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PREFACE

Astute readers will already have noticed that there are now only two editors of "Advances in Parasitology". On the retirement of Professor W. H. R. Lumsden from the senior editorship, the editors and the publishers decided to broaden the range of expertise available to advise upon policy and propose or criticize contributions. An international editorial board composed of experts in as many fields of parasitology as possible has been invited to advise the editors generally and to help on specific topics when required.

We were delighted when the distinguished scientists whose names are listed on p. ii agreed to serve as board members. Their wide experience and knowledge will help us considerably, and cannot fail to improve the coverage and raise the standard of the material included in future volumes. We were particularly glad that Professor Lumsden agreed to serve. The experience he acquired on taking over the major responsibility for "Advances" after Professor Dawes's death was considerable; this experience he willingly passed on to us during our years of friendly and, we believe, fruitful collaboration as joint editors, and we welcome its continuation. Professor Lumsden shares with us a deep interest in this publication, and it is good that this will be actively continued.

We are always happy to receive suggestions for future contributions, either general or specific, and we solicit such proposals from readers. All will be considered sympathetically by us, in the light of comments by appropriate board members when necessary. However, we prefer not to receive unsolicited completed typescripts. We state again our intention to maintain a broad interpretation of parasitology, both applied (medical, veterinary and agricultural) and non-applied (conceptual or theoretical), and to emphasize as far as possible the first word of the publication's title.

1982

J. R. BAKER
R. MULLER

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MAX MURRAY, W. I. MORRISON AND D. D. WHITELAW

International Laboratory for Research on Animal Diseases, Nairobi, Kenya

I. Introduction

The exploitation of genetic resistance to disease is becoming an increasingly important consideration in livestock development programmes, particularly where conventional disease control measures are not effective or are too costly. Such an approach may be directly applicable to African animal trypanosomiasis.

In African trypanosomiasis, the control measures currently in use include diagnosis and treatment, chemoprophylaxis, and control or eradication of tsetse with insecticides. Unfortunately, many years of these strategies have had little effect on the problem at the continental level. There are several factors responsible for this. Firstly, there are 22 species of *Glossina* (tsetse) capable of transmitting infection; these are adapted to a wide range of habitats, thereby contributing to the widespread nature of the disease. Secondly, the three trypanosome species pathogenic for domestic livestock, *Trypanosoma congolense*, *T. vivax* and *T. brucei*, exhibit a wide host range for both domestic and wild animals. Thirdly, the phenomenon of antigenic variation which leads to persistent parasitaemia provides an excellent opportunity for transmission of infection by tsetse. At the same time, the implementation of current control measures poses several problems. The use of drugs, both therapeutically and prophylactically, can be costly because repeated treatments are required and diagnostic facilities are necessary if the drugs are to be used properly. Furthermore, frequent use or misuse can lead to the development of chemoresistance, a risk compounded by the fact that the number of drugs commercially available at present is extremely limited. Tsetse control, followed in some cases by eradication, has been successful in certain regions; e.g. Nigeria, Zambia, Botswana and in South Africa (reviewed by MacLennan, 1981). However, as with drug strategies, the cost is high and it is essential that the eradicated area is kept under rigorous surveillance for several years and protected by natural or man-made tsetse barriers to prevent reinvasion. In addition, the emotive question of environmental hazards created by the use of insecticides arises. At present, there is no effective field vaccine available against African trypanosomiasis. The major constraints to the development of a vaccine include the existence of different species of trypanosomes and of different serodemes within the same species, all with the capability of producing different repertoires of variable antigen types (VATs).

In the face of these problems, increasing attention has been focused on the potential use of genetically resistant or trypanotolerant livestock. There is no clear definition of trypanotolerance. At one extreme, Pagot (1974) defined trypanotolerance as a "racial aptitude [of cattle] to maintain themselves in good condition and to reproduce while harbouring trypanosomes without showing clinical signs of the disease." He recommended that such cattle be

introduced widely into high tsetse challenge areas throughout Africa. At the other end of the scale, Stephen (1966) stated that "tolerance is far from absolute" and concluded that propagation of trypanotolerant breeds was not to be recommended as a satisfactory means of improving the supply of protein in densely populated areas of West Africa. In our experience, both these statements are true for the circumstance under which each author made his observations. The major fact by which trypanotolerance may be defined is based on the field observation that certain breeds of cattle, sheep, and goats, as well as some species of wild animals, can survive in endemic tsetse fly-infested areas without the aid of chemotherapy where other breeds cannot. The term trypanotolerance may be misleading because infection of animals considered to be trypanotolerant can, in some instances, cause severe clinical disease. Thus, such breeds are not truly tolerant but could be described more correctly as exhibiting a greater degree of resistance to the disease; it might be better, as discussed by Wakelin (1978), to use the term reduced susceptibility.

With regard to the economic potential of trypanotolerance, we agree with the views of Stewart (1951) and Chandler (1952) that more information is required on several aspects of this trait before widespread exploitation of trypanotolerant breeds can be recommended. It is important to know the extent of the differences in resistance between different breeds and also within the same breed living at different levels of trypanosomiasis risk, under different management systems in different ecological zones. At the same time, an understanding is required of the mechanism(s) underlying trypanotolerance, the genetics of heritability, and the stability of the trait, i.e. how it is affected by environmental factors.

In the current review, we present and discuss the available information on each of these aspects of trypanotolerance, with regard to cattle, sheep, goats, wildlife and man. We also evaluate experimental results derived from mouse models and consider their relevance to trypanosomiasis of livestock.

II. Origin of Trypanotolerant Livestock

The majority of published information suggests that trypanotolerant livestock are confined to West and Central Africa. While this is broadly the case, there is no obvious reason why they should not have evolved in other regions of Africa infested by the tsetse fly.

Domestic cattle were probably introduced into Africa from the near East around 5000 BC (Payne, 1964; Epstein, 1971). Goats arrived at approximately the same time but sheep did not appear until early in the third millenium BC. These estimations are based on rock paintings and engravings.

Three major breeds of cattle were imported or migrated with nomadic people into north-east Africa. These were the humpless Hamitic longhorn, the humpless Shorthorn and the humped Zebu. The Hamitic longhorn and the Shorthorn would be classified as ancestral *Bos taurus* types while the Zebu would be the *Bos indicus* type. Sanga breeds have resulted from a mixture of Zebu and Hamitic longhorn and/or Shorthorn. The time of origin and the subsequent migration routes of domestic cattle in Africa are shown in Fig. 1.

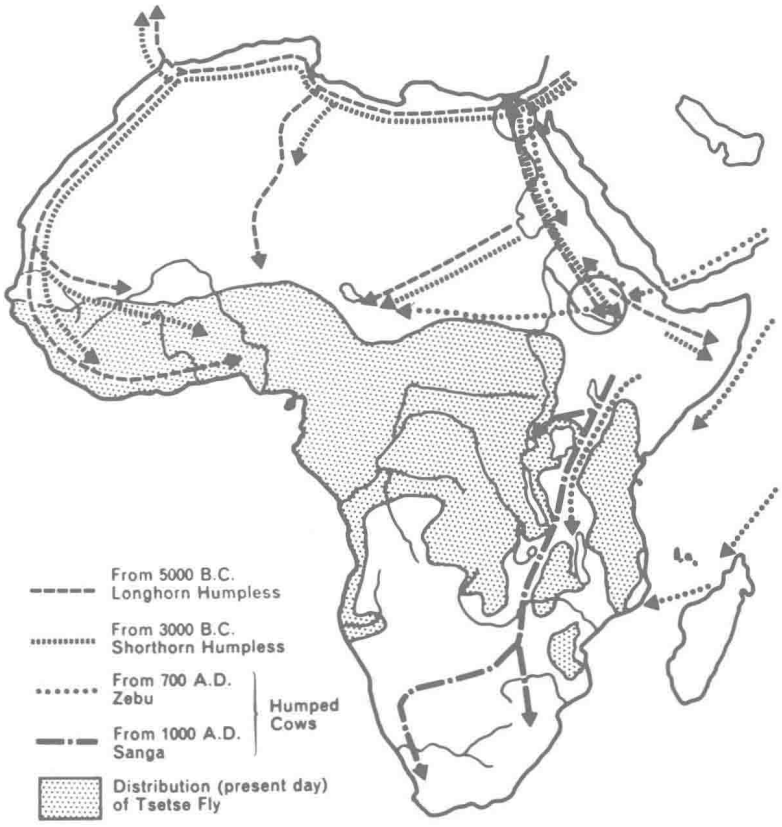


FIG. 1. Map of Africa showing the foci of origin and time of subsequent spread of indigenous breeds of African cattle. Data are based on Payne (1964) and Epstein (1971).

The Hamitic longhorn arrived in Egypt about 5000 BC, while the Shorthorn were first introduced into the same area about 2750 to 2500 BC. Zebu arrived in Egypt between 2000 and 1800 BC and Sanga were recognized between 2000–1500 BC. However, it was not until the Arab invasion of Africa after 669 AD that the number of Zebu imported into Africa rose sharply and the large-scale spread of Zebu and Sanga followed.

TABLE 1

Classification of trypanotolerant cattle[a]

Group	Breed	Estimated no. in millions
N'DAMA	N'Dama	3·4
WEST AFRICAN SHORTHORN (MUTURU)		
Dwarf West African Shorthorn	Lagune/Dahomey Forest Muturu Liberian Dwarf	0·1
Savanna West African Shorthorn	Baoule Ghana Shorthorn Somba Savanna Muturu Doayo Bakozi Kapsiki	1·7
ZEBU × HUMPLESS		2·4

[a] Data from ILCA (1979).

At present, the breeds descended from the Hamitic longhorn, the N'Dama, and from the Shorthorn, the West African Shorthorn, are concentrated in West and Central Africa (Table 1). It is these breeds which are considered trypanotolerant, and they are found largely in tsetse-infested areas. As the tsetse challenge becomes lighter and with northern extension beyond the tsetse belt, Zebu crosses and Zebu become more common and eventually predominate. Thus, it would appear that the presence of the tsetse fly has had a major influence on the eventual distribution of different breeds of cattle. It is then interesting to speculate on the reason for the lack of taurine cattle in East Africa, where *Bos indicus* types are the main indigenous breeds, despite the tsetse. One possible explanation is that rinderpest pandemics curtailed the movement of the trypanotolerant breeds such as the N'Dama which are thought to be less resistant to rinderpest than West African Zebu (Cornell and Evans, 1937).

Another interesting aspect of the migration of the Hamitic longhorn and the West African Shorthorn is that, in addition to moving west and then south into West Africa from the Nile delta (Fig. 1), they crossed into the Iberian peninsula and from there to the rest of Europe and the Americas; e.g. the Hamitic longhorn is represented in Scotland by the West Highland Cattle, in Brazil by the Franquiro, and in Mexico and the southern U.S.A. by the Texas Longhorn. The Shorthorn is partly responsible for the Jersey, Guernsey and Kerry breeds in the British Isles.

III. Evidence for Genetic Resistance to Trypanosomiasis

A. CATTLE

In one of the first accounts of West African livestock, Pierre (1906) recorded the ability of certain cattle to survive in tsetse-infested areas. Subsequently, the resistance of the taurine animals was recognized increasingly in West Africa (reviewed by Godfrey *et al.*, 1964 and ILCA, 1979), as well as in the Sudan (Archibald, 1927). In 1951, Stewart described his experience with what he termed "West African Shorthorn Cattle" in Ghana (Gold Coast) over a period of 20 years from 1929 to 1948. These animals were genetically heterogeneous and comprised Hamitic longhorn, Shorthorns and Zebu. The contribution made by each "breed" appeared to depend on the level of tsetse challenge; the greater the tsetse risk, the smaller the percentage Zebu in each animal. His overall conclusion was that these animals possessed very high resistance to the disease. He pointed out that they were rather small for beef, for work and for milk, but these features had blinded people to their basic value. namely, the fact that the West African Shorthorn lives, breeds and thrives in areas were Zebu and other exotic cattle die of trypanosomiasis. Furthermore, he emphasized that a vast area of West Africa depended on these small cattle and that, although they might be deficient as a market animal compared with Zebu, the development of mixed farming would be impossible without them as the West African Shorthorn cattle provided the peasant with his draught oxen, his manure and his milk.

Stewart (1937, 1951) examined the susceptibility of these cattle to needle challenge with both *T. vivax* and *T. congolense* (including a proven pathogenic strain from Tanzania). He showed that, despite becoming infected, the animals were able to control their parasitaemia and did not develop any overt clinical signs. Similar results ensued when they were exposed to natural tsetse challenge, including *Glossina palpalis*, *G. morsitans* and *G. longipalpis*. While it was found that most animals showed little evidence of clinical disease and some recovered spontaneously, their resistance broke down if the tsetse challenge was high enough or as a result of stress, e.g. lack of grass or repeated bleeding during experimental studies. Furthermore, in a series of crossbreeding studies Stewart (1951) was able to produce much larger cattle than "West African Shorthorn" that still retained a significant measure of trypanotolerance. As a result of 20 years experience, he concluded that, "the creation of trypanosomiasis-resistant cattle is a more practical and natural procedure than mass inoculation of cattle with drugs in attempts to maintain these doped cattle in tsetse areas." In his investigations, Stewart established the basis for recognizing the importance of trypanotolerance and pointed the way for future studies of the resistance of several West African taurine breeds.

1. *N'Dama*

Most studies of trypanotolerance in cattle have focused on the N'Dama which is the main descendant of the Hamitic longhorn in Africa. It is thought that this breed spread in West Africa from the Fouta Djallon plateau in Guinea (Epstein, 1971). It now is the most common trypanotolerant breed in West Africa with an estimated population of 3·4 million (Table 1). Its popularity is probably based on the fact that it is the largest of the trypanotolerant breeds (Fig. 2a; Table 2) and is thought to be the most productive.

Some of the first experimental studies on the extent of trypanotolerance exhibited by the N'Dama were carried out in Nigeria. The superior resistance of the N'Dama to trypanosomiasis was consistently confirmed by comparisons of weight loss, anaemia and survival. This was true regardless of the nature of the challenge. In some experiments, animals were exposed to natural field challenge of *G. palpalis* or *G. morsitans* (Chandler, 1952; van Hoeve, 1972); in others, the animals were challenged with *G. palpalis* infected in the laboratory with *T. vivax* (Chandler, 1958; Desowitz, 1959); and other investigations involved the inoculation of bloodstream forms of *T. congolense* (Chandler, 1958). These studies emphasized the potential of trypanotolerant livestock and presented evidence that trypanotolerance was an innate characteristic (Chandler, 1952, 1958).

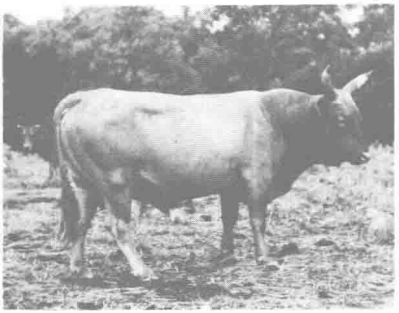
TABLE 2

Weights (kg) of some indigenous African breeds of cattle[a]

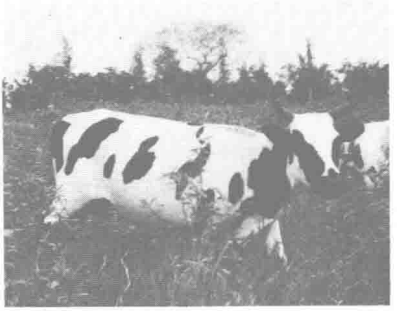
	1 year old	Mature cows
N'Dama	114 ± 14	248 ± 20
West African Shorthorn	79 ± 14	162 ± 20
Keteku–Borgou (Zebu × Shorthorn)	130 ± 10	260 ± 30
Zebu	180 ± 20	300 ± 30

[a] These figures (means ± S.D.) are presented to give some idea of the size of the animals under discussion but vary considerably with management systems. (From ILCA, 1979.)

While there is no question of the general validity of the foregoing results, some of the conclusions might be criticized for the following reasons: the clinical history of many of the animals was not precisely known, the antigenic characteristics of the various trypanosomes to which the animals were exposed was not investigated and, lastly, only small numbers of cattle were available for study. Without these data, it is impossible to define the relative contributions of innate and acquired resistance.



(a)



(b)

(c)

FIG. 2. N'Dama bull (a); West African Shorthorn (Muturu, b); East African Zebu (c): (a) and (b) are reproduced by permission of the International Livestock Centre for Africa, Addis Ababa.