TRYPANOSOMOSIS RESEARCH AT THE CENTRE FOR TROPICAL VETERINARY MEDICINE (CTVM) 1970 TO 1995


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SUMMARY

This review covers aspects of research work carried out on animal trypanosomes at the Centre for Tropical Veterinary Medicine (CTVM) during the last 25 years. The review covers work on antigenic variation, tissue culture, drug resistance, immunology, biochemistry and pathology of Trypanosoma brucei, T. congolense, T. gambiense and T. evansi. It is not intended as an exhaustive review of the subject but focuses on certain aspects of these areas which are presented in relation to work carried out within the broader scientific community.

INTRODUCTION

The pathogenic animal trypanosomoses have had a major influence on livestock productivity in many countries in both the Old and New Worlds. The tsetse transmitted trypanosomoses, Trypanosoma brucei, T. congolense and T. vivax are restricted to Africa where they have been responsible for the exclusion of livestock from large areas of land which is potentially capable of supporting cattle and other ruminants. Probably no other animal disease has had such an influence on cattle distribution both in preventing intensification of livestock production through the introduction of higher performing more productive breeds or in preventing expansion into areas where disease risk is too great for susceptible livestock. Trypanosoma evansi, which is transmitted mechanically by biting flies, has achieved a much wider distribution and is found not only in northern parts of Africa outside the tsetse belts, but also in Asia and South America. Host species principally affected include camels, cattle, buffalo and horses. Trypanosoma vivax too, has spread beyond Africa and is found in South America. The mechanically transmitted trypanosomases have not had as great an influence on livestock as the tsetse transmitted trypanosomases. Nevertheless, serious epidemics of disease were common in the early years of this century particularly in India, Indonesia, Mauritius and the Philippines. Even today, T. evansi causes disease in buffalo which leads to production losses and decreased agricultural output in Indonesia, China, Vietnam and the Philippines. In Africa, trypanosomosis caused by T. evansi is the single most important disease of the camel in Kenya, Sudan, Somalia, Mali and Mauritania. High mortality is sometimes seen in both the tsetse transmitted and the non-tsetse transmitted trypanosomases, but their most significant impact probably comes from chronic trypanosomosis, where abortion, infertility, reduced milk yield, reduced weight gain and lower work output contribute to the lowered provision of animal proteins and lower yields of agricultural products such as maize or rice due to the lack of work oxen or buffalo for ploughing.

The scale of the problems caused by the pathogenic animal trypanosomoses has occasioned a considerable amount of effort in attempting to control the diseases. These have involved a wide spectrum of research studies and the present review highlights some of these aspects in relation to work carried out at the CTVM over the past
25 years. The review is not exhaustive, covering work on antigenic variation, tissue culture, drug resistance and chemotherapy, immunology, biochemistry and pathology, but without attempting to cover the many significant contributions to these fields made by other research workers outwith the CTVM.

ANTIGENIC VARIATION AND SERODEME ANALYSIS

The ability of Salivarian trypanosomes to counter the host’s immune response by producing a large number of antigenically different populations throughout the course of infection in the vertebrate host has fascinated scientists since early in the 20th century (Ritz, 1916). Antigenic variation has continued to attract a high proportion of the international research effort on trypanosomosis, reflecting the rapid expansion in immunology, biochemistry and molecular biology that characterise the last 25 years (Turner, 1992; Hyde, 1990). A considerable amount of work had been done on antigenic variation before 1970 and had established many of the tenets of antigenic variation, particularly the tendency for certain antigen types to appear early in infection irrespective of the infecting variant (predominant antigen types); the reversion to a particular antigen type after cyclical transmission that was a strain characteristic (basic strain antigen) and the classification of trypanosome isolates into groups (serodemes) according to the range of predominant antigen types. The work carried out during this period has been extensively reviewed by Gray (1967), Lumsden (1967) and Gray and Luckins (1976). Results from these studies formed the cornerstone for much of the research on antigenic variation carried out in a number of European laboratories in the last 25 years. These years saw a refinement of many of the techniques developed in the 1960s, in particular the use of cloned populations and standardisation of terminology (Lumsden, 1982). Much of this work, however, concentrated on the easily handled *T. brucei* with the technically more demanding but economically more important species receiving scant attention. At the CTVM, work on antigenic variation concentrated initially on *T. gambiense* and *T. congolense* later moving to *T. evansi* in the late 1980s.

The studies on *T. gambiense* were an extension of those carried out previously at the Nigerian Institute for Trypanosomiasis Research. These studies had suggested that antigenic diversity amongst isolates of *T. gambiense* was more limited than had been found in *T. brucei* with isolates of *T. gambiense* from widely separated areas of Nigeria producing a large number of variable agglutinogenic antigens in common (Gray, 1972; 1973). Later, stocks from Nigeria, Senegal, Uganda and Zaire were also found to show high degrees of similarity in their antigens (Gray, 1974).

At Edinburgh the aim of the studies was to study antigen development in metacyclic-induced infections which had been shown to have important consequences for antigen development in *T. brucei*. The technical problems posed by cyclical transmission of *T. gambiense* caused principally by low infection rates in tsetse was overcome by advances in *in vitro* culture technology that made it possible to generate metacyclic trypanosomes in organ cultures of *Glossina morsitans* (Cunningham, 1977; Cunningham and Honigberg, 1977). Initial results with *T. brucei* showed that infections initiated from *in vitro* produced metacycles expressed a similar range of antigenic types as did tsetse-induced infections (Gardiner et al., 1980a,b). Eventually 5 stocks of *T. gambiense* from Senegal, Uganda, Nigeria and Zaire were adapted to *in vitro* culture conditions and metacyclic forms were used to initiate infections for studies on antigenic development. Results from this study confirmed that there were many similarities in the pattern of antigen development of geographically