Theileriosis in South Africa: a brief review

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Summary: East Coast fever caused by Theileria parva parva has been eradicated from South Africa, but tick-borne infections with other species of Theileria still occur, particularly in cattle and African buffalo (Syncerus caffer). One such infection is Corridor disease caused by T. parva lawrencei, which is controlled by restricting the movement of African buffalo. Other species reviewed are T. parva bovis, T. taurotragi, T. mutans, T. velifera, T. ovis and the genus Cytauxzoon, which are of little or no pathogenic significance.

KEYWORDS: Cattle diseases - Protozoal infections - South Africa - Syncerus caffer - Theileria - Theileria parva.

INTRODUCTION

Since the eradication of East Coast fever from South Africa (i.e. the Republic of South Africa and the independent states lying within its borders) more than 30 years ago, Theileria parva lawrencei (the causative organism of Corridor or buffalo disease) has become the most important Theileria sp. posing a threat to the cattle farming industry in this country. The fact that the African buffalo (Syncerus caffer) acts as a reservoir of foot and mouth disease (FMD) virus used to be the main reason for its confinement to well-fenced game reserves. However, restricting the movement of buffalo, together with the enforcement of quarantine measures and vigorous tick control in areas bordering on Corridor endemic areas, especially when outbreaks occur, has probably contributed largely to preventing the spread of Corridor disease.

Benign theileriosis, caused by T. mutans and T. taurotragi, as well as the apathogenic T. velifera and T. ovis (?) are believed to be prevalent in areas where their specific tick vectors occur. Both T. mutans and T. taurotragi have been incriminated in cerebral theileriosis and Tzaneen disease syndrome, but are apparently of relatively little economic importance.

Cytauxzoon (= Theileria) spp. have been observed in a variety of free-living wild animals in South Africa. However, reports of these organisms as the cause of mortality in their wild animal hosts are very scanty, as is information on the role they might play in the epidemiology of bovine theileriosis.

The occurrence, control, economic importance and continued research concerning the Theileria spp. in South Africa are briefly discussed in this paper.

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THEILERIA SPECIES

THEILERIA PARVA PARVA

Although several tick species have been shown experimentally to transmit *T. p. parva* (14, 17), it is generally accepted that *Rhipicephalus appendiculatus* is the main vector. After the introduction of East Coast fever (ECF) into South Africa in 1902 (21) the disease rapidly spread within the low-lying areas of the country and by 1912 had invaded all the areas within which it could establish and maintain itself (10). Initial attempts to control the disease were aimed at the eradication of vector ticks, particularly *Rhipicephalus appendiculatus* (11). The implementation of short-term dipping programmes, combined with fencing and quarantine of infected areas, eliminated the disease from many areas, but failed to eradicate it completely (10).

Control measures were then intensified and aimed at the early diagnosis of the disease, strict control of cattle numbers, close supervision of short-interval dipping (5:5:4-day cycle) and the adoption of a permit system for the movement of cattle. This intensified campaign led to a steady decline in the number of outbreaks (10), but also revealed the need to eliminate isolated outbreaks of the disease by application of a slaughter policy (11). This latter approach eventually led to the total eradication of the disease in South Africa (1). The last recorded outbreaks of ECF in the Transvaal occurred in 1944 (10) and in the Transkei and Natal in 1954 and 1955 respectively (17). Continued close veterinary surveillance, based largely on the examination of spleen smears from dead cattle, has failed to show any recurrence of this disease in the former endemic areas (4).

An estimated 5.5 million cattle died in South Africa as a result of ECF and the cost involved was enormous (1). An immense effort succeeded in eradicating the disease, but not the vector ticks. The latter are still widespread in the country, and the presence of a highly susceptible cattle population necessitates strict measures to prevent a recrudescence of ECF, either through the reintroduction of the parasite or the transformation (see below) of *T. p. lawrencei* to *T. p. parva*.

THEILERIA PARVA LAWRENCEI

In the past *R. appendiculatus* was considered to be the only vector of *T. p. lawrencei* (17), but recent observations indicate that *R. zambeziensis* (see below) might well be a more important vector (14) (Stoltsz, unpublished observations, 1986).

Corridor disease was the name given by Neitz (16) to a highly pathogenic form of theileriosis that occurred in cattle grazing in the corridor between the Hluhluwe and Umfolozi game reserves in Natal during 1953. Two other outbreaks occurred soon afterwards in the Transvaal on farms bordering on the Kruger National Park (7). Since then, sporadic outbreaks of the disease have been reported from areas bordering on or in close proximity to the Kruger National Park, Umfolozi and Hluhluwe game reserves. These outbreaks have always been associated with the presence of African buffalo (4).

Buffalo also occur in the Addo Elephant National Park, in the Eastern Cape Province, from whence a number have been relocated to other smaller game reserves and game farms elsewhere in the country. To date, however, no outbreaks of Corridor disease have been reported from these areas. Serum samples from a number of buffalo
from this park were tested for the presence of antibodies to *T. p. lawrencei* using the indirect fluorescent (IF) antibody test with *T. p. parva* piroplasm antigen. No antibodies were detected to indicate exposure of these animals to *T. p. lawrencei* (7).

In recent years there has been a great demand for African buffalo for commercial game farming in South Africa. The relatively small buffalo herd at Addo, which was the major source of animals free from FMD and Corridor disease, could no longer meet this demand. As the Kruger National Park is endemic for FMD, the movement of buffalo from this area is prohibited by law.

Buffalo in the Natal parks were recently declared free from FMD, reviving the hopes of owners of private game ranches to obtain buffalo from there. Corridor disease, however, remains endemic in these areas and the relocation of these animals is therefore still prohibited. The major concern in placing this restriction on their movement involves the reported transformation of *T. p. lawrencei* to *T. p. parva* after serial tick passage in cattle (2). However, no evidence has been obtained that *T. p. lawrencei* has reverted to *T. p. parva* under natural conditions in South Africa, despite the opportunity to do so during the more than 30 years since its recognition (4).

The strict control measures currently employed are rendered necessary by the potential ECF threat and by the fact that Corridor disease itself causes mortality rates of $\geq 90\%$ in cattle (17). By law Corridor disease is still considered notifiable, particularly because of its close resemblance to ECF. Buffalo-proof fences have been erected around the above-mentioned game reserves to confine the buffalo to reserves, and outbreaks in cattle are controlled by short-interval dipping and the elimination of buffalo from the premises.

**THEILERIA PARVA BOVIS**

*T. p. bovis* has not been isolated in South Africa. However, both confirmed vectors of this parasite, namely *R. appendiculatus* (17) and *R. zambeziensis* (14), are known to occur over a large area of the country.

The close antigenic relationship among *T. p. lawrencei*, *T. p. bovis* and *T. p. parva* is well recognised (24). Using the immunofluorescence test with *T. p. parva* piroplasm antigen, serological evidence was obtained to indicate the presence of a parasite with *T. parva* antigenicity on two farms in the Eastern Transvaal (7) and one in South West Africa/Namibia (Stoltsz, unpublished observations, 1985). In the absence of ECF and buffalo in these areas the results seem to point to the presence of this parasite. In addition, the aetiological agent in the Tzaneen disease syndrome (see below) retrospectively appears to have been *T. p. bovis* (7).

Considering that *T. p. bovis* is widely distributed in Zimbabwe (19) and that strong evidence exists for its presence in Botswana (Mehlitz and Ehret, 1974; in 7), it seems likely that the parasite was introduced into South Africa by the cattle trade, both legally and illegally, that existed between these countries for many years.

A further reason for the apparent absence of solid evidence for the existence of *T. p. bovis* in South Africa is probably the fact that non-pathogenic strains of the parasite occur, with the mortality rate during outbreaks in endemic areas as low as 1.5% (Matson and Hill, 1969; in 7). It would thus appear that the presence of the parasite could easily be obscured by the presence of other relatively more pathogenic tick-borne diseases like babesiosis and anaplasmosis (4).
Tzaneen disease

In 1937, a disease syndrome was described in the Tzaneen district of the Transvaal. Severe mortality occurred in cattle after they had been transferred from a tick-free area to pastures heavily infested with *R. appendiculatus* (24). At the time of the investigation, only *T. p. parva* and *T. mutans* were known to be present in South Africa. Based on epidemiological findings and the absence of ECF in the area, the aetiological agent was identified as *T. mutans*. It was thought that *R. appendiculatus* secreted a toxin which, with such massive infestations, caused some degree of immunosuppression in the affected animals. During the investigation it was concluded that this, together with stress factors and concurrent infections of babesiosis and anaplasmosis, probably combined to provoke an abnormally severe reaction of *T. mutans* which closely resembled ECF (6).

On the grounds of the aetiological agent being transmitted by *R. appendiculatus* (6), the parasite associated with the Tzaneen disease syndrome was retrospectively identified as *T. taurotragi* (24). More recently, it has been suggested that the causative organism might have been *T. p. bovis* (7). This suggestion was based on the fact that *T. p. bovis* probably occurs in South Africa and is more virulent than *T. taurotragi*. In the absence of any serological evidence, however, these suggestions remain merely speculative.

**THEILERIA MUTANS**

*T. mutans* was originally described in South Africa in 1906 (22). Subsequent reports failed to distinguish between the two benign *Theileria* spp. now known to be present in the country (see below). As a result, much confusion existed as to the true identity of the species referred to as *T. mutans*. Uilenberg (24) concluded that these reports in fact dealt with two different parasites of low pathogenicity: the one transmitted by *Amblyomma* spp. (*T. mutans*) and the other by *R. appendiculatus* (*T. taurotragi*).

In this latter report *T. mutans* was defined as a parasite of African buffalo which may also infect cattle. Usually of low pathogenicity, it is known to be transmitted by at least five African species of *Amblyomma*.

Evidence supporting this definition has been gained subsequently in South Africa. Both De Vos (8) and Stoltz (unpublished observations, 1985) have successfully transmitted *T. mutans* to cattle by subinoculation of blood from buffalo. Furthermore, *A. hebraeum* has been shown to be an efficient vector of *T. mutans* in this country (8).

*T. mutans* appears to be widely distributed amongst both buffalo and cattle populations in South Africa wherever *Amblyomma* spp. occur. All isolates of *T. mutans* observed in this country appear to be apathogenic in cattle. *Theileria* piroplasms are frequently observed during the routine examination of blood smears from healthy cattle in various parts of the country (4). These are considered to be incidental findings and not of any major veterinary or economic importance.

**THEILERIA TAUROTRAGI**

As early as 1909 the presence of a benign *Theileria* sp. transmitted by *R. appendiculatus* was reported in South Africa (Theiler, 1909; in 7). This report and
several others that followed referred to the parasite as *T. mutans*. Only fairly recently was it realised that at least two benign *Theileria* spp. which infected cattle existed in Africa (see above).

In 1981, De Vos (9) confirmed the presence of *T. taurotragi* in South Africa and it is believed to occur quite commonly within the distribution range of *R. appendiculatus* and *R. zambeziensis* in this country.

**Bovine cerebral theileriosis**

Elsewhere in Africa, *T. p. parva* has often been incriminated as the causal agent of a cerebral syndrome, characterised by a number of nervous symptoms and, in particular, circling or turning movements which eventually result in death (7). The pathogenesis of the condition remains unclear; one possibility is that an auto-immune disorder induced by the parasite is responsible for intravascular agglutination of lymphocytes with subsequent embolism, thrombosis and infarction in the central nervous system (25).

Several cases of cerebral theileriosis have been described in South Africa, but given the absence of ECF along with the prevalence of *T. mutans*, these cases were attributed to the latter species (25).

In a 1981 investigation, *T. taurotragi* was identified as a probable cause of cerebral theileriosis (7). In the light of recently acquired knowledge regarding the existence of this second benign species of *Theileria* in South Africa, some doubt has been cast on the accuracy of earlier reports implicating *T. mutans* as the aetiological agent. From this investigation it was concluded that *T. taurotragi* was the main, if not the only, cause of cerebral theileriosis in South Africa (7). It is not clear why *T. taurotragi*, which is usually a benign parasite, should sometimes cause cerebral theileriosis.

Cases of cerebral theileriosis in this country occur sporadically, but the incidence appears to be low (4). On farms where outbreaks occur, dipping is usually advocated to control the vector ticks.

**THEILERIA VELIFERA**

This parasite was first reported from cattle in South Africa in 1979 (3). It is considered to be non-pathogenic and therefore of no economic importance. Piroplasms of *T. velifera* are usually seen in mixed theilerial infections, but as they are easily distinguishable from those of other *Theileria* species occurring in this country, they do not complicate the diagnosis of pathogenic *Theileria* spp.

*T. velifera* piroplasms have been observed in blood smears of buffalo from different localities in South Africa (Stoltz, unpublished observations, 1986) and occasionally also in cattle. It is believed that this parasite occurs commonly within the distribution range of *A. hebraeum* (7), but as a result of its apparent insignificance very few reports exist to indicate its exact distribution.

**THEILERIA OVIS**

This parasite was first recorded in sheep in South Africa in 1929 (5). Transmission by *R. evertsi evertsi* was demonstrated for the first time in 1955 (13).
Many years later Uilenberg studied a South African *Theileria* isolate from sheep and, based on its morphology and successful transmission by *R. evertsi evertsi*, he concluded that it was identical to *T. separata*. However, there may be more than one *Theileria* sp. of sheep and/or goats in this country.

*Theileria* piroplasms are frequently encountered during the examination of blood smears from sheep, but under natural conditions infections appear to be asymptomatic. Mild clinical symptoms have thus far only been observed in splenectomised sheep (13, 17).

**CYTAUXZOON**

Some controversy seems to exist on the exact taxonomic status of this group of parasites. Neitz (18) called attention to the fact that some *Theileria* spp. multiply by schizogony in cells of the histiocytic series and by fission in the erythrocytes, a sound enough reason for including these parasites in a separate genus, *Cytauxzoon*. In a more recent review, however, Uilenberg (24) recognises only the genus *Theileria* and considers *Cytauxzoon* to be a synonym.

Piroplasms indistinguishable from those of *Theileria* spp. have been noted in a number of wild antelope species in this country. These include kudu (*Strepsiceros strepsiceros*) (17), waterbuck (*Kobus ellipsiprymnus*) (17), bushbuck (*Tragelaphus scriptus*) (17), sable antelope (*Hippotragus niger*) (17, 23, 27), blue wildebeest (*Gorgon taurinus*) (17), steenbuck (*Raphicerus campestris*) (17), reedbuck (*Redunca fulvorufa*) (17), duiker (*Sylvicapra grimmia*) (17), roan antelope (*Hippotragus equinus*) (27), gemsbuck (*Oryx gazella*) and tsessebe (*Damaliscus lunatus*) (Stoltz, unpublished observations, 1986). Similar parasites have also been reported in South African antbear (*Orycteropus afer*) (17), warthog (*Phacochoerus aethiopicus*) (17) and giraffe (*Giraffa camelopardalis*) (15, 17).

From these and other reports as well as many unpublished observations it would appear that theilerial organisms frequently occur in a wide variety of wild animals. In most cases, only erythrocytic stages are observed and infected animals appear healthy. But in a number of these, such as duiker, kudu, tsessebe, sable antelope, roan antelope and giraffe, both piroplasms and schizonts have been observed, and infected animals showed clinical signs of disease often resulting in death (17, 23, 27). It therefore appears that under certain conditions of stress these apparently apathogenic organisms could become pathogenic and cause fatalities in their wild animal hosts.

From a practical point of view it should be clear that suitable experimental animals are extremely difficult to obtain for detailed studies of these parasites. As a result, very few experimental investigations have been conducted to determine the interplay of these organisms with cattle and game.

Considering the lack of scientific knowledge concerning the *Theileria* spp. in wildlife (excluding the African buffalo), any detailed discussion on their involvement in the epizootiology of theileriosis in domestic animals remains hypothetical.
Apart from *T. p. lawrencei*, the other *Theileria* spp. occurring in South Africa appear to be of little significance. Their greatest importance lies in their ability to obscure or confuse the diagnosis of *T. p. lawrencei* infections in cattle and buffalo alike. For some years now, research has therefore been directed mainly at the accurate diagnosis, some epidemiological aspects and the possible sterilisation of *T. p. lawrencei* infections in particular.

A great deal of uncertainty still surrounds the exact taxonomic status of the theilerial parasites with *T. parva* antigenicity, namely, *T. p. parva* (causing classical ECF), *T. p. bovis* (causing Zimbabwean theileriosis) and *T. p. lawrencei* (causing Corridor disease). Some authors believe them to be merely different behavioural forms of the same parasite (24). *T. p. lawrencei* is believed to have the potential to change its behaviour to resemble that of *T. p. parva* when tick passaged through cattle, and may lead to outbreaks of typical ECF in areas where the disease has long been extinct (24).

As mentioned before, *T. p. lawrencei* has apparently failed to revert to *T. p. parva* under natural conditions in South Africa. Likewise, limited attempts to transform *T. p. lawrencei* under laboratory conditions in South Africa have also failed (7). This phenomenon is still being investigated, however, and until conclusive results have been obtained it will be considered a potential threat to the cattle farming industry in this country. Consequently, the relocation of buffalo from Corridor endemic areas to non-endemic areas will still be prohibited.

A useful tool in the control of Corridor disease would be a chemotherapeutic drug that would sterilise the infection in carrier animals. Several drugs have been tested under laboratory conditions in South Africa to determine their efficacy in the treatment of *T. p. lawrencei* infections. Although a number have been found to be effective in the treatment of clinical disease, none has been proved to sterilise the infection. In view of the risk of treated recovered cattle developing chronic infections, as proved experimentally in both splenectomised (7) and intact (20) animals, and thus creating opportunities for the parasite to be transmitted between cattle, these drugs have not been registered in South Africa.

For many years, the most widely used and reliable indicator of exposure to *T. p. lawrencei* has been the immunofluorescence (IF) antibody test. Recent observations in East Africa (12) and South Africa, suggesting that antibody levels to *T. p. parva* antigen in carrier buffalo fluctuate between positive and negative levels, have raised doubts regarding the reliability of the test to identify infected animals. Low antibody titres, mixed infections and serological cross-reactions between species such as *T. taurotragi* and *T. p. lawrencei* often lead to inconclusive results (9).

In the event of successful chemical sterilisation of infections in animals, antibody levels alone would not indicate effective sterilisation. For this reason the possibility of a DNA probe as a diagnostic tool is currently being investigated.

In the continued search for more accurate and sensitive diagnostic aids, some interesting observations have been made. The presence of *R. zambeziensis*, a tick closely resembling *R. appendiculatus*, has recently been confirmed in South Africa (26). Under laboratory conditions, this tick has proved to be a most efficient vector of *T. p. lawrencei*. Use of this tick species in transmission experiments has led to
much improved results with the xenodiagnosis of *T. p. lawrencei* infections. Infection rates in the salivary gland acini of *R. zambeziensis* were significantly higher than in *R. appendiculatus* when fed concurrently on the same host. A further development from this finding which is currently being investigated, is the use of purified *T. p. lawrencei* sporozoite antigen from these salivary glands in the IF antibody test and the production of monoclonal antibodies.

Further attempts to confirm the diagnosis of *T. p. lawrencei* infections in carrier animals have resulted in the successful subinoculation of *T. p. lawrencei* infections from both intact and splenectomised carriers into splenectomised cattle recipients. In this way, infections which were neither microscopically detectable, nor transmissible by ticks, resulted in patent piroplasm parasitaemia and serological conversion in recipient animals. Although expensive and cumbersome, this technique might find some application in selected cases where the presence of a carrier state needs to be established.

**CONCLUSIONS**

The situation regarding theileriosis in South Africa appears to be stable at present. The mildly pathogenic *Theileria* species (*T. mutans* and *T. taurotragi*) and the apathogenic species (*T. velifera* and *T. ovis* (?)) are common in South Africa, but apparently of little economic consequence in most cases. Buffalo-associated theileriosis (Corridor disease) caused by *T. p. lawrencei* is still present, but fortunately restricted to well defined areas bordering on certain game reserves where buffalo occur.

Considering the potential ECF threat to the cattle population in this country, either through reintroduction of *T. p. parva* or the transformation of *T. p. lawrencei*, strict control measures will be maintained. Indications are that *T. p. lawrencei* infections will not be easily sterilised and probably not with the existing anti-theilerial drugs. Having shown that recovered intact cattle can infect ticks, the use of chemotherapeutic drugs in infected cattle during Corridor disease outbreaks is prohibited.

Attempts to study possible behavioural changes of *T. p. lawrencei* under conditions of tick-cattle passage will probably continue using different buffalo isolates of this parasite.

Efforts will be made to overcome the problems encountered with the diagnosis of mixed *Theileria* infections. The vector potential of more tick species should be studied for possible xenodiagnostic application.

The *Theileria* parasites and their vectors of game species should be studied in more detail and attempts made to define their role in the epidemiology of theileriosis in domestic animals.

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TEILERIASIS EN SUDÁFRICA: BREVE REVISTA. — W.H. Stoltsz.

Resumen: La fiebre de la Costa Oriental, cuyo agente es Theileria parva parva, se ha erradicado en Sudáfrica, pero todavía subsisten infecciones transmitidas por las garrapatas, causadas por otras especies de Theileria, especialmente en los bovinos y los búfalos de Africa (Syncerus caffer). Una de ellas es la «enfermedad del corredor», causada por T. parva lawrencei, que se controla mediante la prohibición de los desplazamientos de los búfalos de Africa. Las otras especies examinadas, de papel patógeno reducido o nulo, son: T. parva bovis, T. taurotragi, T. mutans, T. velifera, T. ovis y el género Cytauxzoon.

PALABRAS CLAVE: Enfermedades de los bovinos - Infecciones por protozoarios - Sudáfrica - Syncerus caffer - Theileria - Theileria parva.

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