Rev. Sci. Tech. Off. Int. Epiz., 2015, **34** (2), 599-611

The aetiology, pathogenesis and control of theileriosis in domestic animals

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Summary
The *Theileria* genus includes a large number of species of tick-borne parasites that infect domestic animals and wildlife species, predominantly ruminants. These range from species, such as *T. parva* and *T. annulata*, which cause acute lymphoproliferative diseases in cattle resulting in high levels of mortality, to others that are non-pathogenic. In the last decade, several new pathogenic species of *Theileria* have been identified and pathogenic strains of other previously low-pathogenic species have emerged. *Theileria* parasites are characterised by developmental stages within leukocytes and erythrocytes. The capacity of the most pathogenic species to undergo extensive multiplication during intra-leukocyte development is central to their ability to cause disease. However, this is not the sole property responsible for disease, as illustrated by *T. parva*, which grows in a similar manner in buffalo cells but does not cause disease in this species. Because of the highly pathogenic nature of these parasites in livestock and the susceptibility of young animals to disease, control of the diseases is challenging. Control by chemotherapy and prevention of tick infestation has proved expensive and difficult to sustain. Vaccines using live parasites are available for *T. parva* and *T. annulata* and have been used with some success in the field. However, their widespread use has been hampered by practical constraints in production and distribution of the vaccines. Studies of the immune responses in immune cattle have helped to elucidate the protective immune responses and identified a number of parasite antigens that are currently being explored for development of alternative vaccines.

Keywords
Africa – Buffalo – Cattle – Immunity – Sheep – *Theileria* – Tick – Vaccination – Vector.

Introduction

Theileria are tick-borne apicomplexan parasites, which include a number of species that cause economically important diseases of farm animals in tropical and sub-tropical regions of the world (1, 2, 3). They are most closely related to *Babesia*, from which they differ by having a developmental stage in leukocytes prior to infection of erythrocytes. Although *Theileria* have been reported in several mammalian species, the vast majority of *Theileria* species described to date are found in ruminants (4, 5, 6). One important exception is the equine species *T. equi*, which was originally considered to be a *Babesia* parasite (*B. equi*) but was reclassified in 1998 following the discovery of a developmental stage in leukocytes (7). *Theileria* parasites are transmitted by a range of different tick species and the geographical distribution of the parasites is determined largely by the climatic conditions that support the respective tick vector species. Transmission of ruminant *Theileria* occurs transstadially, meaning infections acquired by larval and nymphal ticks are transmitted to new hosts by nymphs and adults respectively. Transmission of *T. equi* by some tick species can also occur intra-stadially, i.e. by the same tick stage transferring from one host animal to another (8). Many of the *Theileria* that infect domestic livestock are also found in wildlife, notably African and Asian buffalo (*Syncerus caffer* and *Bubalus bubalis* respectively), which in some cases are considered the primary mammalian hosts (1, 5, 9, 10). The parasites are usually non-pathogenic in their wildlife hosts.

This review provides a brief summary of current knowledge on the *Theileria* species that cause disease in farm animals

and discusses the pathogenesis of the diseases and methods employed for their control, focusing particularly on the role of vaccination.

Diseases caused by *Theileria* species

A summary of the hosts, geographical distribution and pathogenicity of *Theileria* species that infect domestic animals is provided in Table I. *Theileria* species vary widely in virulence, ranging from production of severe disease, resulting in high levels of mortality, to completely benign. *Theileria parva* and *T. annulata* in cattle and *T. lestoquardi* in sheep are particularly virulent, causing acute lymphoproliferative diseases that result in major economic losses in the affected regions. The last decade has also seen the discovery of novel species of *Theileria* that cause disease in sheep in China and the emergence of apparently more pathogenic strains of *T. orientalis*.

Cattle

Theileria parva is the causal agent of East Coast fever (ECF), which occurs in 11 countries in East and Southern Africa, where 28 million cattle are at risk (3, 11). The disease is characterised by the presence of large numbers of parasitised leukocytes throughout the lymphoid system, clinically evident as lymph node enlargement, and infiltration of other tissues, notably the lungs and gastrointestinal tract, by parasitised cells. In severe cases, extensive lymphocytolysis during the later stages of the disease results in profound cellular depletion of lymphoid tissues and leukopenia, accompanied in the terminal stages by pulmonary oedema (12, 13). The disease causes high levels of mortality in fully susceptible stock. Annual losses due to the disease are estimated at US$300 million. European (*Bos taurus*) breeds are particularly susceptible (14), although the disease also results in up to 10% mortality in indigenous (*B. indicus*) animals (15, 16, 17). Cattle can acquire infection with *T. parva* from ticks that have fed on cattle or African buffalo. Both infections result in severe disease with similar clinical signs, but buffalo-derived infections exhibit lower levels of schizonts in peripheral lymph nodes and very low or undetectable piroplasm parasitaemia (18).

A buffalo parasite closely related to *T. parva*, referred to as *T.* sp. (buffalo), was first described in the early 1990s (19), but has yet to be assigned a formal species name. A recent study in Kenya has demonstrated that this parasite can infect cattle (R. Bishop, unpublished data). A number of parasitised cell lines isolated from cattle that developed severe disease following introduction into an area grazed by buffalo were shown to contain cells infected with *T.* sp. (buffalo). Because *T. parva* was also present in these animals, the role of *T.* sp. (buffalo) in pathogenesis of the disease could not be determined.

Cattle in Africa are frequently infected with a number of other *Theileria* species (20, 21, 22) which rarely cause disease. *Theileria mutans* has very occasionally been reported in association with clinical disease, manifesting as fever, severe anaemia and icteris, with mortality in some animals

Table I
***Theileria* parasites infective for domestic animals**

Species	Hosts	Tick vector genus [a]	Distribution	Pathogenicity
T. parva	African buffalo, cattle	*Rhipicephalus*	Africa	++++
T. sp. (buffalo)	African buffalo, cattle	Not known	Africa	Not known
T. taurotragi	Eland, cattle	*Rhipicephalus*	Africa	–
T. annulata	Cattle, Asian buffalo	*Hyalomma*	Mediterranean Basin, Middle East, Asia	+++
T. lestoquardi	Sheep, goats	*Hyalomma*	Mediterranean Basin, Middle East, Asia	+++
T. mutans	African buffalo, cattle	*Amblyomma*	Africa	+/–
T. velifera	African buffalo, cattle	*Amblyomma*	Africa	–
T. orientalis (incl. *T. buffeli*)	African buffalo, cattle	*Haemaphysalis*	Widespread	+/–
T. uilenbergi	Sheep, goats	*Haemaphysalis*	China	++
T. lowenshuni	Sheep, goats	*Haemaphysalis*	China	++
T. sinensis	Cattle, African buffalo, Asian buffalo, yak	*Haemaphysalis*	China, Africa	–
T. ovis	Sheep, goats	*Rhipicephalus*	Widespread	–
T. equi	Horses	*Dermacenter, Rhipicephalus* [b], *Amblyomma* [b]	Widespread	++

a) Specific tick species have been identified as vectors for most species and are well defined for *T. parva* and *T. annulata*. However, testing of vector competence of different tick species for most other *Theileria* species has been limited
b) *Rhipicephalus microplus* and *Amblyomma cajennse* have been shown to transmit intra-stadially

(23). Such disease usually occurs in older animals that have not previously been exposed to the parasite. Affected animals are also often infected with other parasites, which might contribute to the observed clinical disease.

Tropical theileriosis caused by *T. annulata* occurs in a broad subtropical zone in the Northern Hemisphere extending from northern Africa and southern Europe through the Middle East to Asia. *Theileiria annulata* causes an acute disease similar to that produced by *T. parva* (2). European breeds of cattle are particularly susceptible to the disease and can suffer high levels of mortality. Unlike *T. parva*, which causes only a small reduction in circulating erythrocytes, mild to moderate anaemia is observed in tropical theileriosis, although pathology produced by the schizont stage is usually the primary cause of mortality.

The *T. orientalis* group of parasites, which have a wide global distribution, includes parasites previously assigned the *T. orientalis, T. buffeli* and *T. sergenti* species names. Because of close similarity in morphology and serological cross-reactivity, they are now referred to as a single species, *T. orientalis*, although they exhibit minor sequence differences in the 18s ribosomal RNA subunit gene (6, 24). The *T. sergenti* species name is no longer used, but *T. buffeli* is commonly still used for these parasites in buffalo (both Asian and African). It is unclear whether *T. orientalis* parasites exhibiting minor 18s sequence differences represent distinct species or subtypes of the same species (discussed in 21). Studies in Japan indicate that some *T. orientalis* parasites can cause transient anaemia, with clinical signs in up to 2.5% of animals and occasional mortalities (<0.1%) (22). Outbreaks of disease in cattle attributable to one particular subtype of *T. orientalis* have been reported in Australia and New Zealand over the last eight years (24, 25, 26, 27). This disease, which prior to 2006 was only rarely observed, has occurred in a large number of herds, dairy herds being most severely affected. The main clinical manifestations are fever, haemolytic anaemia of variable severity and mortality in some animals; infection is also associated with an increased incidence of abortion and stillbirths and significant reductions in milk yields in affected herds.

Sheep and goats

Theileria lestoquardi (previously known as *T. hirci*) is genotypically closely related to *T. annulata* and causes a severe disease in sheep; the disease is similar to that caused by *T. annulata* in cattle and can result in high levels of mortality (28, 29). Available evidence, although limited, indicates that *T. lestoquardi* is transmitted by the same *Hyalomma* tick species as *T. annulata* (30, 31). Reports of the disease are mainly confined to the Middle East and north-east Africa, suggesting that the parasite may have a more restricted distribution than *T. annulata*.

About ten years ago, a severe disease of sheep in China, previously assumed to be caused by *T. lestoquardi*, was found to be associated with two novel *Theileria* parasites subsequently designated *T. lewenshuni* and *T. uilenbergi* (32, 33). These species are morphologically indistinguishable and cause similar disease, but can be distinguished by DNA typing methods (34). They are transmitted by *Haemaphysalis quinghaiensis* ticks (35). Infected animals show variable levels of piroplasm parasitaemia. Disease appears to be associated predominantly with the schizont stage and this stage of the parasite is detected in lymph nodes and in a range of internal organs. Morbidity and mortality rates of up to 65% (*T. lewenshuni*) and 75% (*T. uilenbergi*) have been observed in susceptible animals introduced into endemic areas (33).

Horses

Infection of horses with *T. equi* is often asymptomatic but can result in outbreaks of disease characterised by fever, anaemia and lethargy, leading to mortality of some animals (36). Certain strains of the parasite may be more pathogenic than others. Although schizont-infected leukocytes are readily observed in lymphoid tissues of affected animals, disease is largely attributable to destruction of infected erythrocytes (37). Thrombocytopenia and haemorrhage may also occur.

The properties of *Theileria* species that enable them to cause disease

The developmental stages of a highly pathogenic species, *T. parva*, in the bovine host are illustrated in Figure 1. *Theileria*-infected ticks feeding on their mammalian hosts deposit sporozoites at the site of feeding, where they invade leukocytes. The intracellular parasites develop over a number of days to multinuclear schizonts, which then undergo varying degrees of multiplication (depending on the species), before differentiating to produce merozoites. Upon release from the infected cells, merozoites invade erythrocytes, giving rise to the piroplasm stage, which is infective for ticks. Virulence of the different *Theileria* species is strongly influenced by the degree to which they multiply during the schizont stage of development. Unlike most other apicomplexan parasites, *Theileria* reside free within the cytosol of the host cells (38). The highly pathogenic species, such as *T. parva*, *T. annulata* and *T. lestoquardi*, cause activation and proliferation of the infected host leukocytes and, by associating with the mitotic spindle during cell division, the parasites are able to divide at the same time as the host cells, ensuring that infection is retained in the daughter cells (39, 40, 41).

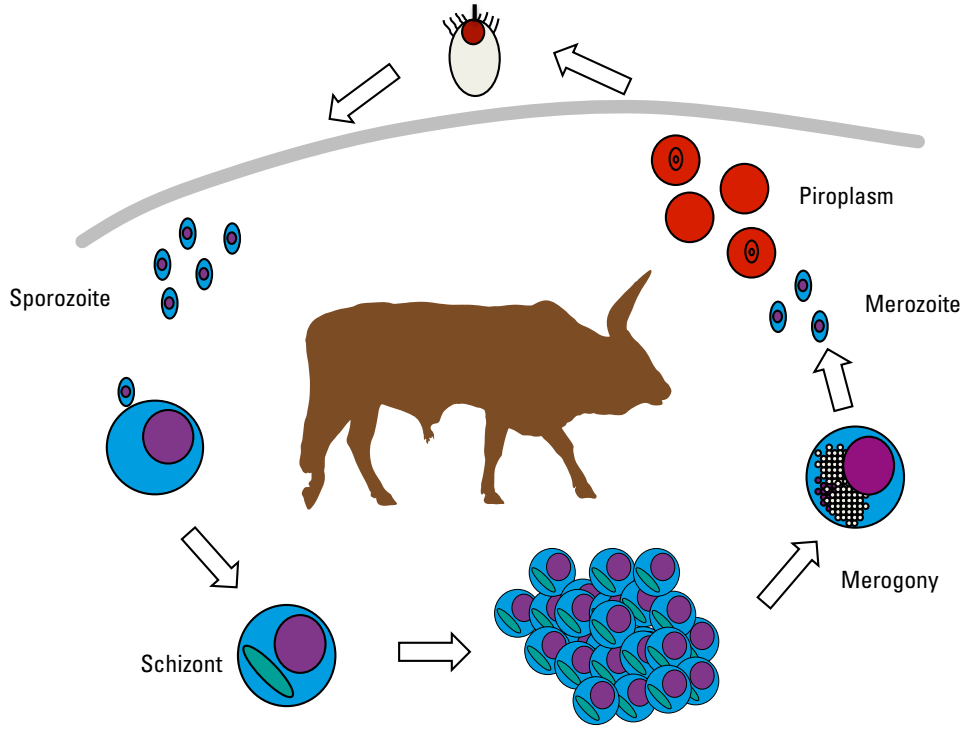

Fig. 1
Schematic representation of the life cycle of *Theileria parva*

This process facilitates rapid parasite multiplication prior to differentiation to merozoites. The intra-erythrocytic piroplasm stage of the highly pathogenic species undergoes little or no multiplication. Nevertheless, the sheer numbers of merozoites produced from the infected leukocytes can result in high levels of piroplasms during the acute stage of infection. Extensive multiplication of the schizont stage of *T. parva*, *T. annulata* and *T. lestoquardi* , as well as *T.* sp. (buffalo), enables the parasitised cells of these species to be cultured *in vitro* as continuously growing cell lines (42, 43). Bovine cells infected with *T. taurotragi* can also be established as cell lines *in vitro*, although this species is non-pathogenic in cattle. Consequently, these parasites are sometimes referred to as 'transforming' *Theileria* species. It has not been possible to culture parasitised cells from *T. lewenshuni* and *T. uilenbergi*, despite evidence that they multiply and cause disease during the schizont stage. The initial development of schizonts of other *Theileria* species is similar but multiplication of the infected cell is more limited and varies between species. Multiplication in these parasites occurs predominantly during the piroplasm stage, but only in a few species does this result in disease.

An important property of all *Theileria* is their ability to establish persistent infections in the face of immune responses that control the infection. In the case of *T. parva* and *T. annulata*, these infections (referred to as the carrier state) are usually not detectable microscopically but can be revealed by polymerase chain reaction (PCR) assays (44) and can be transmitted by ticks. Carrier infections with *Theileria* species that do not multiply during the piroplasm stage rely on persistence of small numbers of schizont-infected cells. The sites of persistence of these cells and how they avoid the immune response are not known.

Host adaptation and susceptibility to diseases

As outlined above, the most pathogenic *Theileria* species are able to transform their host cells, allowing them to be cultured *in vitro* as cell lines. While this property facilitates rapid parasite multiplication, it does not inevitably result in disease. This is best illustrated by *T. parva*, which infects and transforms cattle and African buffalo (*S. caffer*) leukocytes *in vitro* with similar efficiency (45), yet infection of buffalo does not result in disease. This presumably reflects a long period of evolutionary adaptation of buffalo to the parasite, allowing them to control the infection. By contrast, cattle currently present in East and Southern Africa were introduced into Africa from the Middle East within the last 8,000 years (46). Since *T. parva* is not found outside Africa, cattle would have first encountered the parasite within this time period by tick transmission from

the African buffalo. Recent studies involving sequencing of genes encoding polymorphic antigens in field isolates of *T. parva* have indicated that cattle-maintained populations of *T. parva* contain much less antigenic diversity than buffalo-maintained populations (47). This is consistent with previous evidence that buffalo-derived *T. parva* parasites differentiate poorly to the piroplasm stage in cattle and onward transmission by ticks is very inefficient (48). This implies that the subset of *T. parva* parasites currently maintained in cattle have been selected for their ability to adapt to tick transmission in cattle.

As mentioned earlier, some populations of indigenous (*Bos indicus*) cattle residing in ECF-endemic areas exhibit a degree of resistance to the disease (15, 16, 17). Experimental studies carried out in the 1950s, involving challenge of *T. parva*-free indigenous and European cattle with different numbers of infected ticks, demonstrated that both types of animal were susceptible to infection and disease, but larger numbers of infected ticks were required to produce lethal infections in the indigenous animals (15). Hence, these animals appear to have evolved a degree of resistance that allows most of them to survive the levels of parasite challenge encountered in the field. The mechanisms responsible for these differences in host susceptibility to disease are not understood.

Diagnosis

Diagnosis of clinical disease caused by *Theileria* usually relies on clinical parameters and microscopic confirmation of the presence of parasites, either in smears of needle aspirates from enlarged lymph nodes or blood smears. Definitive identification of the *Theileria* species involved sometimes requires the application of species-specific PCR assays (49, 50). Antibody tests based on enzyme-linked immunosorbent assays employing recombinant immunodominant schizont proteins (51, 52), as well as species-specific PCRs, are frequently used in epidemiological studies. A reverse line blot assay involving PCR amplification of a segment of the 18s ribosomal RNA subunit of all *Theileria* and *Babesia* species and subsequent hybridisation of the amplicons with species-specific oligonucleotides has been employed to identify *Theileria* species present in individual animal samples (53).

Disease control measures

Calves infected with several other bovine tick-borne blood pathogens, including *Babesia* species and *Anaplasma marginale*, show enhanced resistance to disease in the first six months of life, enabling them to acquire immunity to these pathogens in regions where the infections are endemic. Such age-related resistance is not seen with *T. parva* or *T. annulata*. Nor is there any evidence that maternally derived antibodies are protective (54, 55). Because of the absence of such protective mechanisms and the fatal nature of the diseases in susceptible stock, control of disease caused by these highly pathogenic *Theileria* is particularly challenging.

A single therapeutic compound (buparvaquone, marketed as Buparvex) is available (56), but its use is limited by cost and the need to treat animals during the early stages of disease to be effective. Moreover, there are recent reports of the emergence of drug-resistant strains of *T. annulata* (57, 58). Control of the disease by prevention of tick infestation requires essentially continuous application of acaricides and is therefore expensive and difficult to sustain. The use of these compounds can also result in selection of acaricide-resistant tick populations. Because of the shortcomings of these control measures, vaccination is seen as the most sustainable option for control of the disease.

Successful vaccination against *T. parva* and *T. annulata* has only been achieved using live parasites. A method of vaccination against *T. annulata*, based on the use of parasitised cell lines in which the parasite had been attenuated by up to 200 passages *in vitro*, was developed in the 1960s (2, 59). Although the immunity obtained by immunising with a single cell line isolate was more effective against experimental challenge with the homologous parasite isolate than heterologous isolates, such cell lines could be used successfully to vaccinate cattle in the field (2). This method of vaccination has been used locally with success in a number of countries since the 1970s (60). Each country has utilised a locally derived culture-attenuated parasite isolate in their vaccine, because of concern about introducing the 'foreign' vaccine parasites into local tick populations. Stocks of the vaccine are cryopreserved in liquid nitrogen and a dose of 10^5–10^6 infected cells (representing <1 ml of cell culture) is administered to each animal.

In contrast to *T. annulata*, reliable induction of immunity to *T. parva* with cultured cells required doses of 10^7–10^8 infected cells (61) and was therefore not economically viable as a means of vaccination. Subsequent studies have provided evidence that induction of immunity against both parasites requires transfer of the parasite from the cells in the vaccine to the cells of recipient animals and that this occurs at a much higher frequency with *T. annulata* than *T. parva* (62, 63). The mechanism of parasite transfer and the reason for the difference between the two parasite species are not understood

An alternative method of vaccination against *T. parva* using live parasites was developed in the 1970s. This involves infection of cattle with sporozoites and simultaneous

treatment with oxytetracycline to delay parasite development, resulting in mild, transient infections (64); a long-acting formulation of oxytetracycline that provides five to six days of activity is used. This so-called 'infection and treatment' protocol provides long-lasting immunity in all animals against large doses of the *T. parva* isolate used for immunisation (65, 66), but only some of the immunised animals withstand challenge with other parasite isolates (64). However, immunisation and cross-challenge studies with different combinations of parasite isolates resulted in identification of a mixture of three isolates (known as the Muguga cocktail), which, when used to immunise cattle, gave broad protection against experimental challenge with different *T. parva* isolates and against field challenge with *T. parva* (67, 68). Despite evidence of efficacy, until recently, use of the Muguga cocktail vaccine in the field had been limited, largely because of the complex process involved in production and quality control of the live sporozoites and the requirement for a cold chain to store and distribute the vaccine. However, recent initiatives to register the vaccine and to establish centres for vaccine production and systems to facilitate its distribution have led to increased field uptake. Nevertheless, the need for an alternative vaccine that can be produced and distributed in a more sustainable manner is widely recognised.

Mechanisms of immunity induced by live parasites

The need for alternative methods of vaccination has driven research to unravel the nature of the protective immune response, with the aim of identifying antigens that could be exploited for vaccination.

A large body of evidence from studies of immunity to *T. parva* indicate that protective immune responses are directed against the schizont-infected cell and that this involves T-cell-mediated immune responses (69, 70). Cattle immunised by infection and treatment generate major histocompatibility complex (MHC)-restricted CD8 T-cell responses following immunisation and challenge, coinciding with parasite clearance (71, 72). These cells show cytotoxic activity against autologous *T. parva*-infected cells and exhibit parasite strain specificity (73, 74). Two further observations provided evidence that these T cells are key mediators of immunity. First, transfer of responding CD8 T cells (but not CD4 T cells) from immune to naive identical twin calves was found to confer protection against parasite challenge in the naive recipients (75). Second, parasite strain specificity of the CD8 T-cell response, which varies between individual animals immunised with the same parasite isolate, correlated closely with immunity following challenge with a cloned heterologous parasite strain (76).

Immunised animals also show strong parasite-specific CD4 T-cell responses (77, 78), which recognise antigen presented by class II MHC on the surface of the infected cells and the majority of them release interferon gamma (IFN-γ) following antigenic stimulation. Although these CD4 T cells do not appear to have a direct role as immune mediators, *in vitro* studies indicate that they may be required for induction and/or recall of effective CD8 T-cell responses *in vivo* (79).

More limited studies of immune responses against *T. annulata* indicate that similar mechanisms of immunity operate with this parasite (80, 81, 82).

Publication of the complete genome sequences of *T. parva* and *T. annulata* in 2005 provided a catalogue of the functional genes, indicating that both parasites encode just over 4,000 proteins (83, 84). Around the same time, development of high-throughput antigen screening methods led to the identification of a number of *T. parva* antigens and epitopes recognised by CD8 T-cell responses (85). These advances facilitated a series of studies to examine the fine antigenic specificity of the CD8 T-cell response, which helped to elucidate the basis of strain specificity of immunity (reviewed in 69). Although some of the antigens that generate highly dominant responses are polymorphic (86, 87), recent studies have shown that others are highly conserved, but suggest that CD8 T cells specific for these antigens may represent a minor component of the immune response (H. Hemmink, W. Weir and W.I. Morrison, unpublished). Hence, the dominance of the polymorphic antigens appears to be an important factor in determining strain specificity of the response.

Approaches to development of alternative vaccines

The above studies of immune responses induced by live parasites have yielded parasite antigens that are being investigated for development of subunit vaccines against *T. parva* and *T. annulata*. An additional approach has been to attempt to vaccinate using antigens from the sporozoite stage of the parasite. Although infection or immunisation with live parasites induces very little antibody against sporozoites, monoclonal antibodies reactive with *T. parva* and *T. annulata* sporozoite surface antigens were found to neutralise the infectivity of sporozoites *in vitro* (88, 89). The antigens recognised by these antibodies have been identified (90, 91) and recombinant proteins have been explored for vaccination (92, 93, 94). Immunisation of cattle with the *T. parva* and *T. annulata* antigens (p67 and spag, respectively) incorporated in adjuvant induced neutralising antibodies in all animals and protection in

up to 50% of animals against experimental challenge with sporozoites. However, field testing of the *T. parva* antigen has given variable and disappointing results (reviewed in 95).

Theileria parva antigens recognised by CD8 T cells have also been tested for their ability to induce immune responses and protection against parasite challenge (85). These experiments used prime-boost protocols involving priming with plasmid DNA or recombinant canarypox viruses followed by a single boost with recombinant replication-defective vaccinia viruses. Animals were immunised simultaneously with five of the antigens in separate DNA or viral constructs and challenged three weeks later with a lethal dose of sporozoites. Most of the immunised animals (19/24) exhibited readily detectable antigen-specific CD8+ T-cell IFN-γ responses following immunisation, but only a proportion of the animals were protected against challenge with a lethal dose of sporozoites (85). However, observations on the CD8 T-cell responses induced by vaccination indicated that they differed quantitatively and functionally from those elicited by live parasites (e.g. they did not exhibit cytotoxic activity in most immunised animals). Current research is investigating alternative antigen delivery systems to achieve improved immune responses and higher levels of protection against parasite challenge (discussed in 69).

Acknowledgements

Some of the work discussed in this paper was supported by a grant awarded jointly by the Department for International Development (United Kingdom [UK] Government) and the Biotechnology and Biological Sciences Research Council (BBSRC) in the UK (grant number BB/H009515/1) and by the Roslin Institute Strategic Grant funding from the BBSRC.

Étiologie, pathogénie et contrôle de la theiléríose chez les animaux domestiques

W.I. Morrison

Résumé

Le genre *Theileria* comprend un grand nombre d'espèces de parasites vectorisés par les tiques, qui peuvent infecter diverses espèces d'animaux domestiques et sauvages, principalement des ruminants. Certaines de ces espèces, notamment *T. parva* et *T. annulata*, sont responsables de maladies lymphoprolifératives occasionnant une mortalité élevée, tandis que d'autres ne sont pas pathogènes. De nouvelles espèces pathogènes de *Theileria* ont été identifiées au cours des dix dernières années, en même temps qu'émergeaient des lignées pathogènes d'espèces précédemment non pathogènes. Les parasites du genre *Theileria* se caractérisent par le fait que certains stades de leur développement se déroulent à l'intérieur des leucocytes et des érythrocytes. La capacité de la plupart des espèces pathogènes de se multiplier de manière extensive pendant le développement intraleucocytaire participe à leur aptitude à déclencher une maladie. Cette propriété n'est toutefois pas le seul facteur d'apparition de la maladie, comme le montre l'exemple de *T. parva* qui a un taux de multiplication similaire à l'intérieur des cellules du buffle sans pour autant causer de maladie chez cette espèce. Ces parasites sont extrêmement pathogènes pour les espèces d'élevage, dont les jeunes sont particulièrement sensibles, de sorte que les méthodes de lutte recourant à la chimiothérapie ou à la prévention des infestations par les tiques s'avèrent coûteuses et difficiles à mener sur le long terme. Des vaccins utilisant des parasites vivants ont été utilisés sur le terrain pour lutter

contre *T. parva* et *T. annulata* et ont rencontré un certain succès. Néanmoins, leur utilisation massive est rendue difficile par des contraintes pratiques liées à la production et à la distribution de ces vaccins. Des études sur la réponse immune chez les bovins ont permis de comprendre le mécanisme des réponses protectrices et d'identifier un certain nombre d'antigènes du parasite, qui font actuellement l'objet de recherches complémentaires en vue de développer de nouvelles solutions vaccinales.

Mots-clés
Afrique – Bovin – Buffle – Immunité – Ovin – *Theileria* – Tique – Vaccination – Vecteur.

Etiología, patogénesis y control de la teileriosis en animales domésticos

W.I. Morrison

Resumen
El género *Theileria* abarca un gran número de especies de parásitos transmitidos por garrapatas que infectan a diversos animales domésticos y salvajes, principalmente a los rumiantes. Entre ellas hay desde especies como *T. parva* y *T. annulata*, que provocan enfermedades linfoproliferativas agudas en los bovinos y causan elevados niveles de mortalidad, hasta otras que no son patógenas. En el último decenio se han descrito varias nuevas especies patógenas de *Theileria* y han aparecido cepas patógenas de especies que hasta entonces presentaban escasa patogenicidad. Los parásitos *Theileria* se caracterizan por atravesar una fase de desarrollo en el interior de los leucocitos y eritrocitos. En las especies con mayor poder patógeno, la capacidad de multiplicarse a gran escala durante la fase de desarrollo intraleucocitaria es un aspecto central de su aptitud para generar la enfermedad. Sin embargo, esta no es la única propiedad responsable de la patología, como evidencia el caso de *T. parva*, que se reproduce de forma parecida en las células del búfalo pero no le causa enfermedad alguna. Está comprobado que, en razón del gran poder patógeno que revisten estos parásitos para el ganado y de la sensibilidad de los animales jóvenes a la enfermedad, resulta caro y difícil luchar duraderamente contra ella con medidas de farmacoterapia y prevención de la infestación por garrapatas. Existen vacunas a base de parásitos *T. parva* y *T. annulata* vivos que han sido empleadas con cierto éxito sobre el terreno. No obstante, la fabricación y distribución de esas vacunas presentan limitaciones de orden práctico que han obstaculizado su aplicación generalizada. Las investigaciones sobre la respuesta inmunitaria de los bovinos han ayudado a desentrañar las respuestas inmunitarias que confieren protección, y actualmente se está estudiando el uso de una serie de antígenos parasitarios para obtener vacunas alternativas.

Palabras clave
África – Búfalo – Ganado vacuno – Garrapata – Inmunidad – Ovino – *Theileria* – Vacunación – Vector.

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