Trypanotolerant livestock: Potential and future exploitation

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The exploitation of genetic resistance to infectious diseases is being given increasing attention in livestock development programmes. This is particularly the case in developing countries where it is estimated that 70 per cent of the world's livestock resources exist but where conventional disease control measures are often not effective, do not exist, or cannot be implemented because of lack of finance or trained manpower.

The problems of increasing livestock production in face of widespread endemic disease are exemplified by tsetse-transmitted animal African trypanosomiasis. At present, tsetse infest approximately ten million km^2 of Africa, affecting 38 countries [1]. It is considered that seven million km^2 of this area would otherwise be suitable for livestock or mixed agricultural development. Currently, about 30 per cent of the 147 million cattle in countries affected by tsetse are exposed to the disease [1]. Information at present available indicates that the overall situation is deteriorating and that, since the 1950s, the areas of savanna infested by tsetse have continued to expand [2]. Thus, with the steadily increasing human population, there is mounting pressure on tsetse-free pasturage and increasing need to utilise the areas currently infested. Several factors contribute to the magnitude of this disease problem in Africa, possibly the most important relating to the methods currently available for control. Because of the phenomenon of antigenic variation exhibited by each of the three species which cause the disease—namely *Trypanosoma congolense*, *T. vivax*, and *T. brucei*—no vaccine is available for field use. At present, control methods involve the use of trypanocidal drugs or tsetse control by means of residual or non-residual insecticides. While such methods can be highly effective in certain situations if properly applied, their net impact at the

continental level is small. This is partly related to lack of manpower trained to introduce these measures, to the cost of implementation, and, lastly, to the massive area involved.

Because of these constraints increasing consideration is now being given to the use of trypanotolerant breeds of domestic livestock in tsetse-infested areas. It has long been recognised that certain breeds of domestic livestock, as well as some species of wildlife, possess the ability to survive and be productive in tsetse-infested areas, without the aid of trypanocidal drugs, where other breeds rapidly succumb to the disease. This trait has been termed trypanotolerance and is generally attributed to the taurine breeds of cattle in West and Central Africa, namely, the N'Dama (Figure 1) and the West African Shorthorn (Figure 2 with several phenotypes listed in Table 1), as well as to their sheep and goat counterparts.

Table 1. *Classification of trypanotolerant cattle [3].*

Group	Breed	Estimated no. in millions
N'Dama	N'Dama	3.4
West African Shorthorn (Muturu)		1.7
Dwarf West African Shorthorn	Lagune/Dahomey	
	Forest Muturu	
	Liberian Dwarf	
Savanna West African Shorthorn	Baoule	
	Ghana Shorthorn	
	Somba	
	Savanna Muturu	
	Doayo	
	Bakozi	
	Kapsiki	
Zebu × Trypanotolerant		2.4

While trypanotolerant breeds of cattle are a well recognised component of livestock production in certain areas of West and Central Africa, they represent only about 5 per cent (8 of 147 million) of the total cattle population in the 38 countries where tsetse occur [3, 1]. Failure to exploit these breeds might be attributed to several factors. It was generally assumed that, because of their small size (Table 2), they were unproductive. Furthermore, it was believed that their trypanotolerance was limited to resistance to local trypanosome populations and that, as a result, their ‘tolerance’ would break down if they were moved to distant tsetse-infested locations where different trypanosome strains existed. Another reason was probably the devastation caused by the rinderpest pandemics of the late 19th century, when the N’Dama, which are believed to be very susceptible to rinderpest, are said to have been particularly severely affected [4].

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 x 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 [3].

However, many of these premises have not been substantiated by more recent investigations. It has been found that the productivity of trypanotolerant cattle relative to other indigenous breeds is much higher than previously believed. Furthermore, it has now been confirmed that trypanotolerance is an innate characteristic and, as such, may be exploited. The present paper reviews the evidence for the genetic basis of resistance to trypanosomiasis, examines the productivity of trypanotolerant livestock, considers the environmental factors which influence the stability of trypanotolerance, evaluates the possible underlying mechanisms, and considers the future potential of the breeds that exhibit this trait.

Evidence in cattle for genetic resistance to trypanosomiasis

As early as 1906, C. Pierre [5] observed the ability of certain taurine breeds of West African cattle to survive in tsetse-infested areas. On the basis of rock paintings and engravings it is thought probable that the taurine Hamitic longhorn, from which the N'Dama is descended, first arrived in the Nile Delta from the Near East about 5000 BC, while the taurine Shorthorn cattle were introduced into the same area about 2750 to 2500 BC [6, 7]. On the other hand, although *Bos indicus* types were recognised in Egypt between 2000 and 1500 BC, it was not until the Arab invasion of Africa after 669 AD that the number of Zebu imported into Africa rose sharply and their large-scale spread followed.

Figure 1. *N'Dama bull in The Gambia. This animal acted as a donor in the embryo transfer project.*

Figure 2. *West African Shorthorn cow (Lagune) in Zaire.*

Figure 4. *East African Zebu in Western Kenya; published with permission from Advances in Parasitology (20).*

Figure 5. *Djallonke ram in Congo.*

Figure 6. *Dwarf West African female goat in Benin.*

Figure 7. *Red Maasai sheep at ILRAD.*

Figure 8. *East African goats at ILRAD*.

Figure 9. *Buffalo at Kenya Veterinary Research Laboratories.*

Figure 10. *Eland at Kenya Veterinary Research Laboratories*.

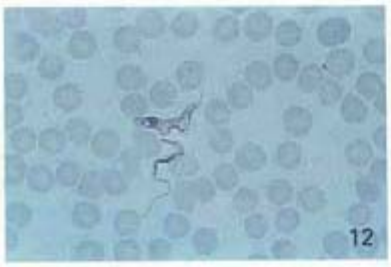


Figure 12. *Slender and stumpy forms of* T.brucei. *Giemsa. x 640 photograph magnification).*

Figure 13. *N'Dama bulls and heifers being shipped from The Gambia to Nigeria.*

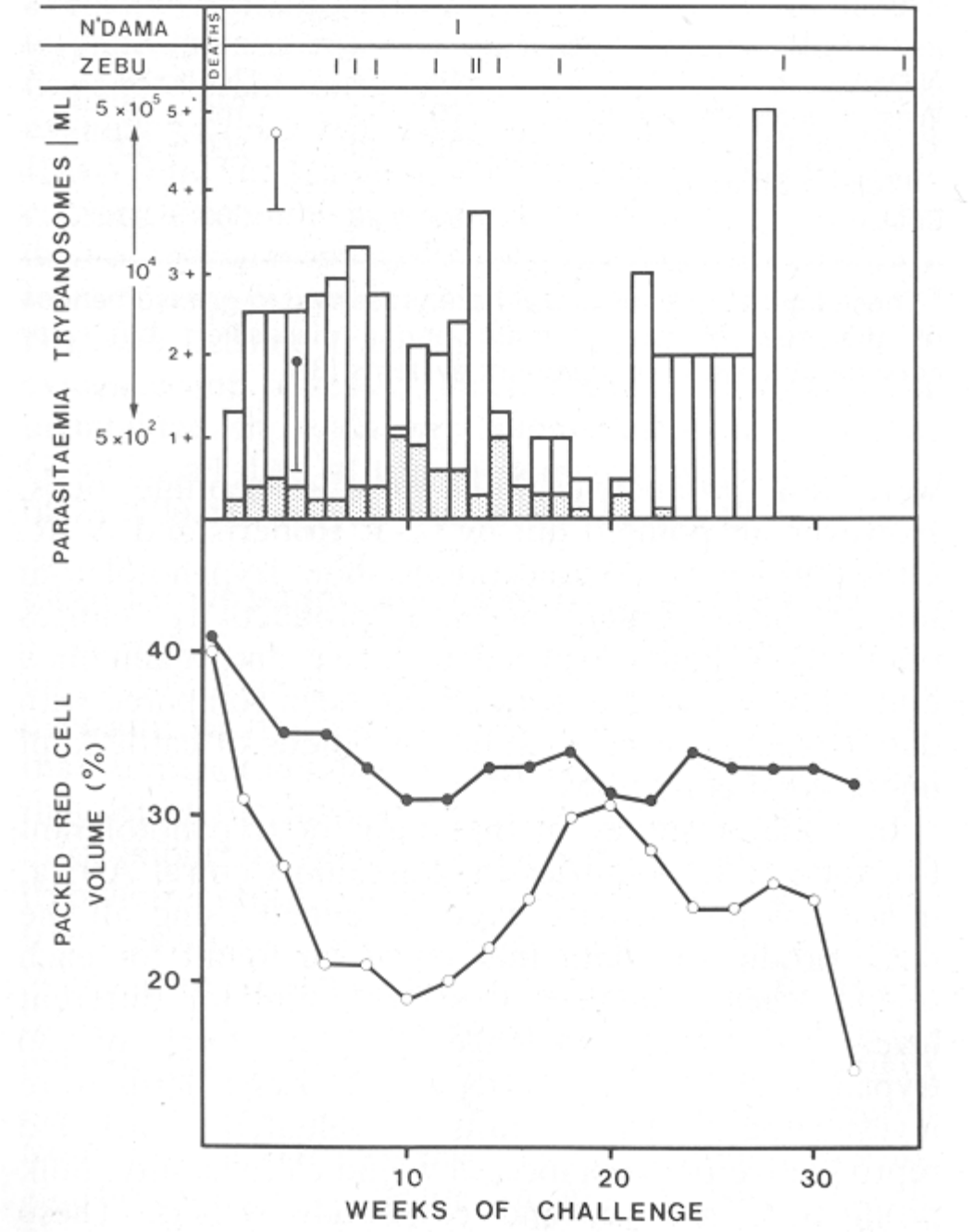
Figure 14. *Implantation of N' Dama embryo into recipient Boran mother on ILRAD ranch.*

Subsequent to Pierre [5], in both field investigation and experimental studies, the resistance of the taurine breeds was increasingly recognised [8, 9, 10, 11]. The validity of these observations cannot be questioned but it was not possible to determine the relative contribution to 'trypanotolerance' of innate and acquired resistance because the history of the animals under study was not known.

More recently, however, it has been clearly demonstrated that breed differences in resistance to trypanosomiasis are an innate characteristic. Using animals that had never been previously exposed to trypanosomes, it was confirmed that N'Dama were significantly more resistant than Zebu to experimental challenge with wild-caught infected tsetse [12, 13], natural field exposure [14, 15], and to trypanosomes inoculated by syringe [16, 17]. The resistance of the West African Shorthorn appeared to be intermediate between N'Dama and Zebu [13].

A striking example of the degree of trypanotolerance exhibited by N'Dama was provided by co-operative work carried out in The Gambia by ILRAD; the National Veterinary Authorities; Glasgow University Veterinary School; and the Rockefeller Foundation, when ten N'Dama and ten Zebu cows were exposed to a natural field challenge from *Glossina morsitans submorsitans* [15]. The animals were two and a half to three years old and had not been previously exposed to trypanosomiasis. All Zebu died of trypanosomiasis within eight months of first exposure (Figure 3). At this time, while all the N'Dama had become infected, they were all in excellent condition, apart from one which had died of anthrax. Later, three N'Dama died of trypanosomiasis 11 to 14 months after initial exposure; these animals had all suffered the stress of parturition and were suckling calves when they succumbed. This difference in survival between the two breeds was associated with the fact that the prevalence, level, and duration of parasitaemia were significantly less in the N'Dama. Correspondingly, this breed developed less severe anaemia. In addition, the N'Dama experienced no abortions and produced live calves, while the Zebu produced no live calves and abortions occurred in both early and late pregnancy. Although some variation in resistance occurred within each breed, the differences found between breeds showed that they existed as two distinct populations.

Figure 3. *The average weekly parasitaemic score in N'Dama and Zebu exposed to a natural challenge of* Glossina morsitans submorsitans*. The hatched areas of the histogram represent N'Dama. The level of the first peak of parasitaemia plus one standard deviation is shown for N'Dama (•) and Zebu (o). PCV values and mortalities are given. The one N'Dama death was due to anthrax; published with permission from Advances in Parasitology (20).*



Further evidence that trypanotolerance has a genetic basis and is not due only to resistance acquired to local trypanosome populations has been provided by the successful establishment of cattle from West Africa in distant tsetse-infested areas of West and Central Africa: for example the introduction of Lagune in 1904 and N'Dama in 1920 into Zaire and more recently N'Dama into the Central African Republic, Gabon, and Congo [3].

There is also evidence that trypanotolerant breeds of cattle may be resistant to several other important infectious diseases. Thus, it has been shown that N'Dama and West African

Shorthorn are very resistant to streptothricosis [18, 19] and they are said to be more resistant to helminthiasis [20]. Furthermore, N'Dama have been reported to be more resistant to tick-borne diseases, including heartwater (*Cowdria ruminantium*), anaplasmosis, and babesiosis [7].

The possibility that genetic resistance to trypanosomiasis might have developed in other regions of Africa and in other breeds of cattle has not been given much serious consideration because most observers believe that, if it did exist to any significant extent, it would be well documented by this time. However, resistance to trypanosomiasis has been reported in local cattle of the Koalib Hills of Nuba Mountains Province in Sudan [21]; these cattle had the appearance of West African Shorthorn. In addition, a few reports exist which describe differences in resistance to trypanosomiasis in certain *B. indicus* types: for example, in Zebu in Upper Volta following needle challenge [22]; in Zebu from Western Kenya following both field and experimental challenge [23, 24; Figure 4]; and in Orma Zebu in South-eastern Kenya exposed to continuous tsetse challenge [25]. However, as the animals in these studies had all been previously exposed to trypanosomiasis, it is not possible to assess the relative contribution of innate and acquired resistance to their susceptibility status. While critical comparative studies on the differences in resistance and productivity remain to be carried out, the degree of genetic resistance in such *B. indicus* types is probably considerably less than in the recognised trypanotolerant breeds. Nevertheless, it would appear that the development of *B. indicus* breeds with a significant degree of resistance is a long-term possibility and could be an important objective in certain situations.

Evidence in sheep and goats for genetic resistance to trypanosomiasis

Although the capacity of indigenous breeds of sheep and goats to survive in tsetse-infested areas is well recognised throughout Africa, experimental evidence that this is the result of an innate capacity to control the parasite and resist the effects of the disease is poorly documented (reviewed in [20]). In West Africa, it is generally accepted that the indigenous Djallonke sheep (Figure 5) and the Dwarf West African goat (Figure 6) are trypanotolerant, and experimental evidence has been presented to substantiate this in sheep [26]. However, the situation with regard to Dwarf goats is far from clear and there are reports demonstrating that Dwarf goats can be highly susceptible to experimental infection [20]. Similarly, there is evidence that indigenous breeds of sheep and goats in East Africa are more resistant to trypanosomiasis than exotic breeds [20]. We have confirmed this experimentally in the case of Red Maasai sheep (Figure 7) in Kenya [20], but have failed to demonstrate in goats any differences in susceptibility between indigenous breeds such as the East African (Figure 8) and imported breeds, following both inoculation of trypanosomes by syringe and experimental tsetse challenge. Nevertheless, there is no question that indigenous breeds of goats do survive under natural tsetse challenge. This enigma might be explained by the fact that some species of tsetse exhibit definite host feeding preferences [27], and, therefore, in an area where several host species exist certain animals will be more liable to tsetse attack and infection than others. Whether this explanation is adequate for small-stock awaits full investigation.

Evidence in wildlife for genetic resistance to trypanosomiasis

It is widely accepted that many species of wildlife are highly resistant to trypanosomiasis, that is, exhibit marked trypanotolerance, despite in some cases being highly attractive to tsetse flies. Findings in early experimental studies (reviewed in [20]) have more recently been confirmed in African buffalo (*Syncerus caffer*) (Figure 9), oryx (*Oryx beisa*), eland (*Taurotragus oryx*) (Figure 10), and waterbuck (*Kobus defassa*) which had not been previously infected with trypanosomes (28]. Following syringe inoculation or experimental tsetse infection with *T.*

congolense, T. vivax, or *T. brucei*, these four species all exhibited a marked degree of resistance to trypanosomiasis. This was reflected in low transient parasitaemias and small temporary reductions in red blood cell levels (Figure 11). An exception to this picture occurred in water buck infected with *T.brucei*; while red blood cell values decreased only transiently, parasitaemia remained high and corresponded to the levels recorded in domestic livestock which develop anaemia. Wild bovidae offer an unique opportunity to study the possible mechanisms that allow the host to resist trypanosome infections and are currently being used for this purpose at ILRAD, in collaboration with the Kenya Veterinary Research Laboratories.

Productivity of trypanotolerant livestock

Until recently, it was a widely held view that, because of their smaller size (Table 2), trypanotolerant breeds were less productive than more susceptible ones. However, as pointed out by C. J. Roberts and A. R. Gray [29], many misconceptions about trypanotolerant breeds have arisen because productivity indices obtained in herds exposed to tsetse and maintained under low levels of nutrition have been compared with data collected from a variety of breeds of cattle kept under good conditions.

In a major survey of the status of trypanotolerant livestock in 18 countries in West and Central Africa, indices of productivity were examined using all the basic production data that could be found for each region, each management system, and for different levels of tsetse challenge [3]. A total of 30 trypanotolerant cattle herds and 20 Zebu herds were investigated. The traits evaluated included reproductive performance, cow and calf viability, milk production, growth, and cow body weight. These parameters were used to compute the index of the total weight of calf and live weight equivalent of milk produced per 100 kg of cow maintained per year. This final index related these production traits back to the actual weight of breeding cow that had to be supported, this being closely connected with maintenance costs. The traits and production indices were derived for two basic management systems, village and ranch or station, and for four levels of tsetse challenge, arbitrarily designated zero, low, medium, and high. Estimates of productivity for Zebu herds under ranch/station conditions in low or tsetse-free areas averaged 38.6 kg per 100 kg of cow maintained per year. This compared with 37.1 kg for trypanotolerant herds in ranch/station conditions in low tsetse challenge areas (Table 3). Thus; the productivity of Zebu was only four per cent higher than that of the N'Dama and West African Shorthorn, strongly indicating that the productivity of trypanotolerant cattle relative to other indigenous types was much higher than previously assumed. Directly comparable data between breeds were not available in many areas because the level of tsetse–trypanosomiasis risk was such that breeds other than trypanotolerant ones could not survive. A striking example of this occurred in field studies carried out by ILRAD in The Gambia from 1975 to 1979. During the course of an eight-month investigation, 21 of 31 Zebu died of trypanosomiasis in an area where the challenge from *G. palpalis gambiensis* was such that only 13 of 37 N'Dama became transiently infected and showed no evidence of disease. Furthermore, of 31 Zebu maintained in a *G. m. submorsitans* area of The Gambia, all died of trypanosomiasis, whereas only 15 of 73 N'Dama succumbed to the disease [20].

Table 3. *Influence of breed on productivity [3].*

Breed	Management	Tsetse challenge	Productivity index (kg)[a]
Zebu	Ranch	Zero-low	38.6
N'Dama and West African Shorthorn	Ranch	low	37.1

[a]Total weight of one year old calf and liveweight equivalent of milk produced per 100 kg of cow per year.

Environmental influences in trypanotolerance

While there is evidence in cattle that the level of innate resistance can be enhanced by previous exposure to trypanosomiasis, it must be emphasised that trypanotolerance is reduced by several factors that affect the host and its environment. One of the most important factors, which affects the stability of trypanotolerance, is the severity of the tsetse–trypanosomiasis risk to which animals are exposed. While critical data estimating the level of tsetse–trypanosomiasis risk are lacking, preliminary findings indicate that as the level of risk increases, productivity falls (Table 4) and that N'Dama can suffer severely from the disease as judged by stunting, wasting, abortion, and even death. In addition, stress (work, pregnancy, parturition, lactation, suckling), intercurrent disease, and poor nutrition have been identified as factors reducing the level of trypanotolerance [20].

Table 4: *Influence of level of tsetse challenge on productivity of trypanotolerant cattle [3].*

Level of tsetse challenge	No. of herds	Productivity index (kg)[a]
Zero	3	40.1
Low	13	31.9
Medium	10	23.2
High	4	18.8

[a]Total weight of one year old calf and liveweight equivalent of milk produced per 100 kg of cow per year

On the other hand, there is now evidence to indicate that cattle, both of trypanotolerant and trypanosusceptible breeds, which survive trypanosomiasis, with or without the aid of chemotherapy, gradually become more resistant to infection (reviewed in [20]). This situation probably causes much of the controversy over the belief held by many that the resistance of trypanotolerant breeds is largely the result of immunity acquired to local trypanosome strains and that tolerance disappears if cattle are moved to distant locations. While exposure to new trypanosome strains will undoubtedly lead to infection, the superior genetic resistance of the trypanotolerant breeds will ensure that their chances of survival and acquiring resistance in new locations will be significantly greater than for trypanosusceptible breeds. This has been shown in several countries in West and Central Africa where trypanotolerant breeds of cattle have been imported and successfully established in tsetse-infested areas where previously other breeds could not survive [3]. However, it must be recognised that the movement of any breed over large distances, with resultant exposure to different diseases, environments, and management systems, involves considerable stress and requires a period of adaptation.

Thus, trypanotolerance does not represent a refractory state. It is essential, therefore, in order to realise the full potential of trypanotolerant breeds, to identify the main factors which affect the stability of the trait so that appropriate management measures—for example, the strategic use of trypanocidal drugs—can be considered under adverse circumstances.

Mechanisms

Increased resistance to trypanosomiasis in trypanotolerant compared to susceptible animals would appear to be related to a better innate ability to respond to the trypanosome and as a result to control and reduce levels of parasitaemia. This capacity has usually been attributed to a superior immune response. Other factors that could also contribute to trypanotolerance include the ability to prevent the development of anaemia, reduced attractiveness to tsetse attack, and increased resistance to the effects of infection due to physiological characteristics which aid survival. Identification of the main factors responsible for trypanotolerance and investigation into their underlying mechanisms, is an important part of ILRAD’s research

programme. These studies should achieve a better understanding of host–parasite interactions which might allow new methods for controlling trypanosomiasis to be devised (cf. later).

1. Immune response

Despite the general belief that differences in their immune response account for the greater capacity of the trypanotolerant livestock to control parasitaemia, the published evidence for this is limited. It has been found that N'Dama with previous experience of trypanosomiasis were able to eliminate trypanosomes more rapidly than Zebu, following renewed challenge. Employing an *in vitro* test that involved the use of sera from the challenged animals to inhibit trypanosome respiration, the activity of N'Dama sera was superior to that of Zebu [11]. Similarly, using a serum neutralisation test, the immune response to trypanosomes was found to be higher in N'Dama than in Zebu [10]. Further evidence that the N'Dama might possess a better immune response was suggested when an association between the greater capacity of N'Dama (compared to Zebu) to control *T. brucei* infections and their ability to recognise at least one of three common trypanosome antigens of 110, 150, and 300 thousand daltons was demonstrated [30]. Such studies need to be extended in domestic livestock to provide more substantial information on the role of the immune response.

In the search for an underlying explanation of the mechanism(s) of trypanotolerance, experimental work has been carried out at ILRAD on inbred genetically homogenous strains of mice that exhibit different degrees of resistance to trypanosomiasis [20, 31]. Some of the experimental approaches used would not be possible in genetically heterogenous breeds of domestic livestock.

It was demonstrated in mice that the rate of differentiation of *T. brucei* from rapidly dividing slender forms to non-dividing senescent stumpy forms (Figure 12), correlated with capacity of the host to control and reduce parasitaemias [32]. Furthermore, the rate of parasite differentiation influenced the kinetics of antibody production, because antibody responses were stimulated by stumpy but not by dividing slender forms of the parasite [33, 32]. In addition, it was shown that the host exerts an important influence on the degree of differentiation exhibited by a given population of *T. brucei*. It was found in mice that two populations *of T. brucei* which were pleomorphic and monomorphic respectively, were equally pleomorphic when inoculated into cattle [34]. When parasites were recloned back into mice they reverted to the original phenotypes. These findings indicated that factors which regulate differences in the rate of parasite differentiation might play a central role in determining host susceptibility to infection.

When parasite differentiation was compared in mouse strains of high and low susceptibility, it was found that the lower level of parasitaemia displayed by the resistant mice was associated with more rapid parasite differentiation and a superior antibody response [31].

The demonstration of a non-dividing late bloodstream form of *T. vivax* [35], together with the report of a similar stage with *T. congolense* [36], indicates that a series of events similar to those described for *T. brucei* might be involved in determining host susceptibility to *T. vivax* and *T. congolense*. As with *T. brucei*, susceptibility in mice to *T. vivax* [37] and *T. congolense* [20] is related to the capacity to control parasitaemia, as well as to better immune responses. Preliminary studies with *T. brucei* suggest that regulation of parasite growth and differentiation may also be important in influencing the susceptibility of cattle and wild bovidae to infection.

Not only are the factors responsible for parasite growth under control of the host but it is also possible to manipulate them using immunostimulants such as *Corynebacterium parvum*. When we treated mice with *C. parvum* trypanosome differentiation occurred earlier, subsequent peaks of parasitaemia were lower and of shorter duration, and mice survived for

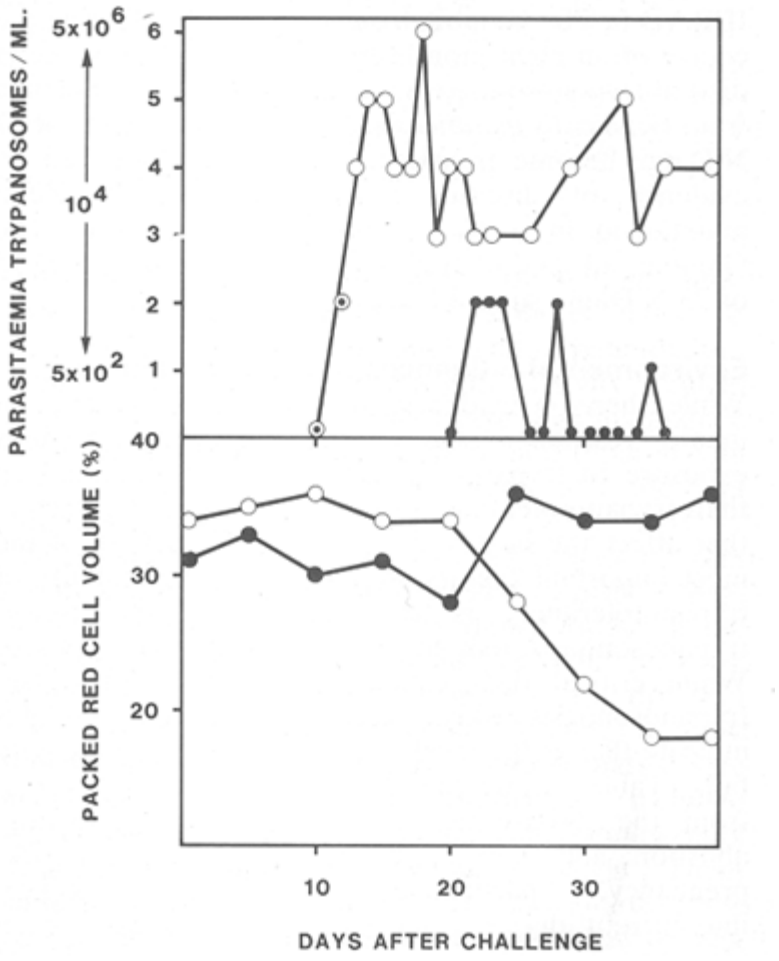
longer. Similar results were achieved with *T. congolense* [20].

These findings suggest that genetic resistance to animal African trypanosomiasis is associated with an event that regulates parasite growth and differentiation and determines how rapidly the immune response is triggered. Identification of the factor(s) mediating this event may be the key to our understanding of the basis of trypanotolerance.

2. Anaemia

One of the major features of infected trypanotolerant animals is that they develop less severe anaemia than more susceptible breeds (Figures 3 and 11). A series of erythrokinetic and ferrokinetic studies of N'Dama and Zebu infected with *T. congolense* or *T. brucei* showed that the anaemia and its underlying processes broadly reflected the numbers of parasites in the blood (reviewed in [20]). Thus, it appeared that the differences in anaemia between N'Dama and Zebu were due to their capacity to control parasitaemia and could not be attributed to differences in innate erythropoietic responses. In contrast to cattle, major differences were found in the severity of the anaemia between the relatively resistant Red Maasai sheep and the more susceptible Merino, despite similar levels of parasitaemia [20]. Also, in wild animals significant anaemia rarely occurs, despite fairly high levels of parasitaemia in some species; for example, in the waterbuck infected with *T. brucei* [28]. It might be that the red blood cells of certain species have a greater capacity to resist the pathogenic effects of trypanosomes or that resistant hosts are able to mount a faster and more efficient erythropoietic response.

Figure 11. *Parasitaemia and PCV in a buffalo (•) and Boran (o) challenged with* Glossina morsitans centralis *infected with* T. congolense*. In contrast to the Boran, the buffalo developed only a low level transient parasitaermia and showed no evidence of anaemia*.



3. Attractiveness to tsetse

Another explanation for survival in areas infested with tsetse is that certain breeds and species are rarely subjected to tsetse attack. As discussed earlier, this might be the reason why sheep and goats in tsetse-infested areas are only rarely infected and are usually in excellent condition, despite the fact that they (especially goats) are highly susceptible to experimental infection. Studies based on blood meal analysis indicate that tsetse exhibit definite host feeding preferences which vary with tsetse species [27]. However, these preferences are affected by a large number of environmental factors, of which host availability is one of the most important [38]. The potential significance of tsetse preferences has been alluded to in small-stock and its possible importance was shown when the attractiveness of cattle and oryx to tsetse fly was compared under critical experimental conditions [20]. It was found that five times as many tsetse were attracted to cattle. Furthermore, full engorgement on cattle of 279 tsetse was recorded during the period of observation, whereas, four tsetse were seen to obtain partial blood meals from oryx during the same time; this was partly the result of oryx killing tsetse with their horns. Whether attractiveness to tsetse differs between breeds of cattle is not known but results from The Gambia, where groups of N'Dama and Zebu were exposed to a high *G.m. submorsitans* challenge (cf above), would indicate that there was no major difference in attractiveness, as all cattle became infected and there was no significant difference between breeds in the time to first detectable parasitaemia [15].

Recently, significant new observations have been made on factors influencing host attractiveness to tsetse. While colour, size, and movement have been considered important, G. A. Vale [39] has demonstrated the overriding importance of host odour and the attractant powers of carbon dioxide and acetone in bovine breath. Another possibly related factor is that cattle suffering from loss of condition are less attractive to tsetse [40].The identification and characterisation of factors which attract, as well as those which repel tsetse [39), may have important implications in the development of novel strategies for the future control of animal African trypanosomiasis.

4. Physiological Factors

Trypanotolerance may also be related to reduced susceptibility to the effects of the infection because of a number of physiological factors possessed by trypanotolerant breeds which aid survival. These factors possibly include superior ability to utilise food, to tolerate heat, and to conserve water. Unfortunately, critical data concerning these parameters are not available. However, where food intake is marginal, as it is in many areas of Africa, breeds with an inherently high maintenance requirement will suffer most, as demonstrated by weight loss or reduced weight gains [41]. Thus, it is likely that trypanotolerant breeds with much lower inherent maintenance requirements are probably better adapted to remain productive in the conditions which prevail in West and Central Africa.

In the same way, what little is known about water conservation and heat tolerance in trypanotolerant breeds would suggest that they have developed considerable capability to conserve water and to tolerate heat. Thus, it was found that N'Dama could withstand not only higher levels of humidity than Zebu [42], but also have been reported to experience a considerable range in rectal temperature from 34.4°C at dawn to 41.1°C in late afternoon [43]. The teleological argument for such a phenomenon is that thermoregulation under cold conditions—that is, less than 20°C for tropical breeds of cattle—requires the use of body energy stores. Thus, when caloric intake is low, energy is conserved by allowing the body temperature to fall [44]. On the other hand, Zebu regulate their temperature within a range of about 2°C and neither periodic heat load nor dehydration have any significant effect on this [45].

With regard to water metabolism, studies in East Africa have shown that the water requirement of the indigenous East African Zebu is about half that of Herefords and is similar to that of several species of wild bovidae, such as the eland [45]. While there is no published information on the trypanotolerant breeds, it is possible that they have adapted to an even greater extent as indicated by the fact that N'Dama turn over less water than Zebu in terms of ml per kg body weight [46].

Potential and future exploitation

African Governments and International Agencies [47, 48] are now recognising that the exploitation of trypanotolerant breeds of domestic livestock, in particular the N'Dama, has immediate potential for utilising tsetse-infested areas to meet the increasing demand for food in Africa. This recognition is based on the knowledge that trypanotolerant breeds of cattle are productive, that their trypanotolerance is innate, and that these breeds have already been successfully established in tsetse-infested regions, where other breeds rapidly succumbed to the infection. It is estimated that an area of some two million km² in West and Central Africa is suitable for trypanotolerant cattle without any additional control measures [47]. FAO [49] considers the average carrying capacity of this region at 20 cattle/km², as compared with the current 3.4/km^2. Equivalent increases would also be possible for sheep and goats; that is, approximately five times as many animals could be maintained. At present, the livestock biomass per inhabitant in West and Central Africa is only 26 kg, compared with 136 kg for the remainder of Africa south of the Sahara and 79 kg for the continent as a whole [3]. Already certain countries, including Nigeria and Gabon, have recognised the potential contribution that trypanotolerant breeds can make to increasing their capacity to meet the growing need for food. As a result, they are importing N'Dama (Figure 13) in order to establish breeding nuclei for future livestock development in tsetse-infested areas.

However, as discussed earlier, trypanotolerant animals can suffer from trypanosomiasis and may even die under certain circumstances; for example, high levels of tsetse–trypanosomiasis risk. Thus, in order to realise the maximum potential of trypanotolerant breeds it is necessary to identify and quantify the environmental factors which influence the stability of the trait so that the appropriate management measures can be instituted. Furthermore, it is important to understand the mechanisms responsible for trypanotolerance with a view to enhancing the trait. Current work at ILRAD and ILCA is being carried out in these two areas. These organisations with inputs from a number of donor agencies, are co-ordinating a network of national research epidemiological and productivity studies. At present, it is planned to include nine countries in West and Central Africa, Zaire, Gabon, Nigeria, Ivory Coast, Congo, Benin, Togo, Senegal, and The Gambia. The objective of these investigations is to evaluate the productivity of trypanotolerant breeds of domestic ruminants, and of other breeds where available, living under different levels of quantified tsetse–trypanosomiasis risk. Once essential baseline data, which are completely lacking at present, are established and meaningful productivity indices, based on performance, economic, health, and tsetse information, are computed, it should be possible:

1. To predict the productive capacity of different breeds living under different levels of tsetse–trypanosomiasis risk; that is, to determine precisely at what level of risk N'Dama cease to be productive and when they need health or improved management care. This knowledge will lead to more efficient use of different breeds and, consequently, to increased livestock production.
2. To evaluate the cost-effectiveness and impact of the introduction of any control method; for example, trypanocidal drugs, tsetse control, improved management, and nutrition.

A recent major development in the exploitation of N'Dama cattle is that the Government of The Gambia is establishing a N'Dama Centre with which ILRAD and ILCA will have major links

and inputs. The main objectives of this Centre are, firstly, to provide channels for marketing and export of stock, and, secondly, to undertake epidemiological studies to evaluate the productivity of N'Dama exposed to different levels of quantified tsetse–trypanosomiasis risk. This project will service some 60 000 N'Dama based in village herds in The Gambia and will be extended into Senegal.

At the same time, ILRAD scientists are carrying out basic research in order to obtain a better understanding of trypanotolerance, especially with regard to the factors which control parasite growth and allow the development of an effective immune response. This knowledge could produce new methods for controlling the disease. For instance, techniques might be devised for enhancing resistance to trypanosomiasis, either by the regulation of parasite growth by the use of suitable drugs, or by recombinant DNA technology (cf later). These studies are being carried out on mice, domestic livestock, and wild bovidae; more recently, embryos from N'Dama in The Gambia have been introduced into cattle at ILRAD to provide animals to extend these investigations (Figure 14).

One of the major constraints to the more widespread use of trypanotolerant breeds of cattle is the limited number available; there are 3.4 million N'Dama and 1.8 million West African Shorthorn [3]. At present, the demand for N'Dama heifers and bulls greatly exceeds the number available for distribution. Furthermore, the period of acclimatisation that animals need to adapt to different environmental conditions, management, and diseases means that a lengthy investment is required before any significant development and economic return can be expected. However, it is probable that a number of these constraints could be overcome by the use of embryo transfer technology in trypanotolerant breeds. In selected situations, such an approach would allow more rapid multiplication of rare breeds, and the production of animals adapted to the local circumstances. The potential of this approach has been further enhanced recently by the production of a monoclonal antibody which recognises the HY antigen, making it possible to select for sex in six-day-old calf embryos [50].

In the long term, the availability of embryos offers the possibility of genetic manipulation by inoculating genetic material into the egg just after fertilisation [51]. The feasibility of this approach was clearly demonstrated when a DNA fragment containing the promoter of the mouse metallothionen-I gene fused to the structural gene of rat growth hormone was microinjected into fertilised mouse eggs [52]. About one third of the mice that developed grew significantly larger than their littermates. Several of these mice also had high levels of the fusion m RNA in their liver and growth hormone in their serum. The potential of this approach in livestock development could be enormous, as it is possible to envisage the introduction of genes selected for specific function, such as, trypanotolerance or growth, into recipients selected for other characteristics.

In conclusion, it would appear that rigorous natural selection, over several thousand years, of characteristics that permit survival in the face of tsetse challenge has provided Africa with a group of animals capable of making a significant contribution towards alleviation of the continent's food problems by allowing more effective livestock and mixed agriculture development in the humid and semi-humid tsetse-infested regions.

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