6 Summary

Studies on the diagnosis, development and distribution of drug-resistant trypanosomes in cattle herds from selected sites of East and West Africa

Tsetse transmitted bovine trypanosomosis or nagana is a major constraint to rural development in much of sub-Saharan Africa. In all these regions the main control method is to cure the disease in cattle through the administration of anti-trypanosomal molecules such as the diamidine diminazene aceturate and the phenanthridine derivative isometamidium chloride. These drugs are in use for more than 40 years. Due to the phenomenon of antigenic variation no vaccine has been developed until now. Furthermore, vector control even though technically feasible, is inherently confronted with problems of sustainability. Therefore, control of the disease will continue to depend largely on the use of trypanocidal drugs for the foreseeable future. However, there have been several reports in recent times indicating an increase of the drug resistance incidence in trypanosomes. The number of case reports on drug resistance is growing, yet there is lack of reliable data at regional level on its true prevalence.

The present study aimed to assess the development and distribution of drug-resistant trypanosomes in cattle herds from selected sites of East Africa (Metekel, north-west Ethiopia; Upper Didessa Valley, west Ethiopia; Mukono County, south-east Uganda) and West Africa (province of Kénédougou, south-west Burkina Faso). Longitudinal field studies were conducted to estimate the incidence of trypanocidal drug resistance in high risk areas. Several *in vivo* and *in vitro* tests were used to characterize the drug sensitivity of trypanosome field stocks. The polymerase chain reaction (PCR) was evaluated and its diagnostic potential to monitor the efficacy of prophylactic and curative treatments tested.

Block treatment of cattle with isometamidium in high trypanosomosis risk villages in Metekel, Upper Didessa Valley and Kénédougou indicated that isometamidum resistance in *Trypanosoma congolense* was widespread but varied in its incidence between villages, indicating a relation with trypanosomosis risk and, possibly, other factors. Field-derived indicators of isometamidium resistance were supported by *in vivo* and *in vitro* demonstration of resistance to both isometamidium and diminazene. Clones originating from cattle primary isolates of *T. congolense* from Metekel and Kénédougou and tested in mice expressed a high level of resistance to both isometamidium and diminazene. It was concluded that chemotherapeutic agents *per se* would not provide a viable option for the control of trypanosomosis at Metekel and Kénédougou on a long-term basis if such resistance at clonal level was highly prevalent. In contrast, there appeared to be no resistance of trypanosomes to the common used drugs in cattle of Mukono. All the same, given the apparent development of resistance to trypanocidal drugs that has occurred in other tsetse-infested areas, anti-trypanosomal compounds should be judiciously applied in Mukono County as well. PCR proved to be a highly sensitive and specific tool to monitor the therapeutic and prophylactic efficacy and disease progression in bovine trypanosomosis. Depending on the availability of financial support, PCR could provide an ideal tool to assess trypansomosis risk in endemic areas and to monitor the success of tsetse and trypanosomosis control programmes.

Since there is no indication that new trypanocidal drugs will become available in the near future, it is of greatest importance that measures be taken to avoid or delay the development of resistance and to maintain the efficacy of the currently available drugs. The most efficient way is the reduction in the number of treatments in order to reduce the selection pressure caused by these drugs. Mass treatments at short intervals should be avoided, particularly in areas of high challenge. Drug use should be reduced through vector control and by decreasing host-vector contact. If resistance to both isometamidium and dimiazene is present at the level

of individual trypanosomes, trypanocidal drug use should be terminated, except for the treatment of clinical cases. Vector control activities should be maximised and cross-breeding with trypanotolerant cattle should be encouraged.