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Review

# Immunogenetic influences on tick resistance in African cattle with particular reference to trypanotolerant N'Dama (*Bos taurus*) and trypanosusceptible Gobra zebu (*Bos indicus*) cattle

Raffaele C. Mattioli [a,*], Vijay S. Pandey [b], Max Murray [c], Julie L. Fitzpatrick [c]

[a] *International Trypanotolerance Centre, PMB 14, Banjul, Gambia*

[b] *Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium*

[c] *University of Glasgow Veterinary School, Bearsden Road, Bearsden, Glasgow G61 1QH, Scotland, UK*

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**Abstract**

In sub-Saharan Africa, tick infestation and tick-borne infections together with tsetse-transmitted trypanosomosis arguably constitute the main parasitological disease complex constraining livestock production. Resistance to tick attack and tick-borne micro-organisms (TBMs) varies among different breeds of cattle. The magnitude of losses due to these parasites is related to an extent to the degree of breed resistance. Generally, zebu (*Bos indicus*) cattle possess a higher resistance to ticks and TBMs than European (*Bos taurus*) cattle. The host's immune system would appear to be the single most important factor that regulates this resistance. This paper reports on the main effector immune mechanisms governing resistance against ticks and TBMs. The cellular immune response appears more effective and stable than humoral immunity in modulating resistance to ticks and TBMs. Similarities between the immune mechanisms employed by trypanotolerant N'Dama (*B. taurus*) cattle, when infected with trypanosomes, and those elicited by tick bites and TBMs seem to exist, particularly at the skin level in the early phases of parasitic invasion. Moreover, there is evidence that in the N'Dama breed, resistance against ticks per se also has a genetic basis. Therefore, the N'Dama appears to be a unique breed in that it exhibits resistance to several parasitic diseases and/or infections, including helminths, when compared to other cattle breeds in West Africa. It is concluded that the multi-parasite resistant traits of the N'Dama breed should be exploited in those areas where trypanosomosis, ticks and tick-borne diseases constrain animal production. This should be of benefit for low-input farming systems where the use of chemicals for prophylaxis and therapy is limited by their relatively high cost. Additionally, the potential

* Corresponding author. Tel.: +220-462928/463270; fax: +220-462924.

*E-mail address:* raf.mattioli@commit.gm (R.C. Mattioli)



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contribution of multiple disease resistant N'Dama cattle should be considered in crossbreeding programmes with exotic dairy breeds for increasing milk production in West Africa. 

*Keywords:* Ticks; Tick-borne diseases; Host resistance; N'Dama; Gobra zebu

## 1. Introduction

In sub-Saharan Africa, ticks, tick-borne infections (TBIs), such as anaplasmosis, babesiosis, cowdriosis and/or tick-associated diseases, such as dermatophilosis (Morrow et al., 1993), together with tsetse-transmitted trypanosomosis, constitute arguably the major pathological parasite complex responsible for limiting animal production (Jordan, 1986; Jongejan and Uilenberg, 1994). The presence of such diseases also constrains the introduction of exotic upgraded cattle with a view to improving the efficiency of livestock industry. In addition, a study conducted in Ghana evidenced that little benefit can be obtained from crossbreeding programmes of indigenous breeds with improved European breeds, due to harsh tropical environment (Rege et al., 1994). A recent report estimated annual world-wide losses associated with ticks and tick-borne diseases to be in the range of 18 billion US dollars (de Castro, 1997). In Africa, losses due to tsetse-transmitted trypanosomosis are evaluated between 6 and 12 billion US dollars per year in the cattle industry alone (Hursey and Slingenberg, 1995).

### *1.1. Breed variation in production losses*

Besides the capacity to transmit a wide spectrum of pathogens, tick infestations per se cause important losses to cattle production. In Australia, losses due to *Boophilus microplus* have been calculated as 0.6 g of liveweight per engorged female in Brahman cattle (FAO, 1984) and up to 1.5 g in Brahman x European crossbred cattle (Sutherst et al., 1983). In Africa, weight-loss in indigenous zebu cattle attributed to each engorged *Amblyomma variegatum* female ranged from 46 to 63 g (Pegram and Oostervijk, 1990; Stachurski et al., 1993). Infestation by *A. variegatum* males can also have a deleterious effect on cattle growth (Pegram and Chizyuka, 1990), although larval and nymphal stages of *A. hebraeum* and *Rhipicephalus appendiculatus* would appear to have a negligible impact on meat and milk production (Norval, 1990). The negative effect of tick infestation as a whole on cattle production is stressed by the evidence that acaricide-treated animals gain more weight than those left untreated (de Castro, 1987).

The magnitude of losses due to tick infestation varies with the genotype of cattle (Lemos et al., 1985; Scholtz et al., 1991), the species of infesting tick (Norval et al., 1997a,b) and the level of infestation (Sutherst et al., 1983). Moreover, within a genotype, losses per tick unit increase with the number of attached ticks (Pegram et al., 1989). Weight loss was reported in Gudali zebu cattle infested with *A. variegatum* (Stachurski et al., 1993), European cattle infested with *R. appendiculatus* (Norval et al., 1988) and European x indigenous African cattle which were multi-tick species infested (Scholtz et al., 1991). Similarly, milk production was reduced by 9 g per each engorging *R. appendiculatus* female in indigenous Sanga cattle (Norval et al., 1997b). In contrast, liveweight gain in Creole zebus was not affected by *A. variegatum* infestation (Stachurski et al., 1988), no significant reduction in weight gain in Kenana (*Bos indicus*) cattle infested with *A. lepidum* (Tatchell, 1988) or no significant reduction in milk production was observed in Sanga and Sanga x Brahman cattle infested with *A. hebraeum* (Norval et al., 1997a).

A pre-immune status to TBIs, so-called endemic stability, often establishes in indigenous cattle through a continuous contact with the infectious agents from early in life. The presence of endemic stability is claimed to be the main factor in limiting losses, mainly expressed in terms of low or absence of mortality due to TBIs in indigenous cattle populations (Lawrence et al., 1980). In field situations, it is difficult to separate the combined effects on productivity caused by ticks and the diseases they transmit. However, Solari et al. (1992) and Meltzer et al. (1995) postulated that the carrier state of *Babesia* spp., *Anaplasma* spp. and *Cowdria ruminantium* does not reduce productivity. In contrast, the detrimental effect of anaplasmosis and babesiosis on cattle production has been reported even under conditions of endemic stability (Mullenax, 1986).

In summary, infestation with ticks may cause production loss measured by reduced growth or milk production. However, not all tick infestations have been shown to result in production loss, and as the effect of endemic stability varies with the TBIs, it is difficult to assess accurately the costs of the carrier state. It can, therefore, be concluded that the occurrence of local tick species and tick-transmitted pathogens, the different bovine genotypes available and expected production targets (i.e. meat, milk or both) are interacting factors that should all be considered in establishing economically efficient cattle production systems in areas affected by ticks (Tatchell, 1992).

### 1.2. Exploitation of natural resistance

The various interpretations of the words 'resistance' and 'tolerance' may lead to confusion. Therefore, in the context of this paper, 'resistance' and 'tolerance' are the terms used to define the ability of certain genotypes of domestic ruminants to limit parasite burdens and/or their pathological consequences.

Natural resistance to a number of vectors and vector-borne micro-organisms exists in ruminants and this varies with breed (Wakelin, 1991). The use of ruminant genotypes possessing an innate resistance trait to trypanosome infections has been recommended as an economically acceptable option to reduce losses due to trypanosomosis in tsetse-affected areas (Murray et al., 1991). Similarly, the use of naturally tick-resistant cattle biotypes should be incorporated in tick control schemes as a means which could contribute to the biological control of tick infestations (Guglielmone et al., 1992; Tatchell, 1992). This assumption is supported by the observation that field burdens of *Boophilus* spp. (Sutherst and Utech, 1981) and *Amblyomma* spp. (Barnard, 1990) are modulated by the presence of tick-resistant cattle. In Australia, host-tick resistance has been successfully exploited in cattle breeding programmes to limit the impact of *B. microplus* infestation (Seifert, 1984). Therefore, breeding schemes based on dual trypanosome and tick-resistant cattle could contribute to:

1. a reduction in the use of chemicals as trypanotolerant animals require a lower number of trypanocidal treatments than susceptible animals (Murray and Black, 1985; Paling et al., 1991b); in the case of ticks, use of acaricides and relative operational costs would be reduced through a lower frequency of acaricidal treatments: cattle would be treated when tick burden is expected to exceed the economic damage threshold (Meltzer and Norval, 1993); in the case of TBIs, available vaccines would be used, in combination with acaricides, only in susceptible animals (McMillan and Meltzer, 1996; Pegram et al., 1996);
2. an increase in the effectiveness of drugs, as naturally-resistant animals respond better to treatment (Doenhoff et al., 1991);
3. a reduction in the risk and the incidence of drug-resistant strains of pathogens and vectors;
4. lower the cost of animal production through a diminished pathological impact and, consequently, a reduced use of drugs.

Two major types of cattle are present in the West African region: *Bos taurus* type, e.g. N'Dama, and *Bos indicus* type, e.g. Gobra zebu (Shaw and Hoste, 1987). In addition to the well known trypanotolerant feature of the N'Dama cattle (Murray et al., 1982), preliminary observations made in West Africa reported that this breed might also possess a certain degree of resistance to tick infestation (Mattioli et al., 1993, 1995a; Koney et al., 1994a). The N'Dama breed seems also to have the ability to resist *A. variegatum*-associated dermatophilosis (Koney et al., 1994a). It is suspected that resistance to dermatophilosis in Creole zebu cattle populations derives from a certain degree of historical crossing with N'Dama cattle (Maillard et al., 1993a,b).

The purpose of this paper is to review the potential mechanisms modulating resistance to ticks and TBIs in hosts with particular reference to N'Dama and Gobra zebu cattle. The practical relevance of breed resistance is considered.

## 2. Mechanisms of resistance to different tick species

The immune mechanisms modulating tolerance to African animal trypanosome infection are genetically based (Kemp et al., 1996). It has been postulated that trypanotolerance in N'Dama cattle has developed through continuous and prolonged contact between host and parasite over several thousand years (Mattioli and Wilson, 1996). A similar hypothesis was made by Bennet and Wharton (1968), Seifert (1971) and Barré et al. (1988b) in relation to the resistance to locally occurring *B. microplus*, *B. decoloratus* and *A. variegatum* ticks in Australian Brahman, Africander and Creole zebu cattle, respectively. This assumption is supported by the fact that imported Brahman zebu cattle, resistant to *B. microplus*, were more susceptible than indigenous Nguni zebus to local infestation of *B. decoloratus* (Rechav and Kostrzewski, 1991). Thus, it appears that resistance to ticks differs with the breed (Clarke et al., 1989; de Castro and Newson, 1993) and with the species of ticks (de Castro, 1991). Several studies have shown that resistance to the one-host ticks *B. microplus* (O'Kelly and Spiers, 1976; Wagland, 1980; Lemos et al., 1985; Brizuela et al., 1996) and *B. decoloratus* (Rechav and Kostrzewski, 1991) is proportionally related to the amount of zebu (*B. indicus*) genes in the breed, although a certain degree of resistance to the former tick species has been observed in Spanish *B. taurus* (Guglielmone et al., 1992). However, evidence for a genetic trait for resistance to multi-host ticks, such as *R. appendiculatus*, in *B. indicus* breeds is not as strong as for one-host ticks (Kaiser et al., 1982; Smith et al., 1989). This supports the view that breed tick resistance might vary with the species of infesting tick (Ali and de Castro, 1993). Thus, heterospecific resistance appears to be low or even absent among different genera of ticks (Rechav et al., 1989), while a certain degree of cross-resistance is expressed to tick species belonging to the same genus (McTier et al., 1981). Studies conducted in N'Dama and Gobra zebu cattle in The Gambia showed the former to possess a higher degree of resistance than Gobras against adult ticks of two genera characterized by long hypostome, such as *A. variegatum*, *Hyalomma truncatum* and *H. marginatum rufipes* (Mattioli et al., 1993, 1995a). In contrast, N'Dama and Gobra zebu cattle appear to be equally susceptible to ticks with short mouth-parts, i.e. *Boophilus* spp. (Mattioli and Cassama, 1995) and *Rhipicephalus* spp. (Mattioli et al., 1998a).

### 2.1. The cellular response to ticks

Walker and Fletcher (1986) suggested that differences in cellular function could exist between mammalians in response to tick bite and that they could also differ in respective immunological effector mechanisms.

Experimental studies investigating the mechanisms of tick resistance indicate that the skin reaction of the host, elicited by tick bite and tick's saliva components, is one of the major factors modulating the response to tick attachment (Brown et al., 1984; Walker and Fletcher, 1990; Adamson et al., 1991; Fivaz et al., 1991). Local skin reactivity is mediated by histamine and other inflammatory mediators. Histamine, derived from basophils and degranulation of mast cells, appears to be directly involved in tick detachment (Kemp and Bourne, 1980) and in inhibiting tick salivation and engorgement (Wikel and Bergman, 1997). Moreover, histamine stimulates host grooming responsible for tick removal (Kaufman, 1989). In bovine skin, higher concentrations of histamine have been found in tick-resistant cattle than in susceptible cattle (Willadsen, 1980). Mast cell degranulation has also been observed in trypanotolerant African buffaloes (*Syncerus caffer*) following tsetse bite while the phenomenon was not reported in trypanosensitive Boran (*B. indicus*) cattle (Grootenhuis et al., 1985). Moreover, quantitative and qualitative characteristics of mediators released by mast cells may vary among animal species (Gordon et al., 1990). Thus, theoretically, a greater release of inflammatory mediators, following tick bite, may occur in trypanotolerant N'Dama cattle, leading to higher tick rejection, than in trypanosusceptible Gobra zebu cattle. The intensity of the inflammation reaction induced by tick bite is an important factor in inducing an effective host response (Kaufman, 1989).

The site of induction of the inflammatory response may help to explain differences in level of infestation among stages and species of ticks. Mast cells in bovine skin are localized at the level of the dermis (Akol and Murray, 1982) but the hypostome of *Boophilus* spp. only reaches the Malpighian layer of epidermis (Moorhouse and Tatchell, 1986, in Kaufman, 1989). Therefore, stimuli derived from *Boophilus* spp. bites might not be effective in evoking a mast cell response either in N'Dama or Gobra cattle. This might partially explain the absence of significant difference between N'Dama and Gobra cattle in the number of attached *A. variegatum* nymphs (Mattioli et al., 1995a), which have a hypostome shorter than adults and similar to that of *Boophilus* spp. Conversely, in the same study (Mattioli et al., 1995a) N'Dama carried a significantly lower *A. variegatum* burden in comparison with Gobra zebu cattle.

In addition to mast cell degranulation, skin biopsies of the point of tick attachment revealed cutaneous infiltration of eosinophils, neutrophils and basophils (Binnington and Kemp, 1980; Walker and Fletcher, 1986). The pathological consequences of this cell infiltration are congestion, oedema and plasma exudation at the tick feeding site with negative effect on tick engorgement capacity (Fivaz et al., 1991). Furthermore, the host's inflammatory skin response is considered as a factor capable of altering other biological traits of the tick life-cycle, such as egg hatching, and larval and nymphal moulting rates (Willadsen, 1980; Adamson et al., 1991). A comparative field study on tick susceptibility reported lower engorgement weight in *H. truncatum* and *A. variegatum* females feeding on N'Dama than in those feeding on Gobra zebu cattle (Claxton and Leperre, 1991). Moreover, under experimental laboratory conditions, a higher hatching rate was observed in eggs laid by *A. variegatum* fed on Gobra zebu than in those fed on N'Dama cattle, while viability of ova of *B. geigyi* did not differ in ticks fed on N'Dama and Gobra zebu cattle (Mattioli and Cassama, 1995). Together, these observations suggest the presence of a different and more effective anti-tick skin reactivity in N'Dama relative to Gobra zebu cattle following tick bites.

### *2.2. The humoral response to ticks*

Several attempts have been made to induce a protective host humoral response against ticks through inoculation of crude or purified tick extracts (recently reviewed by Barriga, 1994; Opdebeeck, 1994). Substances extracted from tick salivary glands stimulate antibody response in the host (Barriga et al., 1991b) and it has been reported that humoral immunity may contribute to tick resistance (Rechav et al., 1991). Brossard (1976) observed that antibody levels in the host correlate with resistance to *B. microplus* adults. Conversely, a negative relationship was reported between antibody titres against salivary gland antigens and resistance to *A. americanum* adults (Barriga et al., 1991a). Salivary gland extracts of *R. sanguineus* adults elicit a humoral response, while antigens derived from larvae and nymphs failed to evoke a detectable antibody response (Hernandez et al., 1994). Lloyd and Walker (1995) demonstrated that salivary material of *A. variegatum* adults is different from that of immature stages. These results would indicate that, among tick species, but also within the same species, larval, nymphal and adult instars vary in their capacity to activate the host humoral immune system. Structural and histochemical changes occurring in salivary glands of adult ticks during feeding determine variations in secretion of pharmacologically active substances (Walker et al., 1985). These substances may counteract the general host immune reaction (Bowman et al., 1997), including the antibody response (Fivaz, 1989). However, no difference was found in antibody levels against nymphal and adult *A. variegatum* salivary antigens between N'Damas and Gobra zebus exposed to field-tick challenge, although the N'Damas carried a significantly lower number of ticks than Gobra cattle (Claxton and Leperre, 1991). Furthermore, the antibody-mediated response to ticks does not seem to provide an effective and long-standing immunity to tick infestations, as high antibody titres are generally observed in highly infested animals (Willadsen et al., 1978; Schorderet and Brossard, 1993). This is also supported by the fact that antibody levels decline following repeated infestations (Barriga et al., 1991a) while resistance to ticks increases (Fivaz et al., 1991; Dossa et al., 1996). It has been shown that resistance is more effectively transferred with lymph node cells than with serum from tick-resistant animals (Wikel and Allen, 1976). Failure of effective humoral immune protection has also been reported in other host-ectoparasite systems: lambs which were highly susceptible to *Melophagus ovinus* had similar high antibody levels as resistant animals, and immunity could not be passively transferred with serum from resistant animals (Baron and Weintraub, 1987). It is thus difficult to ascribe a primary and efficient role in resistance against ticks to the humoral response.

### 2.3. Concluding reflections

From the foregoing observations it can be argued that resistance to antigenic stimuli associated with tick attack is modulated mainly by the host cutaneous cellular responses. The cellular response in the skin has been shown to be due mainly to cells associated with the innate response, i.e. mast cells, eosinophils, neutrophils and basophils. However, the potential contribution of cells associated with an acquired immune response, i.e. T and B lymphocytes, plasma cells, and cells capable of inducing immunity, i.e. macrophages and dendritic cells, should not be forgotten. There is evidence that innate resistance to ticks is conserved during repeated infestations whereas acquisition of resistance is more variable (Barriga et al., 1993), develops slowly, and is subject to immunosuppression (Baron and Weintraub, 1987). The genetic basis of tick resistance in the N'Dama breed is supported by the fact that the degree of infestation of *A. variegatum* and *Hyalomma* spp. in F1 N'Dama x Gobra cattle was at an intermediate level between the highest values observed in Gobra and the lowest levels found in N'Dama cattle (Mattioli et al., 1993). Tick resistance in the N'Dama breed can be altered by repeated infections with trypanosomes (Mattioli et al., 1998b). This finding has been ascribed to immunodepression caused by trypanosomosis. Nevertheless, in the same investigation, where cattle were submitted to continuous field challenges with tsetse and ticks, N'Dama carried fewer ticks than Gobra zebu cattle (Mattioli et al., 1998b). These observations support the view that resistance to ticks in N'Dama cattle is an innate trait, as postulated to exist in other cattle biotypes (Barriga et al., 1993).

In animals repeatedly infested with different levels of ticks, the degree of immune suppression was positively correlated to parasite burdens and increased with number of challenges (Inokuma et al., 1993). Thus, initially, higher tick burdens may increase the level of immunosuppression and render the host more susceptible to subsequent infestations, while repeated challenges of comparatively smaller number of ticks seem to increase host resistance (Schorderet and Brossard, 1993). In field conditions, it has been observed that the kinetics and level of reinfestation is, respectively, more rapid and higher in Gobra than in N'Dama cattle (Mattioli et al., 1998a). This phenomenon could have further interfered with the acquisition and/or conservation of effective mechanisms of immunity (Wikel and Whelen, 1986) to repeated tick attacks in relatively higher tick-susceptible Gobra, compared with N'Dama cattle when animals of both breeds were simultaneously exposed to equivalent field-tick challenge.

Complement also plays a role in tick resistance in guinea pigs (Wikel and Allen, 1977) and rabbits (Heller-Haupt et al., 1983). It has been reported (Wikel and Bergman, 1997) that complement has chemotactic properties for cells involved in the inflammatory reaction to tick bites. Tick bite and trypanosome infection appear to activate similar cascade events of complement components (Doko, 1996; Wikel and Bergman, 1997). Trypanotolerant cattle have the capacity to control complement level when challenged with *T. congolense* (Authié and Pobel, 1990). Thus, it can be postulated that the trypanotolerant trait of N'Dama comprises a factor(s) that contributes to a more effective cellular immune response to tick attack.

## 3. Resistance to tick-borne micro-organisms (TBMs) and relationship with trypanosome infection

The establishment of enzootic stability to tick-borne *Theileria parva bovis* (Fivaz et al., 1989) and *C. ruminantium* (Du Plessis, 1985) infection appears to be related to the challenging dose of the infectious agent. Moreover, the immune competence of the host confers a grade of resistance to *A. marginale* infection which is independent from chemoprophylaxis (Kuttler, 1986). Reduced transmission capacity of *Babesia* spp. has been reported in ticks attached on resistant animals (Francis and Little, 1964). Both the number of infectious kinetes of *Babesia* spp. and the relative infection rate transmitted by *B. microplus* increase with the duration of tick attachment (Gaido and Guglielmone, 1995). In animals, the grooming reflex stimulated by skin reaction to tick bite is accountable for tick detachment (Kaufman, 1989) and is expressed early in the tick-attachment process (Brown, 1985). Additionally, Brossard and Wikel (1997) suggested that the host immune response to ticks may regulate the transmission of *T. parva* and its development in the host. Hence, resistance to ticks may contribute to modulate the transmission rates of TBMs to a sub-pathological clinical level. Moreover, the minimum level of antigen stimulation required for the maintenance of enzootic stability to TBMs will be maintained, as also postulated by Fivaz et al. (1989) for *T. p. bovis* infection.

The occurrence of *A. marginale* (Murray et al., 1981) and *B. bigemina* infections (Kuttler et al., 1988) has been observed in The Gambia. The presence of *Amblyomma*-transmitted *C. ruminantium* has also been recently reported (Mattioli et al., 1994). In field conditions, the absence of mortality or overt signs of tick-borne anaplasmosis, babesiosis and cowdriosis in N'Dama cattle were attributed to endemic stability in traditionally managed N'Dama cattle populations (Kuttler et al., 1988; Mattioli et al., 1997). The same authors postulated, alternatively, the presence of a resistance trait to the above mentioned micro-organisms in the N'Dama breed (Kuttler et al., 1988; Mattioli et al., 1993, 1994, 1997). This conclusion was based on the fact that *A. marginale* antigenaemia remained relatively stable and was independent of the occurrence of potential vectors. In contrast, in Gobra zebu cattle, the *A. marginale* antigen rate fluctuated according to the occurrence of the vector (Mattioli et al., 1995a). Furthermore, a lower frequency of antibody peaks to *B. bigemina* was observed in Gobra than in N'Dama cattle when tick burdens were approximately equal in both breeds (Mattioli et al., 1995a). Similarly, Miller et al. (1984) reported higher antibody titres to *B. bigemina* in N'Dama than in zebu cattle.

Trypanosomosis (Darji et al., 1992) and other blood parasitic infections (Adachi et al., 1993) depress host-immune responses and increase susceptibility to other pathogens (Whitelaw et al., 1979). This phenomenon might explain the higher prevalence of *A. marginale* antigens and the higher mortality rate due to *C. ruminantium* infection observed in Gobra zebu in comparison with N'Dama cattle when animals of both breeds suffered from trypanosomosis (Mattioli et al., 1993, 1994). These two TBMs are taxonomically related (van Vliet et al., 1992) and homologies in immunodominant proteins have recently been reported (Barbet, 1995; Mahan, 1995). Similarities in the immunopathophysiology among other intra- and extracellular blood parasites have also been observed (reviewed by Holmes, 1987; Wright et al., 1988). Hence, the immune mechanisms governing trypanotolerance in the N'Dama breed could also protect against the disease or disorders resulting from other blood parasite infections, or act in synergy with other protective factors in conferring an effective resistance to TBMs. As already mentioned previously, evidence exists that trypanosome-induced immunodepression decreases mainly the humoral response (Rurangirwa et al., 1983) rather than cellular immunity in trypanotolerant N'Dama (Flynn and Sileghem, 1991). Comparative studies showed a more severe lymphocytopaenia in zebu experimentally challenged with *T. congolense* than in N'Dama cattle (Paling et al., 1991a; Williams et al., 1991). Additionally, it was not possible to associate the presence of antibodies with protective immunity to *T. parva* (Allison and Eugui, 1980; Emery et al., 1981; Eugui and Emery, 1981), *C. ruminantium* (Stewart, 1987; Deem et al., 1996) and *Amblyomma*-associated dermatophilosis (Barré et al., 1988a; How and Lloyd, 1988). Similarly, Mattioli et al. (1994) reported that occurrence of *C. ruminantium* antibodies was unrelated to death due to heartwater in experimentally *T. congolense*-infected Gobra zebu cattle. On the other hand, cell-mediated response appears to induce protective immunity to *T. parva* (Morrison et al., 1981) and *C. ruminantium* challenge (Mwangi et al., 1998). Hence, in cattle, cellular immunity may be the major protective immune mechanism against TBMs and the innate response may play a pivotal role. Cytokines are also reported to play an important role in resistance against *C. ruminantium* (Totté et al., 1993, 1996), *B. microti* (Orinda et al., 1994) and *T. brucei brucei* (Magez et al., 1993) infections. N'Damas, in comparison with zebu cattle, have greater levels of co-stimulatory cytokines which activate macrophage proliferation when infected with *T. congolense* (Sileghem et al., 1993). A higher lymphocyte proliferative response was observed in N'Dama resistant to dermatophilosis than in susceptible zebu Sanga type cattle (Koney et al., 1994a). Thus, the higher level of peripheral blood leucocytes found in different populations of the N'Dama breed as compared to various zebu biotypes, such as Gudali (Merlin, 1986) or Gobra (Claxton and Leperre, 1991; Mattioli, personal observation, 1994) may be related to the greater capacity of N'Dama cattle to resist trypanosome and tick-borne infections.

## 4. Concluding scientific remarks

In N'Dama cattle, both trypanotolerance (Karbe et al., 1982; Murray et al., 1984) and resistance to dermatophilosis (Maillard et al., 1993a,b) are under genetic control. African trypanosomes and the TBIs considered in this paper share a common epidemiological feature: the primary immunological host–parasite interface occurs at the skin of the host. In trypanosome infection the cellular skin reaction has been considered important for immunological priming (Akol and Murray, 1982). Dwinger et al. (1986) found a more pronounced cutaneous reaction in domestic and wild ruminants to intradermally tsetse-inoculated trypanosomes to be related to a higher degree of trypanotolerance. Skin response to intradermal injection of tick extracts has also been proposed as a method for assessment of resistance to ticks in cattle (Walker and Fletcher, 1990) in field conditions (Smith et al., 1989): greater skin reaction occurs in more resistant animals (Jongejan et al., 1989). Moreover, inflammatory cells present at skin level following tick bite are believed to be the first effective immune-defence to reduce inoculation rate of tick-transmitted micro-organisms (Wikel et al., 1994) and their multiplication (Musoke et al., 1984). It has been postulated that differences in the capacity to mount immune responses exist among cattle breeds and this might play a significant role in the development of tick resistance (Fivaz et al., 1991). Innate immune mechanisms, whether cellular or humoral, are activated more quickly by antigenic stimuli than acquired defences (Roitt, 1991). It may be possible that N'Dama's skin responds more effectively than Gobra's skin to antigenic and allergic stimuli resulting in limitation of parasite burdens at an early stage of invasion.

Differences in cellular response to tick bite have been reported in *B. indicus* and *B. taurus* (Brown, 1985). In future, histological and functional studies of the skin need to be conducted to investigate the antibody and antigen interactions and immune effector mechanisms involved in the cutaneous response in N'Dama and zebu cattle, such as Gobras, following tick bite and TBM inoculation.

## 5. Practical relevance and conclusion

The N'Dama breed appears to possess not only a natural resistance to trypanosomosis, but also to tick infestation. Moreover, they also show a certain degree of resistance to gastrointestinal nematode infections (Mattioli et al., 1992, 1995b). In all our comparative investigations conducted on different N'Dama and Gobra zebu cattle populations, maintained under different environmental conditions and exposed to various tick challenges, N'Damas consistently carried lower burdens of *A. variegatum* and *Hyalomma* spp. than Gobra zebus (Mattioli et al., 1993, 1994, 1995a, 1998a). These tick genera are directly responsible for serious damage to the skin, the udder and the teats (Uilenberg, 1990), with adverse consequences on calf survival (Asselbergs and Pereira, 1989). In Africa, *A. variegatum* is considered as one of the most harmful tick species (Yonow, 1995) and is also the main vector of cowdriosis (Walker and Olwage, 1987). Moreover, *A. variegatum* is the most abundant tick infesting cattle in the sub-humid and humid zones of West Africa (Vercruysse et al., 1982; Konstantinov et al., 1990; Gueye et al., 1993), including a large part of The Gambia (Mattioli et al., 1995a, 1998a). Infestations with *A. variegatum* and *H. m. rufipes* are often associated with the development of dermatophilosis (Koney et al., 1994b). It has been shown that tick control throughout the year is not economically profitable in indigenous N'Dama cattle in The Gambia (Mattioli et al., 1998a). Moreover, toxicity of acaricide compounds, when frequently used for prolonged periods, might depress weight gain in cattle, as postulated by Pegram et al. (1989) and Fivaz and de Waal (1993). This phenomenon might explain the lower weight gain observed both in N'Dama and Gobra cattle intensively treated with acaricide over 1 year in comparison with untreated cattle (Mattioli et al., 1998a). On the other hand, higher weight gains, exceeding the cost of acaricide application, were obtained in N'Damas through a strategic tick control (Mattioli et al., 1999), i.e. acaricide treatment given only during the period of tick abundance (Pegram et al., 1995). Improvement of milk production in The Gambia is one of the major objectives included in the Livestock Sector Review (1991). Recent studies in The Gambia (Mattioli et al., 1997) and in an equivalent ecoclimatic zone in neighbouring Senegal (Gueye et al., 1989, 1993) indicated that the period of maximum tick infestation in indigenous N'Dama cattle occurs from July to September, with adults of *A. variegatum* and *Hyalomma* spp. congregating mainly on the abdomen and ano-genital and udder region. Therefore, in addition to strategic acaricide application, strategic/selective control, i.e. by spraying the preferential attachment sites of these tick species with an acaricide during their respective periods of abundance, could be discriminately applied to females, and potentially result in a beneficial increase of milk off-take and also on calf growth rate, as emphasized by Kaiser et al. (1988). The endemic stability of tick-borne diseases will also be maintained, as this requires a minimum tick challenge. Additionally, the use of tick-resistant N'Dama will reduce the frequency of acaricide treatments and consequently their cost, as re-infestation following chemical application is more rapid and occurs at a higher level in tick-susceptible Gobra (Mattioli et al., 1998a).

The trypanotolerant trait and the apparent presence of resistance to ticks and tick-related infections in the N'Dama breed should be exploited in those areas where trypanosomosis, ticks, TBIs (particularly cowdriosis) and/or tick-associated infections, such as dermatophilosis, impair animal production. This will be of benefit especially for the low-input traditional farming systems where the use of chemicals to counteract the negative effects of pathogens is limited by their relatively high cost (Itty, 1996) Additionally, the potential contribution of the multiple disease resistance of N'Dama cattle should also be considered in crossbreeding programmes with dairy exotic breeds for increasing milk production in West Africa, particularly in those production systems more market-oriented.

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