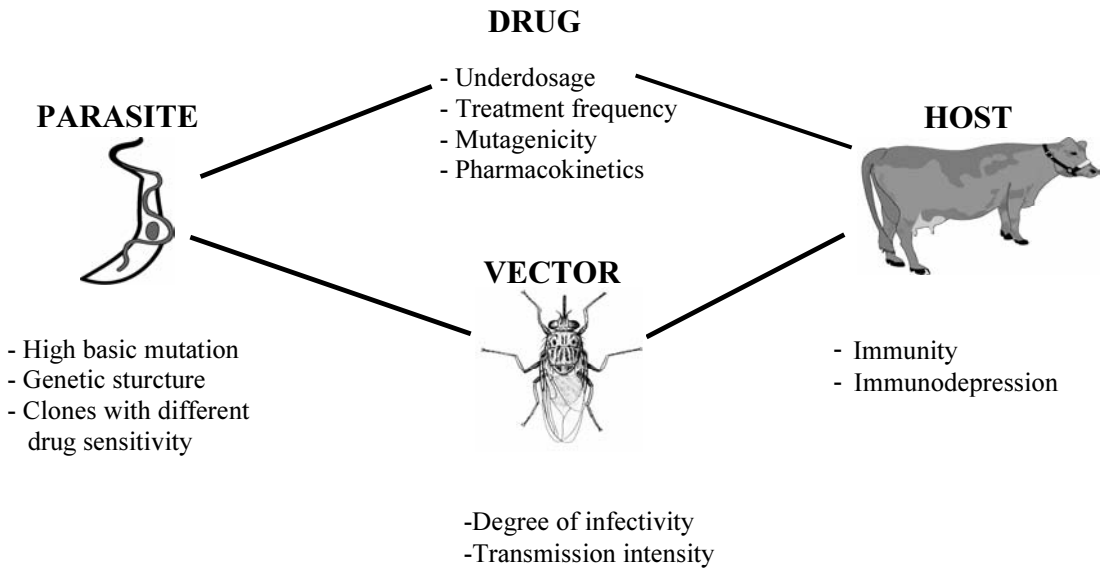

Figure 3.1 Factors influencing the development of drug resistance (Geerts and Holmes, 1998)

Currently resistance to trypanocides has been reported from 15 countries in Africa (Geerts and Holmes, 1998; Diall *et al*., 2003; Mamoudou *et al.,* submitted). Resistance to diminazene and isometamidium has been reported by several authors (Authié, 1984; Chitambo and Arakawa, 1991; Peregrine *et al.*, 1991; Clausen *et al.*, 1992; Codjia *et al.*, 1993; Mulugeta *et al.*, 1997; McDermott *et al.*, 2003; Sinyangwe *et al.*, 2004). Homidium which was previously used extensively as a prophylactic drug was also rendered almost useless by the widespread development of resistant trypanosome strains (Clausen *et al.*, 1992). In addition, the occurrence of multiple drug resistance to diminazene, isometamidium and homidium has been reported in trypanosome populations in five countries, namely Nigeria (Ilemobade, 1979), Kenya (Gitatha, 1979) quoted by Mulugeta *et al.,* 1997, Burkina Faso (Clausen *et al.,* 1992), Sudan (Mohamed-Ahmed *et al.*, 1992) and Ethiopia (Mulugeta *et al*., 1997). Recent reports show increasing resistance to trypanocides in Burkina Faso and Mali (Grace 2005;

McDermott *et al.*, 2003). Other African countries with reported cases of drug resistance include Chad, Uganda, Zimbabwe, Tanzania, Côte d'ivoire, Somalia, Zambia, Central African Republic (Finelle and Yvore, 1962), Mozambique (Jamal *et al.*, 2005) and recently Cameroun (Mamoudou *et al.,* submitted).

3.4.1 Impact of drug resistance

Although resistance has been reported for many years, only recently methodologies have become available for estimating its regional prevalence. Studies applying these methodologies typically report wide variations in levels of resistance or in risk factors from village to village in a given geographical area (Sinyangwe *et al.,* 2004; Tewelde *et al.,* 2004). However, little is known so far on the productivity and the economics of trypanocide use among livestock keepers in Africa. To date, few studies have been carried out on the impact of drug resistance. A study to assess the impact of drug- resistant trypanosomes on the productivity of the local cattle was carried out in the Ghibe valley, Ethiopia, where a high prevalence of multiple drug resistance was reported (Codjia *et al.,* 1993). The study showed that profitable cattle production was possible in a problem area with high prevalence of drug-resistant *T. congolense* and cattle production was able to generate attractive economic returns for owners (Itty *et al.,* 1995). Another study carried out in West Africa (Affognon *et al.,* in press) suggests that in spite of drug resistance, livestock keepers in Burkina Faso and Mali under-use trypanocides and they could increase the profitability of cattle production if they increase the amount of trypanocide use. Experiments have shown that high levels of treatment in mice infected with resistant trypanosomes can prolong lifespan even if there is no complete cure (Mdache *et al.,* 1995) and this may also be true for cattle. While several authors have observed a loss of virulence and loss of fitness in drug resistant trypanosomes (Berger *et al.,* 1995; Mutugi *et al.,* 1995) more recent studies have contradicted this (Rowlands *et al.,* 2001). Further research is necessary to study the pathogenicity of drug sensitive and drug resistant strains of trypanosomes.

3.4.2 Detection of drug resistance

Four types of techniques are commonly used to identify drug resistance: tests in ruminants, tests in mice, in *vitro assays* and field tests (Kaminsky and Brun, 1993; Peregrine; 1994 Holmes *et al.,* 2004). Standardized protocols for the tests in animals have been developed, which should allow better comparisons of data on a temporal and spatial basis (Eisler *et al.,* 2001).

The *test in ruminants* provides direct information using recommended doses of trypanocides. The tests consists of infecting a group of cattle or small ruminants with the isolate under investigation and later, when they are parasitaemic, treating them with various dosages of trypanocides (Holmes *et al.*, 2004). All trypanosome isolates grow well in ruminants and data obtained from the tests are directly applicable to the field. But the test is time consuming, impractical and very expensive if only one isolate of trypanosome per animal is tested. However, the *test in mice* can be used as a single-dose test or a multi-dose test (Eisler *et al.,* 2001). The objective of the multi-dose test is to obtain more detailed information by determining the CD50 or CD80 values (curative dose that gives complete cure in 50% or 80% of the animals) for a given trypanocidal drug (Holmes *et al.,* 2004). In the single-dose test, a large number of trypanosome isolates is tested at a single discriminatory dosage-1mg/kg for isometamidium and 20 mg/kg for diminazene (Eisler *et al.,* 2001). The advantages of the mouse assay are that it is cheaper than the test in cattle and that it is feasible in less well equipped laboratories. There are several disadvantages, however. Mouse sensitivity tests cannot be employed to investigate the sensitivity of strains of *T. vivax* (Sones *et al.,* 1988) and not all cattle isolates of *T.congolense* are rodent infective (Geerts and Holmes, 1998). It can not be reliably used to predict curative doses for cattle because of the differences in the pharmacokinetics and metabolism of trypanocidal drugs in the two animal species.

For the *in vitro* evaluation of drug sensitivity, procyclic, metacyclic or bloodstream forms of trypanosomes can be used. The advantage of *in vitro* assays is that large numbers of isolates can be examined. However the use of metacyclic and bloodstream forms is considered more reliable than the use of procyclic forms (Holmes *et al.,* 2004). An interesting alternative is the drug incubation *Glossina* infectivity test (DIGIT), in which the trypanosomes are exposed to the drug *in vitro* for a short time and thereafter fed to tsetse flies to check whether or not they develop into metacyclic forms (Clausen *et al.*, 1999). This technique distinguishes resistant from sensitive isolates and does not require experimental animals, but it does require a ready supply of teneral tsetse flies from an artificially reared colony (Holmes *et al.,* 2004).

Several authors reported the application of *field tests* to assess trypanocidal drug resistance (Eisler *et al.,* 2000; McDermott *et al.,* 2003 and Tewelde *et al.,* 2004). Analysis of data on frequency of infections after block prophylactic or curative drug treatment allows to identify suspected cases of drug resistance. However, standard parasitological methods used in the

field, such as the phase-contrast buffy coat technique (BCT) (Murray *et al.,* 1977), suffer from relatively poor sensitivity (Paris *et al.,* 1982) and poor ability to identify mixed infections and distinguishing between trypanosome species.

3.4.3 Trypanocidal drug-ELISA

The use of trypanocidal drug-ELISA in combination with parasite detection tests has given promising results for the detection of resistant trypanosomes (Geerts and Holmes, 1998). A competitive ELISA allowing the detection of small amounts of isometamidium in serum of cattle (Eisler *et al.,* 1996) has been validated in cattle under experimental and field conditions. When trypanosomes are found in the presence of a concentration of 0.4 ng/ml isometamidium in the blood resistance is strongly suspected. Further, an ELISA has also been developed for the detection of homidium bromide (Murilla *et al.,* 1999) and diminazene (Karanja *et al.,* 2002). However, these ELISA tests give an indication on the resistance situation at the level of the herd, not on the sensitivity of a trypanosome population at the level of the individual animal (Geerts and Holmes, 1998).

3.4.4 Molecular tests for the detection of drug resistance

Molecular biology provides tools for sensitive and specific diagnosis based on DNA sequence recognition and amplification. The polymerase chain reaction (PCR) permits identification of parasites at levels far below the detection limit of the commonly used parasitological techniques (Geysen *et al.,* 2003). PCR has been shown to be a sensitive method for the diagnosis of trypanosome infections in experimentally and naturally infected cattle (Kukla *et al.,* 1987; Moser *et al.,* 1989; Desquesnes and Tresse, 1996; de Almeida *et al.,* 1997). PCR has also been used to monitor the efficacy of diminazene aceturate treatment in cattle experimentally infected with *Trypanosoma brucei* (Clausen *et al.,* 1999). Under natural challenge, PCR and DNA probe hybridization were used to confirm the effectiveness of isometamidium chloride prophylaxis in cattle infected with *T. brucei* and *T. vivax* populations (Clausen *et al.,* 1998). The potential of PCR as a method to detect drug failures in cattle was also reported by Gall *et al.* (2004).

Amplified Fragment length Polymorphism (AFLP) was used recently by (Delespaux *et al.* (2005) to compare the genome of 2 isogenic clones of *T.congolense* in order to search for mutations that might be correlated with the resistance of these trypanosomes to isometamidium. The correlation between the single dose mouse test and the PCR-RFLP test

was consistent in 30 of the 35 tested isolates. Preliminary results show also that Single Strand Conformation Polymorphism (SSCP) allows the detection of *T. congolense* resistance to diminazene (Delespaux *et al.,* 2006). A *T. congolense* putative gene (TcoAT1) presenting a high similarity with the adenosine transporter 1 gene (TbAT1) of *T.brucei* and coding a putative P2-like nucleoside transporter was screened by SSCP for point mutations possibly linked to changes in sensitivity to diminazene. Using the commonly accepted criterion for sensitivity to diminazene, being a CD80 of 20 mg/kg in the mouse test, there was a correlation of 84.6% (22 out of 26 isolates). Although PCR, RFLP and SSCP need a well equipped laboratory, they could provide a rapid and convenient tool, suitable for large-scale surveys of drug-resistant trypanosomes in livestock.

3.4.5 Delaying the development of trypanocidal drug resistance

In the past, the most important guidelines to avoid or to delay the development of drug resistance were considered to be the use of the 'sanative' pair of drugs (alternate use of isometamidium or ethidium and diminazene) and the avoidance of subtherapeutic concentrations of trypanocidal drugs (Whiteside, 1960; Holmes *et al.,* 2004). However, in case of multiple drug-resistance, which seems to occur more and more frequently (Clausen *et al.,* 1992; Codjia *et al.,* 1993; Mulugeta *et al.,* 1997; McDermott *et al.,* 2003), the concept of sanative pair is no longer valid. The most efficient way to delay the development of drug resistance remains the reduction of drug selection pressure by decreasing the number of treatments (Geerts and Holmes, 1998). It is therefore strongly recommended that control of trypanosomosis should not rely solely on drugs. An integrated approach should be adopted using vector control, to reduce the tsetse challenge, along with reduced frequency of drug dosing. Where such measures have been adopted, the results have been impressive (Fox *et al.,* 1993; Peregrine *et al.,* 1994). In West and Central Africa, the use of trypanotolerant livestock combined with limited drug use may be appropriate in areas of high tsetse challenge (Diall *et al*., 1992; Holmes *et al.,* 2004). Generally, the exposure of parasites to subtherapeutic drug concentrations and uncontrolled use of trypanocidal drugs and the lack of proper diagnosis are considered as the major causes of increasing development of drug resistance throughout Africa (Clausen *et al.,* 1992; Geerts and Holmes, 1998). Given the fact that in many countries drugs are often administered by unskilled persons, errors may easily occur in calculating the correct doses for the treatment of the animals. Furthermore, there is an increasing number of generic products available on a somewhat loosely regulated market,

and some of these have questionable efficacy and many contain lower doses of drug than the stated amount (Holmes *et al.,* 2004).

A ban on the use of quinapyramine in cattle is also recommended by PAAT (Programme Against African Trypanosomosis) to avoid the problem of cross-resistance with other drugs.

Rational Drug Use (RDU) is the cornerstone of efforts to combat resistance (WHO, 2001). However, RDU has rarely been applied to livestock systems in developing countries. A complication is that most animal health treatments in Africa are given at community level, and RDU strategies need to be applied at both the farmer and service provider level (Grace, 2005).

3.4.6 Containment of drug resistance

At community level, there is reasonable evidence that when irrational drug use is controlled, resistance levels decline (Binyon and Cooke, 2000); several studies show evidence of a critical threshold of use below which resistance declines even without total removal of the antimicrobial (Seppela *et al.,* 1997). But in general, once resistance is established, it is difficult to remove and prevention is considered preferable. While much is known about the management of antibiotic resistance, to date no studies have been carried out on containing trypanocide resistance and there are important unanswered questions on the mechanisms of resistance (single or multiple), genesis of resistance (uni-or multi-focal), spread of resistance to new areas (role of vectors and cattle movement) and persistence of resistance. But it is known that AAT cannot persist in the absence of tsetse and so vector eradication should be an effective means of eliminating resistance. Methods for eradication of localised tsetse populations are highly effective and community-based bait methods, using insecticide-treated cattle and traps, are particularly attractive for being low cost, environmentally-friendly and empowering to local communities; these could be used to eliminate pockets of resistance, although the low sustainability of vector control throws doubt on their appropriateness as a long-term, large-scale trypanosomosis control operation (Brightwell *et al.,* 2001; Randolph *et al.,* 2003). Uncertainty surrounding the effectiveness and permanence of resistance containment can be reduced by complementing epidemiological field studies with mathematical models (Austen and Anderson, 1999). Models have been successfully developed for modelling relationships between antibiotic use and resistance and have proved useful for designing more effective resistance control programs (Bonten *et al.,* 2001).

3.5 Tsetse and trypanosomosis control activities on the Adamaoua plateau in Cameroon

Transmission of animal trypanosomosis on the Adamaoua plateau has been attributed to three tsetse species (*Glossina morsitans submorsitans, G. fuscipes fuscipes* and *G. tachinoides*). The invasion of this area of the country did occur around 1950 (Banser, 1979; Hurault, 1993). At that time, about 40% of the national cattle herd was stocked on the Adamaoua plateau (Banser, 1979). The important impact of this invasion by tsetse flies on the cattle industry is easily discernable. The disastrous effect on the economy of the over-run areas was of course immediate and far reaching. To the cattle grazer-families, there was a sliding and uncontrolled loss of wealth as all production parameters such as fertility, birth rate and weight gain dropped steadily while mortality rates rose in alarming proportions in their herds (Banser, 1979). Following this disastrous situation, there was massive emigration from the infested regions. This exodus created a more collective and communal disaster in the area. In Tignere, the most badly affected district, the cattle population dropped from 300.000 prior to tsetse invasion to 35.000 (Banser, 1979). In the 1970s, there were almost no cattle anymore in the Tignere area (Boutrais and Cuisance, 1995).

In order to control this situation, a twice yearly anti-trypanosomosis campaign (from 1960 to 1975) was instituted by the government in the affected regions of the Adamaoua and in the North and East Cameroon. These campaigns provided preventive treatment at the start of the transhumance and curative treatment upon return or in the case of illness (Hamadama, 2001). These mass treatments alone consumed an average of 600.000 doses of isometamidium chloride (Trypamidium®, Rhone-Mérieux (currently Merial) and 300.000 doses of diminazene aceturate (Berenil®, Hoechst) yearly (Banser, 1979). In 1967, with the objective of controlling the vectors of trypanosomosis, a tsetse control unit was created in the extreme northern part of the country. This unit launched a ground-spraying campaign with DDT (Dichlorodiphenyl triclorethane) (Banser, 1979). Under the auspices of the Lake Chad basin commission the operational capacities of the unit were intensified through a regional project between Cameroon and the Federal Republic of Nigeria (from 1970-1974). To reinforce the vector component of the fight against bovine trypanosomosis, the government created in 1974 a specialized service in the Ministry of Livestock charged with tsetse eradication. This service, which had its headquarter in the priority cattle-production centre of Ngaoundere in the Adamaoua highlands, incorporated the far northern unit to form in 1979 a Special Mission of Tsetse Eradication (MSEG: Mission Spéciale pour l'Eradication des Glossines).

The far northern field station continued ground spray with DDT whereas the Adamaoua field station resorted to aerial spraying with helicopters because of the hilly terrain. However, despite the control efforts, persistent re-infestation of tsetse-cleared pastures on the Adamaoua plateau increased from 100.000 hectares in 1988 to 200.000 hectares in 1989 and 400.000 hectares in 1990 (Cuisance, 1991). Another invasion of tsetse occurred in 1990 spreading over the Adamaoua region from Tignere to Galim and in Mayo Banyo (Boutrais and Cuisance, 1995; Hurault, 1993). During the dry season in 1989-1990 ground spraying of pastures with insecticides (Thiodan and DDT) was carried out (Cuisance, 1991)

Two aerial spraying campaigns on the Adamaoua plateau in 1991-1992 and 1994 resulted in effective control of tsetse flies from the re-invaded zones (Cuisance and Boutrais, 1995). To prevent reinvasion of tsetse flies from the valley, a barrier consisting of targets and traps was put in place after aerial spraying. However, bush fires destroyed most of the targets and traps soon after deployment in 1994. Thereafter, the barrier was replaced by a program of insecticide treatments of cattle. At the end of 1994, a preliminary evaluation of the tsetse control activities in Adamaoua showed that the eradication campaign on the plateau had not been 100% effective and that some pockets of *G. m. submorsitans* and *G. f. fuscipes* had survived (Cuisance and Boutrais, 1995). Since then, no further entomological and parasitological information is available.

3.5.1 Aerial spraying of insecticide

The Adamaoua highlands project benefited from two years of entomological studies prior to spraying operations. Following the results of these studies, 800,000 hectares of pastures were programmed for helicopter spraying, but subsequent findings increased the area to about 1,000,000 hectares (Banser, 1979). The aerial spraying was followed by an entomological survey in order to assess its efficacy. The first helicopter operation campaign took place in the dry season 1976/1977. During 3 campaigns since then an area of about 5.700 km² altogether has been reclaimed. About 500 km² out of this area was sprayed twice due to remaining flies or reinvasions of flies (Scholz, 1979). The great advantage of the application of insecticides by helicopter is that spraying can take place in hilly areas which are not easily accessible and which would be impossible to reach using ground spray operation. At the end of 1979 the size of area treated on the Adamaoua plateau was about 10,000 km² (Scholz, 1979). From 1977 until 1987 more than 21,000 km² was treated with a total cost of

30,290,000$ US financed by the World Bank, FAO, GTZ and the government of Cameroon (Cuisance *et al.*, 1987).

Entomological surveys indicated a re-infestation of about 100,000 hectares in 1988 (Cuisance, 1991). Therefore another aerial spraying campaign was launched in March 1989. The annual report of MSEG for 1991 confirmed the re-infestation of more than 300,000 ha in the Faro and Deo Division. In 1991-1992 and 1994, two aerial spraying campaigns cleared more than 400,000 hectares of the tsetse re-infested areas (Cuisance and Boutrais, 1995) (Figure 3.2). At the end of eighteen years (1976-1994) tsetse control activities with aerial spraying 3,200,000 ha of pastures had been cleared (Fig 3.2) (Ndoki, 1994). Three pyrethroids were used during these campaigns: Deltamethrin ULV® (3.2 g/l), Fendena® (alphacypermethrin : 6 g/l) and Solfac® (cyfluthrin : 7.5 g/l). The only organochlor compound used was Thiodan ULV® (endosulfan: 25g /1).

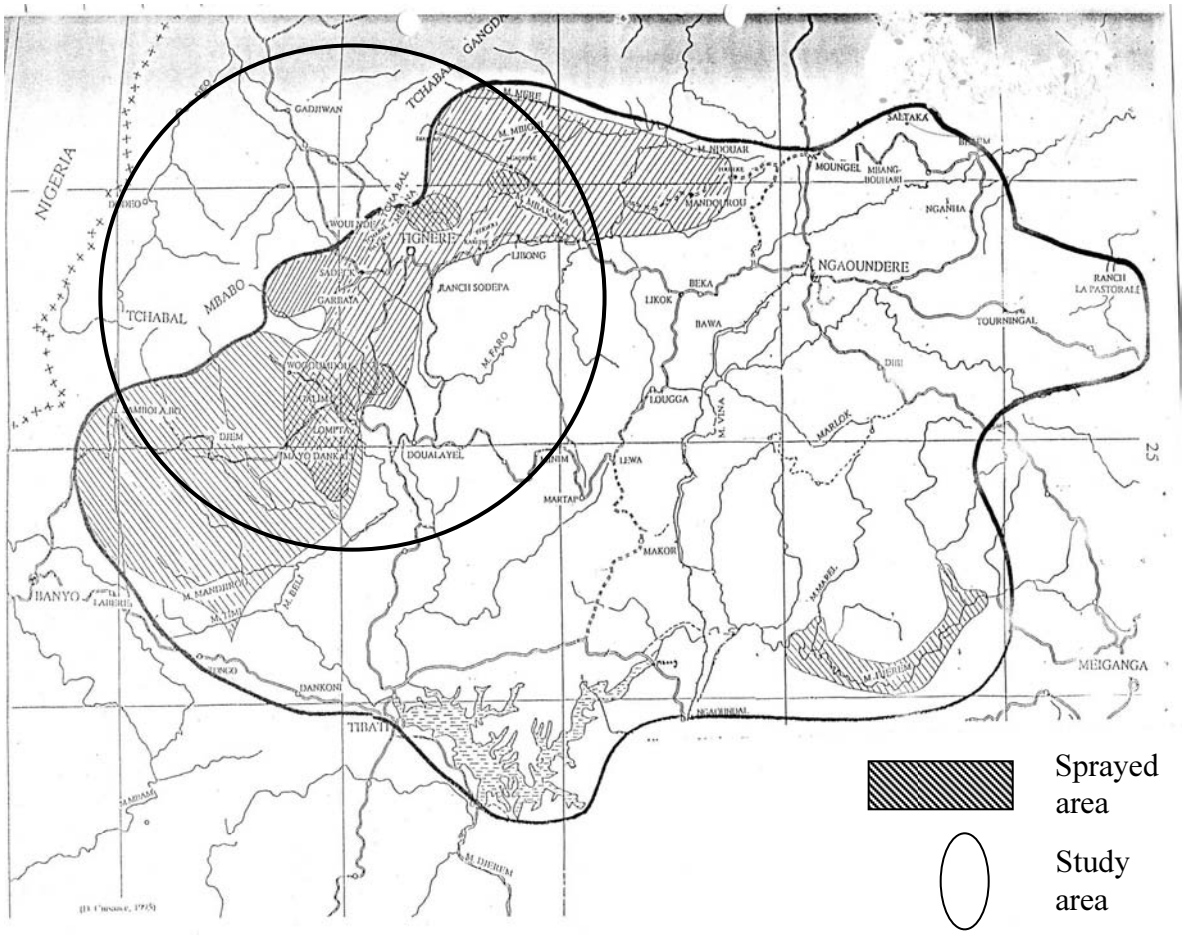

Figure 3.2 Sprayed area with helicopter on Adamaoua plateau, Cameroon, 1976-1994 (source: MSEG)

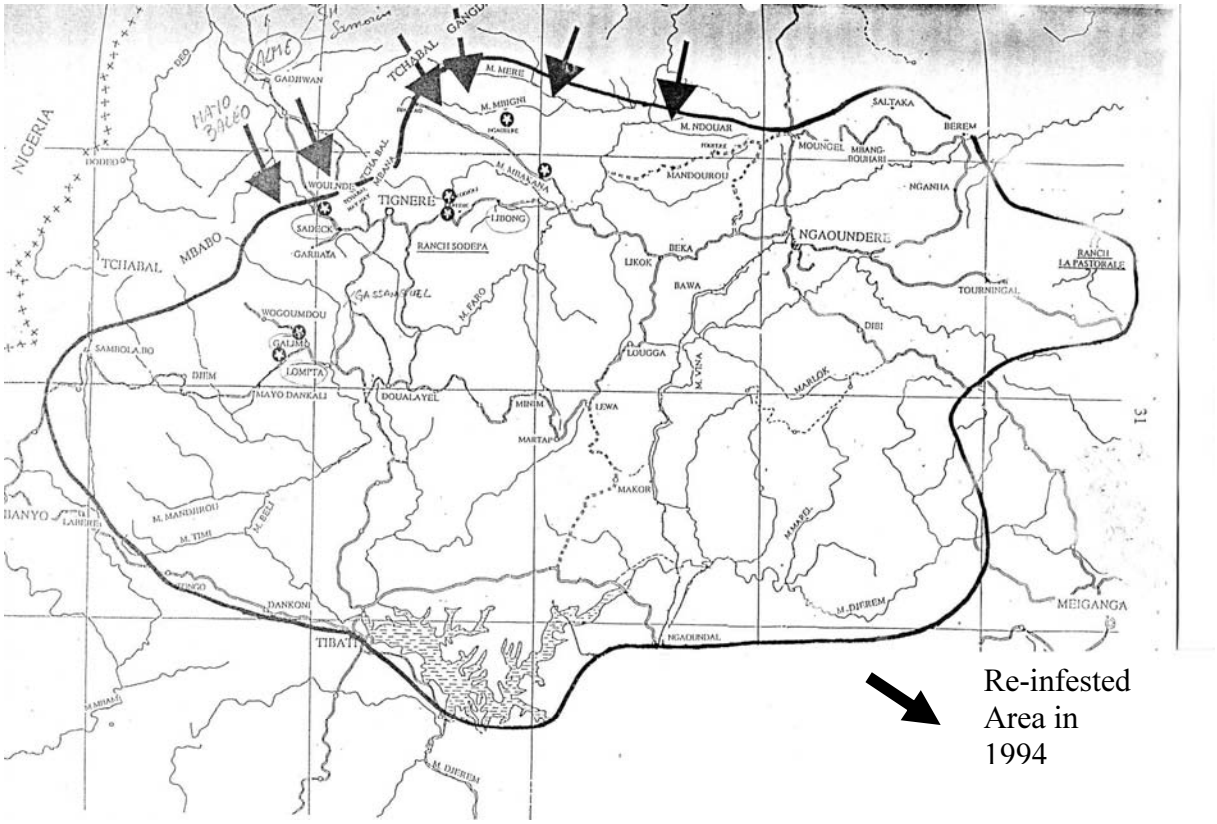

Figure 3.3 Map of aerial spraying showing the re-infested areas of the Adamaoua plateau, Cameroon (source: Cuisance, 1995)

3.5.2 Reinvasion of sprayed areas and tsetse dispersion

The potential reinvasion of sprayed areas by tsetse flies is a serious concern in any control or eradication program. Without preventive measures the perimeter of any area that has been cleared of tsetse is likely to become re-infested by adjacent tsetse populations. Re-invasion pressure is most serious during the rainy season when tsetse distribution increases with favourable conditions (World Bank, 1987). After 14 years of the eradication campaigns tsetse flies were cleared in the major part of the Adamaoua plateau. However, it was difficult to prevent re-invasion after each aerial intervention (Fig 3.3) (Cuisance, 1991).

Causes of reinvasion

1. Accessibility of some areas

Some regions of the Adamaoua plateau are difficult to access due to a network of rivers with ravines (Cuisance, 1991). Another factor, which affects the efficiency of the helicopter, is the hilly terrain in the Adamaoua highlands. Numerous steep hills with deep river beds are difficult to spray even with a helicopter (for safety reasons) and in order to avoid water

pollution insecticides were not sprayed near water courses (Scholz, 1979). Even when insecticide treatments by helicopter are applied, they might not reach the dwelling places of *G.m.submorsitans*.

2. Remanence of the insecticides used

In order to follow up the ecological recommendations and choices imposed by the World Bank, four insecticide products were used separately or in association. However, the insecticides used should have a remanent effect of at least two months due to the length of raining season in the Adamaoua (Cuisance and Boutrais, 1995). This was not always the case. Particularly with Solfac®, the living tsetse flies were found shortly after spraying (Ndoki, 1994), which mean that the adult fly population was probably decapitated, but that there was a limited effect on the cohorts of flies which were present as pupae in the ground and were had still to emerge.

3. The movement of cattle herds between infested and cleared areas

Cattle markets and transhumance are potentially dangerous activities, which are not always compatible with the goal of tsetse eradication (Cuisance, 1991). Since there was a lot of commercial exchange of cattle between the markets of Tchabal Mbabo and Banyo, the cattle herds had to pass trough reinvaded zones which increased the risks of introducing tsetse flies into cleared zones (Boutrais and Cuissance, 1995). Similar risks are associated with the transhumance. At the beginning of the dry season the MINEPIA services usually organize the departure of the herds into transhumance from the cleared into the infested zone (Koutine plain). Cattle are supposed to be treated with isometamidium before departure; the return of the herds takes place at a particular fixed date after the curative treatment of animals and compulsory individual spraying with Butox at the post of Wouldé or Sadeck (by staff of MSEG). In 1990 however, because of the increasing pressure of tsetse during the end of the dry season and at the beginning of the rains, cattle owners would like to return faster and secretly (avoiding spraying with insecticides) from the infested plain to the plateau. This obviously results in the introduction of tsetse into the plateau.

4. Tsetse invasion via roads

The road from Tignere to Kontcha constitutes “a privileged way” for tsetse to penetrate the clean zone. This track is a non-negligible road in the dry season. It crosses the highly infested zone of the Koutine plain. The biggest tsetse threat originates from the forest area where the

flies have never been controlled and which borders the tsetse-infested game reserves of Faro (Boutrais and Cuisance and Boutrais, 1995). Vehicles climb the cliff at a slow speed allowing tsetse to follow them (attraction by mobile objects) and to be carried into the cleared zone. In spite of poor means, MSEG maintained the Sadeck check point on top of the cliff where vehicles are inspected and sprayed (dieldrine) by two agents. Between 5 and 20 tsetse were caught every month on vehicles depending on the season, which is an indication of the potential role this road plays in the reinvasion phenomenon (Cuisance, 1991). David *et al.* (2002) reported that in theory, only one pregnant female tsetse needs to cross any barrier once to re-establish "a population of flies". Sadeck and Garbaya check points are separated by two river networks, one of which was highly infested. Forest galleries being very close, tsetse easily came up at the altitude, mainly where galleries were dense and water was abundant (Cuisance, 1991).

5. Problems with re-invasion barriers

Various methods may be employed to reduce the re-invasion of tsetse flies, but in general the aim of all tsetse control programs should be to finish each phase at a more easily defendable line (buffer zone or barrier) which may be either natural or man-made (World Bank, 1987). A chronic lack of financial means during the last four years of the programme did not allow MSEG to play its role in clearing certain reinvaded zones and in the protection of the clean zone against re-invasion (Cuisance, 1991). Barriers can be made efficient, but can never guarantee 100% success against re-invasion; movement across barriers commonly occurs, frequently associated with animal, human or vehicle movements (David and Randolph, 2002).

Dispersion causes

Progression and regression of *G. m submorsitans* is influenced by many factors:

- Modification of the vegetation: clearing by people occupying an area or thickening of the vegetation when people leave the area.
- Constant movements of cattle herds along certain tracks.
- Increase of warthog population after the epizootic of African swine fever in 1984 (Nuckechap and Gibs, 1985; Balis, 1987) and probably also due to decreased hunting and consumption of these animals (due to increasing islamization) and the increasing area of maize fields.

- Spontaneous movements of these tsetse species. It has been noticed in many countries that at the end of the dry season/ beginning of first rains (April-May) tsetse have an invading behaviour. Davies (1977) reported progress of 10-15km/year in Nigeria.

Concluding on factors responsible for re-invasion Davies (1977) and Brightwell (1992) quoted by (David and Randolph, 2002), stated that the seasonal expansion up and down the river system, and into savannah regions during the wet season, allowed tsetse to re-colonize areas from which they were cleared, either naturally or artificially.

3.5.3 Insecticide treatments of cattle

Tsetse are exceptionally sensitive to insecticides and it is unlikely that resistance to insecticides will emerge because of their low genetic variation (due to low dispersal rate), low reproductive potential and selection for the most energetically-efficient individuals (Krafsur, 2003). Three methods of application of insecticides to livestock were used on the Adamaoua plateau: dips (Thomson *et al.*, 1992), sprays (FAO, 1994) and pour-on's (Bauer *et al.*, 1995).

Dips

This method consists of bathing animals in a deltamethrine solution. In order to be efficient against tsetse, animals must be dipped every 2 to 5 weeks according to the local tsetse pressure and the animal density should be 2 to 10 heads per km^2 (Okello-Onen *et al.*, 1994).
This approach is effective if it is continuously applied on the majority of animals in the same region. However, this method requires a dense network of dipping tanks distributed over the whole area and well maintained (Cuisance, 1991). It was used intensively at the Faro ranch (near Tignere). The animals were dipped once a week during the rainy season and once every two weeks in the dry season. Deltamethrin (Butox®) was used at a concentration of 50 g..a.i. per liter water. Authorities as well as herdsmen recognised the beneficial effect of this acaricidal and insecticidal treatment which resulted in significant allowing reduction of the trypanocide use from 2,08 to 0,35 treatments per year (Cuisance, 1991). When Butox® was replaced by Supona® (chlorfenimphos) in 1986-87, significant losses occurred due to trypanosomosis. Even though Butox is twice more expensive than Supona, the profit remained very important (Cuisance, 1991).
According to the authorities of the Faro Ranch:
-There was a gain in fertility (the number of live calves/100 reproductive female increased from 35 - 50 to 60 - 75%).

-There was a considerable decrease in the use of trypanocidal treatments/year. In the past, 1/3 of the cattle grazed in tsetse infested zones, whereas now half of the cattle are grazing in infested zones.

In the Ranch of Malombo, the use of Butox® since 1985 has brought down the frequency of trypanocides from 3, 97 to 0, 14 treatments per year (Cuisance, 1991).

According to (Vale and Torr, 2004), dipping is one of the most cost-effective means of applying insecticides.

In conclusion, in the Adamaoua as well as in other West African countries as reported by Gao *et al.* (1990) and Wilson *et al.* (1991), dipping is one of the best methods to fight against cattle ticks and tsetse flies under good pasture management conditions. However, in the Adamaoua, almost all dips are located in the East, not far from the vast tsetse eradication front (Cuisance, 1991). The inconvenience is that an enormous investment is necessary in dipping tank construction and therefore it is less practiced by cattle breeders on the Adamaoua plateau. Currently, dipping is rather used to control ticks in the Adamaoua region. The number of dipping tanks has not considerably increased. Up to now there are no dips in the tsetse infested zone. However, some dips were constructed in the buffer zone. Epizootics of trypanosomosis did occur in 2004-2005 in Mandourou (buffer zone) after stopping dipping cattle in one of the ranches (Hamadama, pers. communication).

Sprays

When there is no dip available, application of insecticides can be done by spraying. Tsetse flies have been controlled successfully using insecticide-sprayed cattle in a number of operations (Chizyuka and Liguru, 1986; Thompson and Wilson, 1991; Bauer *et al.,* 1992). In the Adamaoua region the cattle herds were sprayed each year at the return of transhumance before the herd left the infested zone. Breeders from Dibi and Tournigal recognized the positive effect of sprays (Cuisance, 1991). Pulverization of the animals with Butox® was carried out each week in the rainy season (Cuisance, 1991). In 1994, some rich cattle owners sprayed their herds even every three days. In the dry season insecticide was applied once every three weeks. However, overdilution of the product was also reported with a small bottle of Butox being diluted in fifteen liters of water. Foulbe treated 80 heads of cattle with an amount of insecticide which was for 15 animals (Boutrais and Cuisance, 1995). The inconvenience of spraying is that one must use a vaporizer which is very expensive for cattle breeders. When the animals are quite big some expensive infrastructure is even necessary in

order to apply the spray correctly. Inhalation risk of products by man and accidents due to high dose have been common.

Currently, spraying is very commonly used to control tsetse flies in the Adamaoua. The majority of cattle breeders in the buffer zone and the infested zone use this method (Personal observation). It is important to notice that during the transhumance in the dry season many cattle breeders from neighbouring Nigeria and Plateau have a pulverizator and spray their animals. According to Hargrove, (2003 b), achievement of good tsetse control, requires treatment of large numbers of small herds rather than small numbers of large herds. This seems to be the case in the Adamaoua region.

Pour-ons

Pyrethroids can be applied as pour-on on the back or the flank of the animal. The product quickly diffuses into all parts of the body (Bauer *et al.,* 1995; Leak *et al.,* 1996). Due to its easiness to use, cattle breeders use pour-on's more and more as an alternative to spraying and dipping. In Cameroon, already in 1988 the MSEG realised a study in the far North of the country by applying Ectopor® (cypermethrin) pour-on once a month to control *Tabanidae, Stomoxys* and *Culicoides*; the proliferation of which had provoked an epizootic of trypanosomosis. Results were very satisfactory (Cuisance, 1991). In Ndigou village the tsetse fly density dropped from 8-10 to 0, 1 flies per trap and the prevalence of cattle trypanosomosis decreased from 30% to 1-2% (Cuisance, 1991).

In 1990, MSEG used Ectopor® on a herd of 150 animals in Galim during 4 months, then on 1000 heads during 2 months. These experiments had a high "psychological impact" on the cattle breeders in the Galim region which was highly infested by tsetse at that time. The product was considered as very efficacious by the cattle owners, who were very much impressed by the excellent results (Cuisance, 1991). Similarly, during the rainy season the use of Bayticol® pour-on every 15 days on half of the cattle herd of Libong region gave excellent results against cattle ticks and all biting insects (Cuisance, 1991).

According to Ndoki (1994), the method is efficient in areas of medium density of tsetse permitting a great level of reduction in the consumption of trypanocides. He recommended this technique for the protection of slaughter cattle on their way to the "abattoir" and during transhumance.

From these experiments and observations it can be concluded that pour-on insecticides are very efficient and easy to use without any cost either of purchase or maintenance of

equipment. In order to allow efficient control of tsetse, they must be applied on the greater part of the cattle herds of the region. Unfortunately, in the 1980s and 1990s pour-on's were six times more expensive than a pulverization application (3800 FCFA/ animal/ year against 608 FCFA/ animal/ year) (Cuisance, 1991).

Nowadays this practice (pour-on or spraying) is obligatory for all cattle breeders going on transhumance in Adamaoua (Hamadama, 2004). Under the supervision of MSEG technicians, cattle breeders who want to go on transhumance must buy an insecticide and treat their animals. At the end of that treatment, they receive a certificate of transhumance from veterinary service at the final destination. At the return they carry out the same treatment. This approach allows the cattle breeders to protect their animals from trypanosomosis and simultaneously allows MSEG to protect some pastures from tsetse reinvasion.

Figure 3.4 Photo showing the insecticide treatment of cattle on the Adamaoua plateau, Cameroon

Supply of insecticides and equipment for insecticidal treatments

In the past there were often shortages of insecticides and pulverisers (Cuisance, 1991). Similarly, there are regular lacks of trypanocidal drugs. To overcome this situation, the cattle

breeders organized themselves and collected money to buy the insecticide and the necessary equipment. Some cattle owners lent their pulverisers to others (Boutrais and Cuisance, 1995). Nowadays there are many private companies of veterinary drugs and some insecticides are available in the Adamaoua (Table 3.1). In some villages, the cattle breeder organizations sell veterinary medicines. CAMVET (a private company of veterinary supplies) sold about 260 l of Cypermil® (a cypermethrin pour-on formulation) in the Faro and Deo Division during the dry season (2003-2004). According to the CAMVET representative, much more product can be sold (Van den Bossche, 2004).

Table 3.1 Insecticides commonly used to treat cattle on the Adamaoua Plateau

Products	Trade names	Manufacturer	Methods of use
Deltamethrin	Butox®	Roussel-Uclaf Paris France	Pour-on, Sprays and Dipping
	Spoton®	Pitman-Moore ltd, Harefield England	Pour-on
Cypermethrine	Ectopor®	Ciba-Geigy S.A. Bale, Switzerland	Pour-on and Sprays
	Cypermil ®	Ouro Fino Brazil	Pour-on and Sprays
	Eradic®	Calliope France	Dipping and Sprays

3.5.4 Screens and traps as barriers

In 1990, it was proposed by Cuisance (Cuisance and Boutrais, 1995) to combine the use of screens/traps barriers with the insecticidal treatment of cattle herds as barriers. However, the reduction of MSEG funding did not allow the implementation of this recommendation until 1993. In 1993, with limited means (suspension of BIRD loan) the implementation was experimentally started using 1014 screens impregnated with deltamethrin (28 March -29 May 1993). However, the lack of decentralized points of control (non-construction of control posts) forced MSEG to intervene from Ngaoundéré, with limited follow up (Cuisance and Boutrais, 1995). In 1994, with the agreement with the World Bank, the tsetse control activities started again.

Implantation of the screen/traps barriers

Each defence line constituted of two rows (sometimes four) of screens impregnated with insecticides at an interval of 50-100m. On each row, the screens were placed every 150m.

Inside those rows, traps were added without a system of collection but were impregnated with deltamethrin to reinforce the barriers (traps are more attractive than screens). From December 1993 onwards about 3500 screens and 140 traps were progressively deployed along open tracks. In June 1994, more sentinel traps were put in place and 23 fly rounds were organised in order to assess the efficacy of these barriers. To increase the efficiency of screens and traps two olfactory products (octenol and acetone) were used.

Maintenance and control of barriers

All screens and traps were impregnated with K. Othrin® (deltamethrin) and were retreated twice by pulverization between December 1993 and July 1994. According to Cuisance. (1995), product dosages and re-impregnation intervals were done correctly. But from 1993 onwards, the first thefts and degradation of traps/screens were reported (MSEG, 1993). The absence of decentralized control teams equally hindered the regular clearing of vegetation at the immediate surroundings of screens and traps. In December 1994 about 90% of the barrier systems were destroyed by a bush fire during dry season. The loss was estimated at about 28,300,000 FCFA (43,300 Euro). Besides economic losses, this massive destruction demoralised the senior staff and technicians who had worked hard to order the material, install and make it work correctly and then saw it disappearing without possibility to help (Cuisance and Boutrais, 1995).

The efficiency of the barrier system before its destruction

Screens were set up and maintained during almost a year (December 1993 to December 1994). According to Cuisance. (1991) the vast screen/trap barriers were quite effective and played a non-negligible role in preventing reinvasion. Some cattle breeders were convinced that the barriers worked well and affirmed that without them they would not have been able to stay where they were; only one tsetse was found inside the barrier, while at a distance of some meters of the first lines of screens, they were many (Cuisance and Boutrais, 1995).

3.5.5 Program of insecticide treatments of cattle in the buffer zone

At the end of aerial spraying campaign, the MSEG created a buffer zone in order to act as a barrier to tsetse invasion between the valley and the Adamaoua plateau (Boutrais and Cuisance, 1995). Therefore it was advised that all local herds in the buffer zone should be treated regularly with insecticides (pyrethroids). In 1994, the fight against the tsetse flies reached its climax, tsetse having been pushed back to the area which they occupied by the

end of fifties or beginning of sixties (Boutrais and Cuisance, 1995). The buffer zone in the North of Adamaoua had screens and traps to intercept the first moves of tsetse. Behind that barrier, all herds had to be impregnated with insecticides. These cattle herds acted as a kind of second line of defense against tsetse invasion and protected all livestock on the plateau. Cattle breeders present in the buffer zone had and still have a great responsibility not only towards their personal herds but also towards all livestock of the Adamaoua (Boutrais and Cuissance, 1995). In order to assess the efficacy of these regular insecticide treatments of the cattle herds in the buffer zone, longitudinal parasitological and entomological surveys were carried out in the 3 zones of the study area (valley, buffer and plateau), the results of which are reported in this study (see Subsection 4.2).

3.5.6 Trypanocidal treatments of cattle on the Adamaoua plateau

Nowadays chemotherapy in the Adamaoua region is used as preventive treatment with isometamidium chloride at the start of the transhumance and curative treatment upon return or in the case of illness with diminazene aceturate.

Table 3.2 Trypanocides commonly used to treat cattle trypanosomosis on the Adamaoua Plateau

Drug	Trade name	Pharmaceutical Company	Country of origin
Diminazene aceturate	Berenil®	Hoechst Veterinär GmbH	Germany
	Diminaphen®	Phenix Pharmaceutical (Kela)	Belgium
	Diminavet®	Pharmaed mc.	Canada
	Diminazen®	Medrodex. Inx	Canada
	Sangavet®	Vetoquinol	France
	Survidim®	Laprovet	France
	Trycip®	Cipla	India
	Trypadim®	Merial	France
	Pirofort®	Ouro Fino	Brazil
	Veriben®	Ceva	France
Isometamidium chloride	Trypamidium®	Merial	France
	Samorin®	Merial	France
	Securidium®	Laprovet	France
Homidium bromide	Ethidium®	Laprovet	France
Homidium chloride	Novidium Chloride®	Merial	France
	Ethidium Chloride®	Merial	France

Since the cattle owners usually treat their animals without adequate veterinary supervision as well as insufficient control of the locally available trypanocidal drugs (Table 3.2) (substandard or fake drugs are probably imported from neighbouring Nigeria and used), it is not surprising that drug resistance is suspected by the cattle owners and the veterinary services. In order to verify whether resistance to trypanocidal drugs is a real problem in the Adamaoua, surveys were carried out at herd level and also at the regional level in this study (see Subsection 4.8 and 4.10)

3.5.7 Organisations involved in tsetse and trypanosomosis control in the Adamaoua

Livestock is very important for the rural economy of theAdamaoua. Most of the purchases are now made with money obtained from livestock. The constitution of groups of cattle breeders has become a major component in many development projects (Boutrais and Cuissance, 1995). In the Adamaoua plateau two groups are involved in tsetse and trypanosomosis control: BOSCUDA (Bororo social and cultural development association) and UGICETA (Union des GIC pour l'éradication de tsé-tsé en Adamaoua).

UGICETA

This organisation was created in 1994 within the framework of the PDSE (Projet de développement du secteur élevage) financed by the World Bank from 1987 to 1995. It consisted of 8 delegates from breeder groups and 4 MINEPIA (Ministry of livestock, fisheries and husbandry) technicians. The goal of UGICETA was the protection and the valorisation of the tsetse cleared zone. This organisation worked in close collaboration with MSEG. In 2003, UGICETA financed a terrestrial spraying campaign in the pastoral zone of Mboula. This work was done by MSEG technicians (Abah Samuel, pers. communication). UGICETA was financed by the French cooperation in a program of GESEP (Gestion sécurisée des Espaces Pastoraux). The funding was used to buy equipment and consumables (vehicles, office equipment), for personal training and assistance in the field and allowed UGICETA to involve all cattle breeders of the Adamaoua plateau in this organization. Nowadays, UGICETA is no longer funded by external donors. It has become a Federation of cattle breeders of the Adamaoua and its financing comes from cattle market taxes (Bobbo Bakari, pers communication).

PALTAV

PALTAV (Programme de lutte contre la trypanosomose animale et ses vecteurs) is a government organisation financed by PPTE funds (pays pauvres et très endettés). The PALTAV technicians take care of the training of cattle breeders, e.g how to use trypanocidal drugs and insecticidal products.

MSEG

The 'Mission Spéciale d'Eradication des Glossines' (MSEG) was created in 1974 by a presidential decree with as main objective the fight against tsetse flies, principal vectors of bovine trypanosomes. Nowadays the mission of the MSEG is to keep pastures free of tsetse flies through the maintenance of screen and traps barriers; the follow up of the insecticide treatment of cattle in the buffer zone and also the treatment of the animals at the beginning and at the end of the transhumance. MSEG is also involved in terrestrial spraying, entomological surveys and training of cattle breeders.