Theileria parva infections

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Adapted from:

1. Lawrence, J.A., Perry, B.D. & Williamson, S.M., 2005. East Coast fever, in: *Infectious diseases of livestock*, edited by Coetzer, JAW & Tustin, RC. Cape Town: Oxford University Press Southern Africa.

2. Lawrence, J.A., Perry, B.D. & Williamson, S.M. 2005. Corridor disease, in: *Infectious diseases of livestock*, edited by Coetzer, JAW & Tustin, RC. Cape Town: Oxford University Press Southern Africa.

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INTRODUCTION

Theileriosis is a general term used for infections in cattle with one or more of a number of *Theileria* species. Some of these may cause only mild or subclinical disease in cattle (so-called benign theileriosis), whilst others are extremely pathogenic, resulting in high mortality and severe economic losses. By far the most important and pathogenic *Theileria* species affecting cattle in Africa south of the Sahara is *Theileria parva.*

Video link: http://www.youtube.com/watch?v=km9tKR_oJ3M

**Terminal stage of East Coast fever:
severe dyspnoea and recumbency**
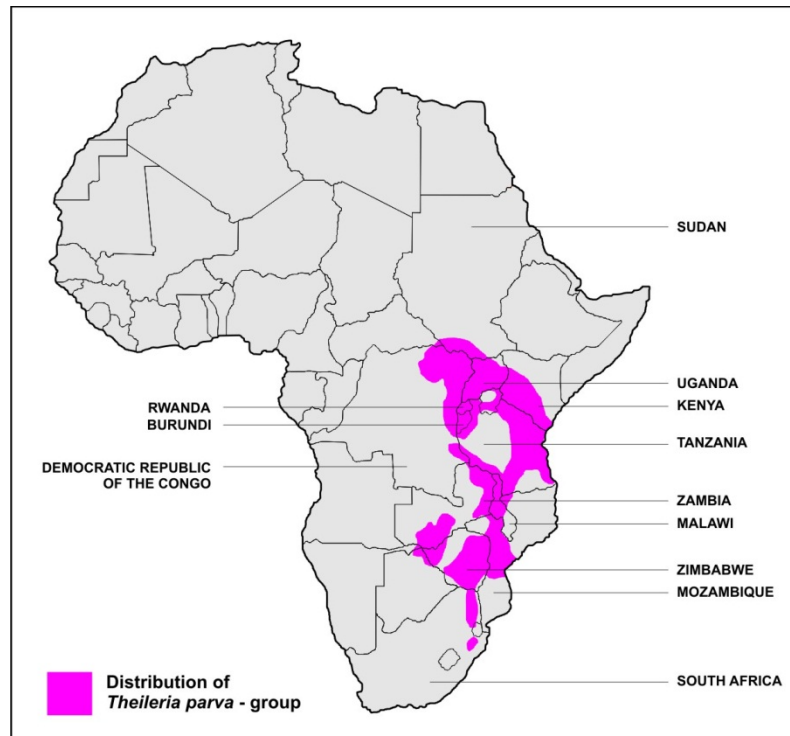
Distribution of the *Theileria parva*-group parasites in Africa

Theileria parva infection is considered by many to be the most important tick-borne disease of cattle in eastern, central and southern Africa and is transmitted mainly by the brown ear ticks *Rhipicephalus appendiculatus* and *Rhipicephalus zambeziensis*. Infections typically cause an acute, often fatal disease of cattle, characterized by fever, enlargement of the lymph nodes and dyspnoea.

***Rhipicephalus appendiculatus* male**

Based on certain clinical and epidemiological parameters observed in some countries of southern Africa, three forms of the disease are usually recognised: East Coast fever, Corridor disease (or buffalo disease) and Zimbabwean theileriosis (or January disease), each respectively caused by one of the three sub-types of *T. parva.* Although these are unlikely to be true subspecies of *T. parva*, the trinomial nomenclature is often retained for convenience to differentiate, firstly, those parasites transmitted mainly between cattle, causing classical East Coast fever (ECF) and characterised by large numbers of schizonts and piroplasms (*T. parva parva* or cattle-derived *T. parva*);

African buffalo (*Syncerus caffer*), the main reservoir host of Corridor disease

secondly, strains from the African buffalo (*Syncerus caffer*) causing Corridor disease or Buffalo disease in cattle and characterised by the presence of small numbers of schizonts and very few or no piroplasms (*T. parva lawrencei* or buffalo-derived *T. parva*), and thirdly, parasites of intermediate character, maintained in cattle in the absence of buffalo and producing the generally less pathogenic Zimbabwean theileriosis or January disease (*T. parva bovis* infection). However, differentiation into three subspecies seems to be an over-simplification of the situation as it exists in nature, since there appears rather to be a gradual range of parasites between the two extremes and infections of genetically diverse populations of parasites may occur concurrently in the same host.

East Coast fever occurs widely through the range of its main vector in eastern, central and southern Africa north of the Zambezi River. It was introduced into the region south of the Zambezi River in 1901/02 and spread through most of the range of its vector but was subsequently eradicated.

The disease was first described in 1902, following its introduction into Zimbabwe, as an unusually virulent form of babesiosis. It was initially named Rhodesian redwater, but later referred to as African Coast fever, the name being subsequently modified to East Coast fever. Although it has been proposed that the organism be named *Theileria parva parva* to distinguish it from other subspecies of *T. parva* which cause diseases that can be differentiated from East Coast fever on epidemiological grounds, it has since been agreed that classical East Coast fever be known as cattle-derived theileriosis and that it is caused by the same parasite as that causing Corridor disease and January disease.

East Coast fever has long been endemic in eastern Africa. The parasite probably originated from buffalo populations in eastern Africa and became adapted to cattle following their introduction and dissemination

in the region. It spread widely through the region during the early part of the 19th Century as a result of European settlement, which involved changes in patterns of movement, extensive use of ox-drawn transport, and importation of susceptible cattle from overseas.

East Coast fever was introduced into the area south of the Zambezi River in the period 1901 to 1903 by cattle which were imported from Kenya and Tanzania for the purpose of restocking the region after the ravages of the rinderpest epidemic of 1896 and the Anglo-Boer War. The disease was subsequently eradicated in a prolonged campaign consisting of movement control, tick control, destocking of infected pastures, and slaughter. The disease has persisted in the region north of the Zambezi River to the present day and is a major constraint on the development of cattle production.

Corridor disease closely resembles East Coast fever and is caused by infection with buffalo-derived *Theileria parva* strains transmitted by ticks from African buffaloes. The disease was first recognized in 1934 in Zimbabwe as a form of pathogenic theilerial infection distinguishable from East Coast fever on clinical, pathological, parasitological and epidemiological grounds. Previous occurrences in the region may well have been obscured by the widespread prevalence of East Coast fever. Twenty years later the disease was recognized in South Africa and the causal organism was then identified as a new species, *Theileria lawrencei,* in 1955. It was later proposed as a subspecies of *T. parva*, namely, *T. parva lawrencei*. Subsequent investigation has revealed that the parasite is *T. parva* and is the same as that causing East Coast fever and Zimbabwe theileriosis, although the distinction between these diseases has been retained and remains useful for descriptive purposes.

The disease was named buffalo disease, for obvious reasons, and Corridor disease, because the first outbreak in South Africa occurred in the corridor between the Hluhluwe and Umfolozi Game Reserves in KwaZulu-Natal. It occurs sporadically throughout East, Central and southern Africa wherever there is contact between cattle and infected African buffaloes in the presence of the ticks, *Rhipicephalus appendiculatus*, *R. zambeziensis* and *R. duttoni*. After foot-and-mouth disease, it is the most important disease transmitted from the African buffalo to cattle and is a major constraint to the acceptance of the presence of buffaloes in cattle-raising areas for purposes of conservation or recreation.

Zimbabwe theileriosis similarly is an acute, frequently fatal disease of cattle caused by *T. parva* infection. The disease was first recognized and distinguished from classical ECF in Zimbabwe in 1936. It has been variously known as January disease, because of its seasonal occurrence, and Fortuna disease, after the farm on which it was first recognized. It is known officially in Zimbabwe as "theileriosis". The disease was described by Neitz under the name Rhodesian malignant bovine gonderiosis, and attributed to a new species, *Theileria* (*Gonderia*) *bovis*, but the parasite was declared in a footnote to that paper to be synonymous with *T. lawrencei*, the causal organism of Corridor disease. The name *T. parva bovis* was subsequently proposed for the parasite to differentiate the disease which it causes from Corridor disease. The disease resembles ECF, but the seasonal occurrence of theileriosis in Zimbabwe, and the fact that infections can be milder than in ECF, justifies the continued use of the terms January disease and Zimbabwe theileriosis. There is currently no sound scientific reason for retaining the subspecies

classification, as the parasite causing the disease is indistinguishable from cattle-derived *T. parva* from elsewhere in East and southern Africa. It is worth noting that *T. parva* isolates have been made in East Africa which show either the lower virulence or parasitological features associated with some *T. parva* strains causing January disease. The disease causes a significant number of deaths each year in Zimbabwe, necessitating the implementation of intensive dipping regulations to control its vector.

EPIDEMIOLOGY

Buffalo-derived *T. parva* is morphologically and serologically indistinguishable from cattle-derived *T. parva* and has an identical life cycle. It is mainly transmitted by *R. appendiculatus,* although *R. zambeziensis* replaces *R. appendiculatus* as the vector in the more arid areas of southern Africa. Epidemiological evidence suggests that in Angola the disease is transmitted by *R. duttoni.*

Theileria parva, the causal organism of East Coast fever, alternates between cattle and the tick in its life cycle. The sexual stage of development occurs in the gut of the tick following ingestion of piroplasms in the erythrocytes of the ox. Completion of development occurs in the immature stages of the tick only after they have detached from the host. As the tick moults, a club-shaped motile kinete forms within the zygote. This is liberated into the body cavity and migrates to the salivary glands via the haemolymph. The kinete invades an epithelial cell of the salivary gland, and develops into a large syncytial sporoblast within which many thousands of minute elongated sporozoites develop during the early part of the next feeding stage of the tick.

The sporozoites are liberated into the saliva and inoculated into the skin of the ox as the tick feeds. They enter lymphocytes and develop within them, becoming multinucleate schizonts after a period of about three days. Differentiation into the schizont stimulates the host lymphocyte to transform into a lymphoblast and thereafter the schizont divides in synchrony with the host cell as it undergoes mitosis. Schizont-infected cells proliferate exponentially, becoming distributed throughout the lymphoid system, with metastasis of infected cells to non-lymphoid tissues also occurring. Initially the schizonts have large chromatin particles and are called macroschizonts. The macroschizont is often known as a "Koch's body" or a "Koch's blue body", the latter name emphasizing its appearance when stained by a Romanowsky technique. Later, a generation of schizonts called microschizonts develops with small chromatin particles. Merozoites liberated from the microschizonts invade the erythrocytes, in which they are frequently referred to as piroplasms, thus completing the life cycle.

Schizonts are found intracellularly in lymphoblasts in lymphoid tissues throughout the body (including lymph nodes, spleen, thymus, Peyer's patches and the lymphoid aggregations in parenchymatous organs which are a feature of theilerial infections) as well as in the blood.

The majority of intra-erythrocytic piroplasms are rod-shaped, but round or oval forms are also seen. Although usually single, there may be several parasites in one erythrocyte in heavy infections.
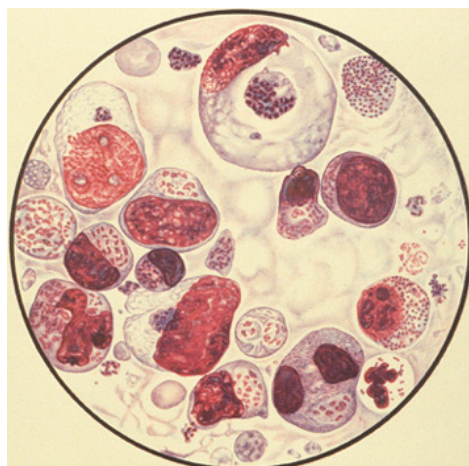
Impression smear from prescapular lymph node: drawing oflymphoblasts and lymphocytes containing macro- and microschizonts. Note several schizonts are extracellular after disintegration of lymphocytic cells

Theileria parva depends on its vector tick *R. appendiculatus* for transmission from host to host. The potential distribution of East Coast fever is thus restricted to those areas of eastern, central and southern Africa where ox and tick co-exist. In eastern and central Africa, this includes much of Kenya, Uganda, Rwanda, Burundi, the eastern part of the Democratic Republic of Congo, areas of southern Sudan bordering Uganda and much of Tanzania. In southern Africa its range is more limited, and it is confined to the northern and central regions of Malawi, the northern, eastern and central regions of Zambia, and the Tete Province of Mozambique, all lying to the north of the Zambezi River.

Theileria parva is probably originally a parasite of African buffalo (*Syncerus caffer*), which has become adapted to cattle. It has been found to infect waterbuck (*Kobus defassa*) under natural conditions, and the Asiatic buffalo (*Bubalus bubalis*) under experimental conditions. It is not infective to other ungulates, nor to any species of laboratory animal.

The classical disease is seen in cattle of European origin which have been exposed to infected ticks. Cattle of African origin have a very variable response to infection and the disease may be insignificant or subclinical in Zebu calves born from immune dams and raised in endemically infected areas.

Within the infected areas, the incidence of the disease can vary widely depending on numerous factors, including the abundance of the vector and the susceptibility of the host. This situation is commonly referred to as endemic stability. However, endemic stability to *T. parva* infection appears to be relatively

limited in its distribution and may not be achieved easily. The more common situation seen in the region is that of endemic instability, in which varying degrees of clinical disease are experienced.

Epidemic East Coast fever occurs when the disease is introduced to areas previously free of the disease, and often occurs on a seasonal or secular basis at the margins of *R. appendiculatus* distribution.

In the field, transmission of East Coast fever takes place only through the medium of the tick vector. The natural vector is *R. appendiculatus*, a common parasite principally infesting the ears of cattle and other herbivores in the more humid areas of southern and eastern Africa.

Zimbabwe theileriosis occurs sporadically on the highveld of Zimbabwe during the period December to May. The strictly seasonal occurrence of clinical disease coincides with the seasonal distribution of adult *R. appendiculatus*. Development of antibodies to *T. parva* has been demonstrated in cattle in the field during the period September to November, indicating that transmission by nymphs, which has been demonstrated experimentally, may cause subclinical infection.

Most cases occur between January and March and the disease usually affects cattle over the age of one year; it is rarely seen in calves. Primary outbreaks usually occur in herds with a moderate to heavy tick burden and are often associated with new additions to the herd. The disease may appear in the resident cattle (suggesting initiation of infection by introduced carriers) or in the introduced cattle (suggesting introduction of susceptible animals into an endemically stable environment). Morbidity in an outbreak is usually less than 10 per cent. The disease is likely to recur each year on an infected property unless good tick control is achieved, but shows little tendency to spread to neighbouring properties.

Serological evidence suggests that infection with the parasite is widespread in both the highveld and lowveld of Zimbabwe. It is not yet known whether the limited occurrence of clinical disease, in spite of the widespread prevalence of infection, is evidence of the existence of avirulent strains of the parasite or of an endemically stable balance between virulent strains and cattle.

Other members of the genus *Rhipicephalus* and several *Hyalomma* spp. have been shown to be capable of transmitting *T. parva* in laboratory conditions. There is, however, no evidence to suggest that any tick other than *R. appendiculatus* plays a significant role in transmission of the disease in nature.

Rhipicephalus appendiculatus is a three-host tick, and transmission of *T. parva* is achieved only by nymphs infected during the preceding larval stage or by adults infected during the preceding nymphal stage. Ticks will transmit infection if, during the preceding stage of development, they have fed on an ox with circulating piroplasms. Infective cattle may be clinically ill, recently recovered, or persistent carriers. Transovarial transmission does not occur, nor is there transmission between larva and adult if the intervening nymph feeds on a non-susceptible host.

Artificial transmission of *T. parva* can be achieved by the inoculation of a suspension of sporozoites prepared from homogenized tick salivary glands or whole ticks, the so-called GUTS (ground-up tick

supernatant) preparation. The method is widely used for the characterization of isolates of *T. parva* in cattle and for the infection and treatment method of immunization. A second method of artificial transmission is by the inoculation of schizonts. Infection can be transmitted to recipient cattle when very large numbers of infected donor cells are administered subcutaneously. The critical factor appears to be the ability of the inoculated cells to survive for a sufficient period for the parasite to transfer to the recipient host cells — this depends on the degree of histocompatibility between donor and recipient.

Transmission of *T. parva* by the inoculation of blood can be achieved but the results are very erratic as success depends on the presence of sufficient numbers of infected lymphoblasts in the circulation.

Buffalo-derived *T. parva* can be considered to be a group of *T. parva* strains which are adapted to tick transmission within the African buffalo population, including the red dwarf buffalo (*Syncerus caffer nanus*), wherever a suitable tick vector of the parasite occurs. It is universally distributed in wild buffalo throughout eastern, central and southern Africa, except in the Addo Elephant National Park in South Africa. It is usually non-pathogenic in this species although fatal disease can occur following experimental infection. The parasite persists indefinitely in infected buffaloes in both schizont and piroplasm form and can be recovered consistently by tick transmission or culture of lymphocytes from such animals.

Buffalo-derived *T. parva* is not well adapted to the ox and, when transmission from buffalo to ox occurs, it usually fails to complete its development; many cattle die before sufficient time has elapsed for development of piroplasms, and in those that survive, piroplasms are very scanty and recovered animals are not commonly infective for ticks. In southern Africa the disease is self-limiting within a population of cattle once it is removed from the source of infection. Onward transmission from cattle has been demonstrated experimentally and in eastern Africa repeated passage of infection in cattle has resulted in a change of the character of the organism on a number of occasions, the parasite behaviour and the disease that it causes becoming indistinguishable from classical East Coast fever. This change is attributed to a "transformation" of the parasite as it adapts to the ox, but an alternative explanation, namely that the phenomenon represents selection of a *T. parva* strain from a mixed population in the buffalo, must also be considered. There is no evidence that "transformation" of buffalo-derived *T. parva* occurs in the region south of the Zambezi River, where classical East Coast fever is absent. This may reflect the infrequent contact between buffalo and cattle in the region. Furthermore, the seasonal appearance of the various tick stages reduces the likelihood of an animal being infected by one stage and infection being acquired by the following stage, since piroplasms are present only transiently and at a low level. In contrast, in eastern Africa, all tick stages may be present on the animal at the same time.

Buffalo-derived *T. parva* has been shown to infect a waterbuck (*Kobus ellipsiprymnus defassa*) from which infection was transmitted to ticks; this was not achieved using cattle-derived *T. parva*. Buffalo-derived *T. parva* will also infect and cause fatal disease in the Asiatic domestic buffalo (*Bubalus bubalis*).

Buffaloes in *T. parva* endemic areas become infected soon after birth and the vast majority survive to become extremely efficient carriers of *T. parva* and remain so even in the absence of reinfection. Almost

all buffaloes in endemic areas in eastern Africa are *T. parva* carriers and ticks feeding on carrier buffaloes become heavily infected. Corridor disease occurs only in cattle that graze pastures on which African buffaloes are or have recently been present. Such situations occur where buffaloes and cattle regularly share the same pasture, where cattle are moved into or through buffalo areas or where buffaloes stray from their natural habitat or game reserves into farming areas. It is not always easy to detect the presence of wild buffaloes in a farming area. They may travel long distances and remain hidden in wooded areas, and the presence of a single buffalo for a relatively short period may be sufficient to cause a serious outbreak of disease amongst the cattle.

Possibilities for infection occurring in southern Africa are limited as buffaloes do not usually inhabit densely populated or intensively farmed land. Contact is most common in the vicinity of game parks or in extensive cattle-raising areas with a substantial wildlife population. Increasing density of human population and the policy of prohibiting buffalo/cattle contact as a foot and mouth disease control measure are likely to reduce the prevalence of the disease progressively in the future. However, in South Africa game ranching in conjunction with or in the absence of cattle is becoming increasingly more popular in certain areas. As one of the so-called "Big Five" African game trophy animals, the buffalo is amongst the most sought-after game species for introduction to many game farms and game conservation areas in South Africa. Buffaloes which are Corridor disease- and foot and mouth disease-free are in short supply for stocking purposes and consequently have an exceedingly high commercial value.

In eastern Africa, the absence of game fences, the mode of life of cattle-keeping pastoralist communities and the widespread distribution of the buffalo populations all contribute to Corridor disease being a more significant problem.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Clinical signs and pathology

East Coast fever in the classical form is characterized by pyrexia, enlargement of the superficial lymph nodes, severe pulmonary oedema and wasting. It usually terminates in death.

The incubation period is generally about 15 days from the time of attachment of the infected tick, but may range from eight to 25 days. The period and the course of the disease become shorter as the challenge is increased. The first clinical signs are fever and increases in pulse and respiration rates. There may be a sharp decline in milk production. The parotid lymph nodes, which drain the ear to which the infected tick has attached, are enlarged. After a few days the animal becomes depressed and lethargic. Anorexia may develop but is not inevitable. Lachrymation commonly occurs together with oedema of the eyelids, and

may be accompanied by photophobia. The animal is often constipated. There is a generalized enlargement of the superficial lymph nodes; the prescapular and precrural nodes become very prominent.

The disease usually progresses over a period of about 15 days, but may terminate after five days or be prolonged to 25 days. The fever remains high, although in a small proportion of cases there may be a temporary remission for one or two days. Appetite and rumination become increasingly depressed and there is a severe loss of body condition, increasing weakness and ataxia, and frequent recumbency. Constipation is succeeded by diarrhoea and there may be blood and mucus in the faeces. Opacity of the cornea may develop and petechiae may be detected in the mucous membranes, especially those beneath the tongue and in the vulva. Anaemia and icterus have been reported but are inconsistent. Pregnant cows may abort.

In the terminal stages of the disease dyspnoea develops, with an increased respiratory rate, a watery cough and the discharge of frothy fluid from the nostrils. Evidence of pulmonary oedema and hydropericardium may be detected on auscultation. Sternal and submandibular oedema may be present. The enlarged superficial lymph nodes begin to regress, the rectal temperature falls to subnormal levels, and the animal becomes recumbent and dies in a coma.

A small number of animals, usually about five per cent, may recover, but convalescence is prolonged and the animals may remain emaciated and unproductive for months.

The disease may assume a less severe form in animals with partial immunity or inherent resistance, but pyrexia and enlargement of superficial lymph nodes remain constant features and, in calves, may be accompanied by persistent unthriftiness. Mild disease has also been reported occasionally following infection of fully susceptible animals with strains of *T. parva* of reduced virulence.

In the Asiatic buffalo, the disease resembles that in the ox, but in the African buffalo infection is invariably subclinical or mild.

Zimbabwe theileriosis exhibits the same clinical features as East Coast fever except that the course is often shorter and death may occur three to four days after the first onset of signs. Sometimes one of the presenting signs is blindness associated with corneal opacity. Clinical disease is often accompanied by evidence of heavy infestation with *R. appendiculatus.* Mortality in the field may reach 90 per cent in severe outbreaks, but many animals recover from experimental infection and serological evidence suggests that subclinical or mild infection may be common.

The most prominent feature seen in a carcass of an animal that died of *T. parva* infection, is often the severe accumulation of fluid in the lungs, frequently also accompanied by large amounts of froth in the trachea and bronchi. In Corridor disease lymphoid hyperplasia and lymphoid infiltrations are generally not very advanced at death, and macroscopic lymphoid aggregations in the kidneys are uncommon.

Video link: http://www.youtube.com/watch?v=xaCUiMtfs0s

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**Severe pulmonary oedema and mild hydrothorax.
Also note the petechiae on the serosal surfaces**
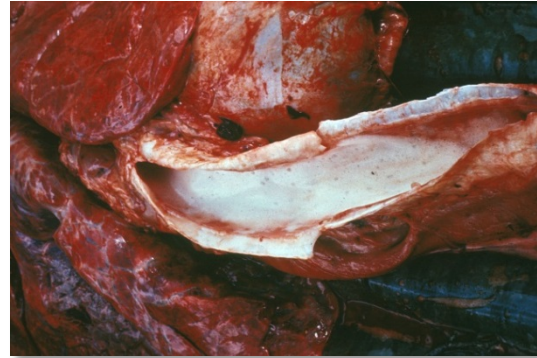
Trachea containing a copious amount of froth
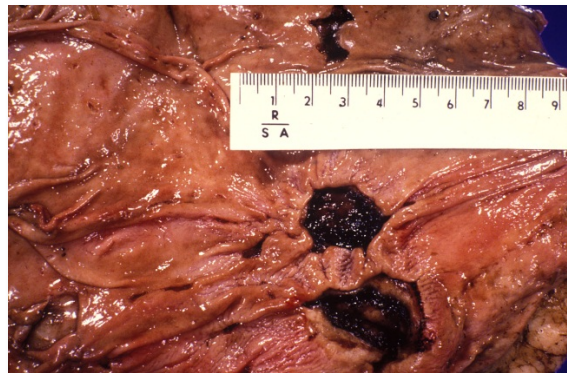
**Thickened congested mucosa and ulcers which are
associated with mucosal lymphoid hyperplasia**

The lymph nodes are usually enlarged and sometimes severely congested. The spleen may also be enlarged and the kidneys often have whitish nodules of varying sizes on their surface. Ulcers or superficial erosions may be found in the abomasum or in the intestinal mucosa. Although not always very obvious, anaemia may also be present.
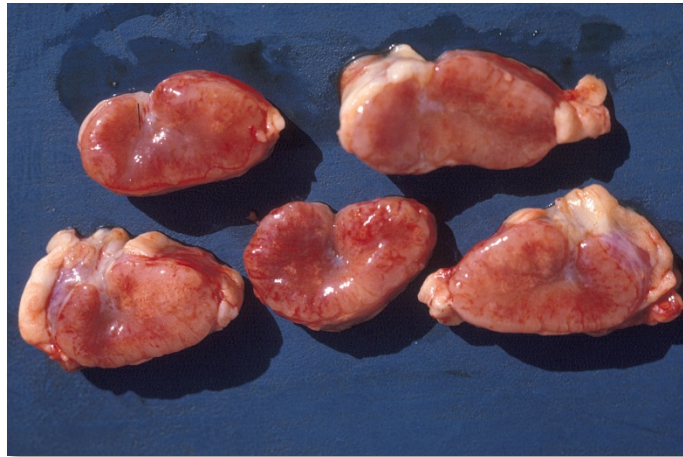
**Enlarged superficial lymph nodes showing
congestion and oedema**

Generally, the schizonts and piroplasms of different *Theileria* species cannot be differentiated morphologically, but the presence of schizonts and/or large numbers of piroplasms is usually indicative of clinical disease.

Laboratory confirmation

The diagnosis of classical East Coast fever is based on the characteristic clinical signs and lesions, and may be confirmed by demonstration of schizonts in lymphoblasts and, in the later stages of the disease, piroplasms in erythrocytes. In the live animal they can be demonstrated in smears prepared from peripheral blood and fine-needle aspirates of superficial lymph nodes. In the dead animal, impression smears prepared from the cut surface of the spleen and any enlarged lymph nodes should be examined.

The diagnosis of Corridor disease depends on the recognition of similar characteristic clinical signs and pathological changes, and on the microscopic demonstration of schizonts in a situation where cattle/buffalo contact is known or may be presumed to have occurred. In marked contrast to East Coast fever, the parasites are usually very scanty and a prolonged search of smears of a selection of lymph nodes and spleen may be necessary to demonstrate schizonts. The presence of piroplasms does not provide supportive evidence as these are more likely to result from incidental infection with non-pathogenic *Theileria* species.

The immunofluorescent antibody test (IFAT) and specific enzyme-linked immunosorbent assay (ELISA) are both applicable for detecting antibody after exposure to *T. parva.* Molecular diagnostic techniques based on the polymerase chain reaction (PCR) provide an attractive option for detecting persistently infected animals. However, these tests do not distinguish buffalo-derived from cattle-derived infections.

Differential diagnosis

Clinically, East Coast fever and Corridor disease must be differentiated from other febrile conditions which usually terminate fatally after a course of one to two weeks and which feature progressive emaciation, respiratory distress, diarrhoea, corneal opacity, and lymphoid hyperplasia, e.g. rinderpest, bovine virus diarrhoea/mucosal disease and bovine malignant catarrhal fever. Normally benign *Theileria* species infections (e.g. *T. mutans* and *T. taurotragi*) may occasionally cause clinical disease and even mortality, and even sub-clinical infections may complicate the diagnosis of *T. parva*.

In babesiosis and anaplasmosis, anaemia and icterus are the major presenting signs. The clinical picture in East Coast fever may be complicated, however, by secondary respiratory infections or by concurrent infection with other haemoparasites.

A definitive diagnosis of East Coast fever is possible if microscopic examination of blood and lymphoid tissues reveals large numbers of theilerial parasites. If only small numbers of schizonts and piroplasms are present in association with *R. appendiculatus* ticks and severe clinical illness, the possibility exists that the disease under investigation is not classical East Coast fever but is caused by infection with buffalo-derived *T. parva* (i.e. Corridor disease). Where schizonts are few and a variable number of piroplasms are encountered in mildly affected animals, the presence of another species of *Theileria* should be considered, or it may be that the *T. parva* infection is incidental. The presence of piroplasms in association with anaemia, minimal lymph node enlargement and few, if any, schizonts is likely to indicate *T. mutans* infection.

To distinguish between the different species of *Theileria* microscopically may be extremely difficult when relatively mild infections are occurring, particularly as mixed infections are frequent in the field, the most common of these being combinations of *T. parva*, *T. taurotragi* and *T. mutans*. Morphologically the piroplasms are difficult to differentiate, except for those of *T. velifera,* and the schizonts are indistinguishable, except for those of *T. mutans.*

Serological examination of recovered animals may permit a retrospective differentiation at the species level with species-specific ELISAs available for *T. parva* and *T. mutans* and standard IFAT for others. Biological transmission of the parasite may also provide a means of differentiation at the species level, but is expensive and requires experimental cattle.

A number of molecular, biochemical and immunological tools is available which enables differentiation between *Theileria* spp. Polymerase chain reaction (PCR) combined with oligonucleotide DNA probes detecting ribosomal RNA sequences can be applied to lymph node, blood and culture material, even when only small quantities are available. Species-specific monoclonal antibodies are also valuable; either recognizing piroplasms or, where applicable, schizonts in cell cultures using the IFAT. More recently, species-specific PCR assays have been developed to distinguish *T. parva, T. taurotragi*, *T. mutans* and *T. buffeli.*

The differentiation between the various disease manifestations caused by *T. parva* is based on epidemiological, clinical, pathological and parasitological factors, and on the implications of the diagnosis in relation to the animal health control policy of the country. Veterinarians in countries which have eradicated (or are on the verge of eradicating) East Coast fever are far more careful to make a distinction between the forms of disease than those in regions where East Coast fever is endemic.

CONTROL

In countries such as South Africa, where cattle-associated *Theileria parva* (or classical East Coast fever) has been eradicated, control of buffalo-associated *Theileria parva* (or Corridor disease) depends mainly on maintaining infected buffalo in well-fenced game reserves to avoid any contact with cattle.

Video link: http://www.youtube.com/watch?v=kfkel4eseU8

Buparvaquone has proved to be a valuable therapeutic agent for the treatment of clinical theileriosis. Treatment does not eliminate the parasite from the host, however, and recovered animals usually remain carriers. For this reason, the treatment of *Theileria parva* infections in some countries, like South Africa, has been prohibited.

Corridor disease responds to treatment with buparvaquone and halofuginone, but as the course of the disease is usually short it may be difficult to institute treatment in time for it to be effective. In South Africa, the treatment of diseased animals is not permitted by law.

Protective immunity to *T. parva* persists for at least five years after natural infection. Vaccines have been developed that consist of a crude suspension of sporozoites prepared from adult ticks which have fed as nymphs on infected cattle, have moulted, and have been prefed on rabbits for three to four days to allow the sporozoites to mature. The suspension is mixed with glycerol as a cryoprotectant and stored, deep-frozen, at -70 0C or in liquid nitrogen. Aliquots are titrated in susceptible cattle to determine an optimum dose for immunization. The stabilate is inoculated subcutaneously into the cattle to be immunized and simultaneously an intramuscular injection of 20 mg/kg of a long-acting oxytetracycline preparation is administered. Alternatively, two injections of 10 mg/kg of a standard oxytetracycline preparation on Days zero and three or four may be used. Infection develops to a mild or subclinical level and the animals are thereafter resistant to challenge, both experimental and natural, although infection may persist and the animals may remain asymptomatic carriers.

The infection and treatment technique provides good immunity against the homologous immunizing strain, but is not consistently successful against unrelated strains. Therefore efforts have been directed towards finding a "master" stock or combination of stocks which, when used as the vaccine, give protection against a wide range of antigenically distinct *T. parva* parasites. On the basis of extensive cross-immunity trials, three isolates, identified as cattle-derived *T. parva* Muguga and *T. parva* Kiambu 5 and buffalo-derived *T. parva* Serengeti transformed, have been combined in the so-called "Muguga cocktail". This mixture provides protection against most isolates from outbreaks of East Coast fever in eastern Africa and is used in Tanzania, Uganda and Malawi.

The infection and treatment technique is relatively expensive and cumbersome, but it is being implemented on an increasing scale in a number of countries and has generally proved successful. A liquid nitrogen cold chain is essential in order to maintain parasite viability and, compared to other veterinary immunizations, more training and expertise are required for the vaccine to be delivered safely and effectively.

Immunization against *T. parva* by inoculation of schizont-infected lymphoblast cultures, has proved to be impractical, as very large numbers of cells are required to establish infection consistently.

There are no vaccines readily available to control buffalo-derived *T. parva*. Cross-protection experiments in cattle, monoclonal antibody studies and genotypic analysis have shown that isolates of *T. parva* from buffalo are antigenically more varied than those from cattle. The "Muguga cocktail" and other cattle-derived *T. parva* vaccines will thus often fail to protect against natural challenge in situations where buffalo-derived *T. parva* infections are prevalent in cattle Experiments indicate that the disease is better controlled by the infection and treatment method of immunization using local isolates. Buffalo-derived *T. parva* is more difficult to control using conventional oxytetracycline dosing during immunization and higher reactor rates tend to occur. Buparvaquone controls the post-immunization reactions better than oxytetracycline but can be over-effective leaving cattle partially or fully susceptible.

In the absence of an effective vaccine, control of East Coast fever has depended in the past, and continues to depend, on the prevention of infestation of susceptible cattle with infected ticks.

In eastern Africa, where susceptible animals are being kept in situations of high risk, and separation of buffalo and cattle is not an option, strict tick control must be practised to prevent disease outbreaks. If the cattle are indigenous Zebu-type, endemic stability may be established whereby calves born to immune dams are infected while young and most become immune with few deaths.

In southern Africa control of the disease is based on the prevention of contact between buffaloes and cattle wherever possible. Game reserves in cattle-raising areas which contain buffaloes should be securely fenced and the introduction of buffaloes into farming areas for purposes of game ranching or safari hunting should be strictly prohibited, unless the buffaloes can be certified free from infection. The growing demand for buffaloes far exceeds the limited supply of Corridor disease- and foot and mouth disease-free animals which are suitable for non-endemic areas. In an attempt to help supply the local demand in South Africa of such animals, Corridor disease-free buffaloes have been bred successfully from Corridor disease-infected parent stock obtained from a foot and mouth disease-free area by rearing them in an environment free from tick vectors. Although transmission of infection by tick vectors to the progeny can be eliminated in this way, the calves must be monitored for possible transplacental infection with *T. parva*.

When an outbreak of the disease does occur, the usual procedure is to remove the cattle to uninfected pastures, to institute strict tick control procedures and to attempt to locate the source of contact and thus prevent future recurrences. As the disease is usually self-limiting in cattle, prolonged quarantine of infected herds is rarely indicated, but outbreaks should be monitored carefully for several months to ensure that cattle-to- cattle transmission does not occur.

SOCIO-ECONOMICS

East Coast fever, if uncontrolled, may cause over 90 per cent mortality of the susceptible cattle following its introduction into a region. In an area where it is endemic, mortality among locally adapted Zebu-type cattle may be negligible but there is evidence that the disease causes a significant reduction in growth and productivity. Susceptible cattle introduced into an endemic area are very vulnerable to infection and the cost of the control measures required is a continuous financial burden on both livestock owners and state veterinary services.

As one of the Big Five African game species, African buffalo are highly sought after animals in the highly lucrative ecotourism industry in South Africa. In order to prevent *Theileria parva* from spreading from buffalo to cattle, only buffalo from known disease-free herds, or buffalo bred under strict experimental conditions, which have been certified free of *Theileria parva*, have been allowed to be translocated to

non-endemic areas. As a result of the limited supply of such "disease-free" buffalo, these animals may fetch exorbitant prices at sales, but also attract unscrupulous traders who may be selling infected buffalo to unsuspecting clients.

IMPORTANT OUTBREAKS

Sporadic outbreaks of Corridor disease in cattle occur in South Africa where inadequate separation between cattle and infected buffalo is maintained in brown ear tick endemic areas.

OTHER *THEILERIA* SPECIES

At least four other *Theileria* species are known to infect cattle in Africa south of the Sahara. *T. mutans* and *T. velifera* both probably have buffalo as their original host and are transmitted by ticks of the genus *Amblyomma.* Some strains of *T. mutans* appear to be more pathogenic, causing occasional anaemia in calves.

T. taurotragi is a parasite of eland that is frequently found as a sub-clinical infection in cattle. However, under specific conditions, sporadic fatal infections, which may be difficult to differentiate from *T. parva* infections, and are commonly referred to as Tzaneen disease or Turning sickness (cerebral theileriosis), may confuse the diagnosis of *T. parva.*

T. annulata is widely distributed in North Africa, the Mediterranean coastal area, the Middle East, India, the former USSR, and Asia. It causes tropical or Mediterranean theileriosis and is transmitted by ticks of the genus *Hyalomma.*

Three species of *Theileria* have been distinguished in sheep and goats, based largely on their relative pathogenicity in these hosts. Mortality can approach 100% with *T. lestoquardi* (formerly *T. hirci*), which is found in southern Europe, Africa, and throughout Asia. It is transmitted by *Hyalomma anatolicum* ticks in Asia. Mildly pathogenic *Theileria* spp. (e.g. *T. ovis* and *T. separata*) are also widely distributed and are mainly transmitted by *Rhipicephalus evertsi* ticks in Africa and *Haemaphysalis punctata* ticks in Europe.

FAQS

1. **Do buffalo develop any clinical signs of disease when infected with *T. parva*?**

   No, although clinical signs have been observed in buffalo calves kept in captivity.

2. **Are cattle and African buffalo the only animals susceptible to infection with *T. parva*?**

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Generally, yes. However, an experimental infection with a buffalo-derived isolate has been reported in defassa waterbuck (*Kobus defassa*) in East Africa. However, waterbuck do not generally appear to be susceptible to infection, or play a significant role in the epidemiology of the disease.

3. **Does endemic stability to *T. parva* develop in cattle raised in endemic areas?**

A degree of endemic stability can be achieved in indigenous breeds raised in *T. parva*-endemic areas, but this is generally not as well-developed as in the case of other tick-borne diseases such as babesiosis, anaplasmosis and heartwater.

4. **Why is the infection and treatment method of vaccination not more widely used to immunize cattle against both cattle-derived and buffalo-derived *T. parva*?**

Production, storage, distribution and administration of the vaccines are highly specialised and expensive. In addition, it would seem that no single parasite isolate of *T. parva* will provide immunity to all field strains, thus requiring inclusion of several parasite isolates in the vaccine. This has raised concerns that foreign parasite strains (not endemic in particular areas or countries) may be introduced with the vaccine, which may result in disease outbreaks in cattle already immune to local strains of the parasite.

5. **Can buffalo be bred and raised to be "Corridor disease-free"?**

Yes. Provided breeding stock and their off-spring are kept in a vector-free environment, no infection of calves should occur. Although transplacental infection is probably extremely rare, the possibility exists that calves may become infected in utero. Therefore, it is recommended that the progeny of infected parent stock be screened for infection by specific and sensitive molecular diagnostic tests.

6. **What are the differences, if any, between East Coast fever (ECF) and Corridor disease (CD)?**

Classical ECF is generally regarded as being caused by *T. parva* genotypes which are readily transmitted amongst cattle in the absence of buffalo. In cattle, the infections are usually characterised by high piroplasm parasitaemias and high schizont parasitoses. CD, on the other hand, is generally regarded as *T. parva* genotypes which are predominantly transmitted from buffalo to cattle, are not readily transmissible amongst cattle, and are characterised by low piroplasm parasitaemias and low schizont parasitoses in cattle.

7. **What role, if any, do African buffalo play in the epidemiology of East Coast fever?**

Buffalo are regarded as the original host of *T. parva* and it is generally accepted that. ECF represents the selection a subpopulation of *T. parva* parasites that are better adapted to cattle-

cattle transmission from buffalo. Due to the diversity of *T. parva* genotypes present in buffalo populations, such selection of parasites that can readily be transmitted amongst cattle, may occur wherever cattle and buffalo share common grazing, even in areas where classical ECF has long been absent. The variety of genotypes potentially transmitted from buffalo to cattle may also preclude the development of an effective vaccine which will protect against all field strains of *T. parva*.

8. **How does the infection-and-treatment method of vaccination against ECF differ from those against other important tick-borne diseases of cattle?**

   The vaccines against babesiosis, anaplasmosis and heartwater are blood-based vaccines in which infective blood is used as a vaccine and treatment is usually only administered if clinical signs of disease are observed in vaccinated animals, or, in the case of heartwater, at the time when vaccine reactions are expected to occur. In the case of ECF vaccination, infective sporozoites (derived from infected ticks) are used to infect animals and tetracycline treatment is administered at the time of vaccination.

9. **What role, if any, do the so-called benign theilerioses of cattle play in the epidemiology of ECF?**

   The most important role that they play is that they may complicate or confuse the diagnosis of *T. parva.* This is especially true of *T. taurotragi* which occasionally may cause clinical signs which closely resemble those caused by *T. parva*.

10. **Is the distribution of East Coast fever and Corridor disease limited to the distribution of the brown ear tick *Rhipicephalus appendiculatus*?**

    No. It may also occur within the distribution range of the closely related tick species *R. zambeziensis, R. duttoni* and, possibly, *R. nitens*.

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