Review

Review on camel trypanosomosis (surra) due to *Trypanosoma evansi*: Epidemiology and host response

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Trypanosomosis is the most important and serious pathogenic protozoal disease of camel caused by *Trypanosoma* species. *Trypanosome evansi* parasite has a wide range of distribution throughout tropical and subtropical regions of the world. Mostly, camels suffer from trypanosomosis caused by *T. evansi* that is transmitted mechanically, non-cyclically, by haematophagus flies such as horseflies (*Tabanus*) and stable flies (Stomoxys) which are endemic in Africa, Asia and South America, although in America the vampire bat also acts as a vector as well as reservoir hosts. The disease manifests itself in different forms: acute, sub-acute, chronic and in-apparent. Anaemia appears to be a major component of the pathology of surra and generally the degree of anaemia might be considered as an indicator of the disease severity. Control of camel trypanosomosis depends mainly on the use of curative and prophylactic drugs even though this strategy is faced with various problems. Surra has a wide host spectrum, the main host species varies with the geographical region. In Africa, beyond the northernmost limits of the tsetse fly belt, and in parts of East Africa, camels are the most important host, whilst in Central and South America the horse is principally affected. In Asia, a much wider range of hosts is involved, including cattle, buffalo and pigs. The disease is most severe in horse, donkey, mules, camels, dogs and cats. *T. evansi*, like other pathogenic trypanosomes induce a generalized immune-suppression of both humoral antibody response and T cell- mediated immune responses. As a result, in the long term, the host's immune responses fail and it succumbs to either the overwhelming parasite load or to secondary infection, consequently leading to occurrence of the trypanosome-induced immunopathology. This paper reviews the epidemiology of the disease and host response against the parasite.

Key words: Trypanosomosis, *Trypanosome evansi,* flies, hosts.

INTRODUCTION

Trypanosoma evansi (*T. evansi*), the protozoan parasitic cause of camel trypanosomiasis (Surra), constitutes one of the major veterinary problems worldwide (Omer et al., 2004). The disease is an important single cause of economic losses, causing morbidity of up to 30.0% and mortality of around 3.0% camels in Ethiopia (Njiru et al., 2001; Tekle and Abebe, 2001), in which, as in most dry lands of Africa and Asia, camels are the principal source of income and food for millions of pastoralists and has a population of approximately over 0.807 million heads of

dromedary camels (Central Statistical Agency of Ethiopia (CSA), 2010), placing it at the third position in camel rearing countries after Somalia and Sudan, then followed by Mauritania and Kenya in that order (Food and Agricultural Organization of the United Nations (FAO), 2008).

  T. evansi is transmitted mechanically, non-cyclically, by haematophagus flies such as horseflies (Tabanus) and stable flies (Stomoxys) which are endemic in Africa, Asia and South America; although in America the vampire bat

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also acts as a vector as well as reservoir hosts (Urquhart et al., 1996). Surra is manifesting itself both in acute and chronic forms. Affected camels show fever, anorexia, marked generalized edema and deteriorate rapidly and die; the chronic form is characterized by progressive loss of body weight, intermittent high fever, marked generalized muscular atrophy, pale mucous membranes and occasionally abdominal edema. Affected camels also may exhibit a characteristic sweet odour due to an increase of urinary ketone. The chronic form is most common and is likely to present an association with secondary infection due to immune-suppression caused by *T. evansi* infection (Olaho-Mukani et al., 1993; Ahmed, 2008).

Treatment recommendations and strategies for chemotherapeutic control depend on information of trypanosomosis risk and the prevalence of trypanocidal drug resistance in the area. Sensitive diagnostic techniques are required to detect the parasite and the efficacy of trypanocidal drug treatment. Parasitological methods used in the diagnosis of *T. evansi* in camels are considered easy, rapid and economic. However, they are not sufficient to detect all trypanosome infected animals, especially in case of low parasitaemia and also in the chronic form of the disease (Ahmed, 2008). The serological test such as the card agglutination test (CATT) is used for the detection of antibodies circulating in the serum of infected camels, the test could be used under both laboratory and field conditions. It is a quick, simple and easy to perform and sensitive method. However, serological techniques are not always distinguishing current from past infection due to the prolonged persistence of antibodies in the blood of treated animals (Luckins et al., 1988). Particularly in these cases of treatment success evaluation, DNA based techniques, as polymerase chain reactions (PCR) are useful. These DNA tests are considered sensitive and specific. With the introduction of molecular diagnostic techniques, several diagnostic assays based on the detection of trypanosomal DNA by PCR have been developed.

Surra has a wide host spectrum, the main host species varies with the geographical region. In Africa, camels are the most important host, whilst in Central and South America the horse is principally affected. In Asia, a much wider range of hosts is involved, including cattle, buffalo and pigs. The disease is most severe in horse, donkey, mules, camels, dogs and cats. In Ethiopia, the occurrence of Surra reported as it has been associated with camel rearing areas (Tekle and Abebe, 2001; Getachew, 2005; Basaznew et al., 2012). Because of the range of agro-ecological zones and the diverse farming systems in which the disease occurs, and its debilitating effects on a variety of livestock, surra has attracted international attention in recent years, with a focus on formulating and implementing effective control strategies aimed at increasing productivity and achieving a decrease in mortality and morbidity (Obihiro, 1998). Therefore, in this review, the epidemiology of surra and host response to *T. evansi* infection are presented, as researchers provide both historical perspective and summarize the latest discoveries which will help in the design of effective diagnosis, treatment and control of camel trypanosomosis.

CAMEL TRYPANOSOMOSIS (SURRA)

History and origin of the disease

The causative agent, *T. evansi*, was discovered by Griffith Evans, in 1880 in infected camels and horses in India. The local Indians had a local name for the disease – Surra, meaning emaciated (Al-Rawashdeh et al., 2000). Since then, studies have shown that *T. evansi* is related to the African trypanosomes and is thought to have evolved from *T. brucei,* the cause of nagana in animals in Africa.

It is thought that *T. evansi* evolved from its ancestors along the edges of the tsetse fly belt in Africa and from there was spread via infected camels used for trade with India (Hoare, 1972). Continuous mechanical transmission by blood-sucking flies in the absence of *Glossina* caused the loss of cyclic transmissibility and gave rise to a predominance of slender parasite forms.

The parasite

Taxonomy and identification

Trypanosomes are unicellular flagellar protozoa belonging to phylum Sarcomastigophora, the order of Kinetoplastidae, family of Trypan-somatidae and the genus of trypanosome, under the *Salivaria* group. The sub genus Trypanozoon includes the pathogenic species *T. evansi, T. brucei* and *T. equiperdum* (FAO, 2000). Because the trypanosome shows variation in its antigen coat, there are antigenic differences between isolates of *T. evansi*. There is limited, equivocal information concerning the existence of strains of *T. evansi* of different pathogenicity (Queiroz et al., 2000). However, some strains are referred to colloquially as highly pathogenic' but this may be a result of host- vector factors, such as stock and insect densities and the susceptibility of host species (Hoare, 1972). *Trypanosoma evansi* is morphologically identical with and indistinguishable from slender forms of other members of the subgenus *Trypanozoon* and is described as monomorphic but may be pleomorphic in some strains with length of 15 to 34 µm. Leaf-like slender forms are characterized by a long free flagellum, which may be up to one half of the length of the organism with narrow and drawn out posterior end (Queiroz et al., 2000).
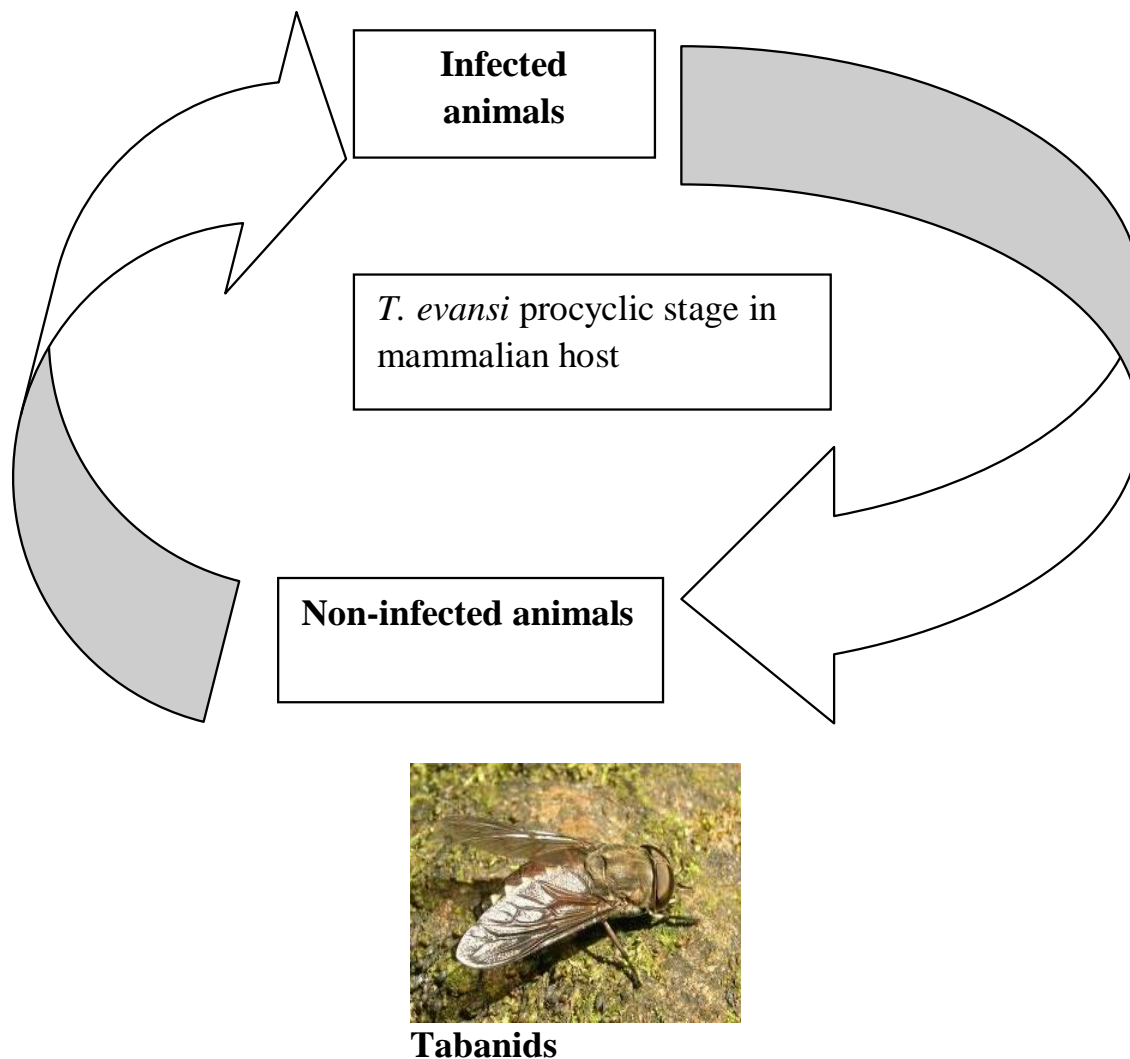
Figure 1. Life cycle of *Trypanosoma evansi.*

Life cycle and transmission

Replication of the trypanosome occurs by longitudinal binary fission both in the host and in the vector with the flagellum and kinetoplast dividing together (Liu-Liu et al., 2005), but in the noncyclically transmuted *T. evansi* developmental stages were not observed in any of the mechanical vectors. Consequently a procyclic or insect stage (epimastigotes) does not exist in *T. evansi* which is attributed to lack of maxi circles in the kinetoplast DNA (Ellie et al., 1999) (Figure 1). The non-cyclical transmission of trypanosomes is aided by biting flies and thus, in the absence of *Glossina,* the transmission is maintained in the ecosystem. Biting flies, such as *Tabanids* (horse flies)*, Stomoxys and Hippoboscids* transmit *T. evansi* mechanically through their mouthparts when they feed on more than one host within a short interval because the trypanosomes remain infective for only a short period (Evans et al., 1995).

Clinical manifestations

T. evansi can infect a variety of hosts and causes a species-specific pathology. In camels trypanosomosis occurs both in chronic and acute formes (Payne et al., 1990). The acute form of the disease in camel may last for up to three months and is characterized by irregular fever, reduced appetite and water intake, as the disease progresses hump disappear (FAO, 2000), recurrent kerato conjunctivitis and urticarial plaques on the neck and flank, dependent oedema under the belly, marked depression, dullness, loss of condition, the hair coat become dull and rough with loss of hair at the tail and often rapid death (Luckins, 1998). There is also pallor of mucous membranes of the eye, a fluctuating temperature with initial peaks of up to 410C and the urine usually has a characteristic smell increases in body temperature correspond with peaks of parasitaemia (Kohler-Rollefson et al., 2001). Anaemia was observed to be a major

clinical finding in camel Trypanosomosis in Morocco (Rami et al., 2003). Chronic cases are most common and develop recurrent episodes of fever. Some camels develop oedema in their dependent parts of the body, urticaria plaques and petechial haemorrhages in serous membranes. Death finally ensures if untreated however; some may harbour trypanosomes for 2-3 years thus constituting reservoirs of infection to susceptible camels and hosts. Other well documented field reports are death ,abortion, and nervous signs like circling movement and trembling, unusual aggressiveness, running aimlessly and sudden collapse in severely stressed and over worked camels (Luckins, 1998) .

Diagnosis

Trypanosomiasis is diagnosed by demonstrating the parasite. However, because dromedaries are usually far away from laboratory facilities, a tentative diagnosis can be reached without microscopy, by taking into account the owner's observations and clinical examination of camels in the field. The chronic form is most common in camel and may present an association with secondary infections due to immunosuppressant caused by *T. evansi* infection, and this complicates clinical diagnosis (Luckins, 1992). The parasites can be detected in blood 13 to 16 days after an infective fly has had a meal to confirm infection. Parasitological diagnosis is mainly carried out by the direct microscopic examination of wet or stained blood films. However, the test has a poor sensitivity. One often less than 50% due to parasitaemia is intermittent (Yadvendra et al., 1998). The implication of this is that in most situations *T. evansi* is under-diagnosed and the level of infection may be greater than what is frequently reported. In these circumstances, concentration methods such as the buffy coat or haematocrit centrifugation technique are necessary, as they increase the sensitivity of microscopic examination (Reid et al., 2001). Mini-anion exchange centrifugation technique (mAECT) is also one of the most sensitive method for trypanosome detection in blood and is based on a purification technique and adapted for diagnosis of animal infections with *T. brucei* and *T. evansi* (Gutierrez et al., 2004).

Serological and molecular tests have strengthened the diagnosis of camel trypanosomosis. Antibody techniques including complement fixation test (CFT), enzyme-linked immunosorbent assays (ELISA) have been used (Reyna-Bello et al., 1998). Others like indirect fluorescent antibody test (IFAT) and card agglutination test (CATT) can also be employed (Connor, 1994). The CATT/*T. evansi* based on the RoTat 1.2 VAT is a quick and easy test which can be performed under field conditions for serological diagnosis of surra in dromedary camels. Even though Ab-detection tests are sensitive, it cannot distinguish current from cured or past infections (Luckins,

1988). Demonstration of trypanosomal antigens in the blood of the infected animal would be synonymous with parasitological diagnosis (Voller and Desavigny, 1981). With the introduction of molecular diagnostic techniques, several diagnostic assays based on the detection of trypanosomal DNA by PCR have been developed. PCR is reported to be more sensitive than conventional parasitological techniques in a number of hosts and has the advantage that it can identify parasites at the species level (Gutierrez et al., 2004).

Treatment and control

Treatment of surra depends largely on four drugs: suramin, diminazene aceturate (Berenil), melarsomine (cymelarsan) and quinapyramine. Suramin and quinapyramine have been used for the treatment of *T. evansi* infection in camels, and only recently melarsomine (cymelarsen) was introduced for the treatment of surra in camels because of the problem of drug resistance. Most drugs are either not curative such as homidium bromide, or are too toxic for camels such as diminazene aceturate (Bourdichon, 1998). Treatment of *T. evansi* infected camels in Morocco with melarsomine (cymelarsan) reduced the sero prevalence level from 58 to 19% within a year (Rami et al., 2003). Drug resistance is known to occur amongst *T. evansi* isolates and there have been reports of its occurrence in several different countries in Africa and Asia. In Sudan, from a place named Kassala (near the west border of Ethiopia), an isolate of *T. evansi Kassala/4* stock was found to be resistant to the curative action of Suramin even at the maximum tolerated dose of Suramin for mice (Abebe et al., 1983), which was attributed to an extensive and repeated use of Suramin in that area a similar problem may be expected in the adjacent Metema areas of Ethiopia.

The aim of prevention is to break the vector transmission cycle in camels and should be directed towards elimination of trypanosomes from the blood of animals or elimination of the vectors from the environment (Luckins, 2000). However there is no obvious way of developing exclusion zones for animals on grazing land and limited likelihood that vector control will be successful, compared to tsetse-transmitted trypanosomes (Jones and Davila, 2001) as the population of biting flies are extremely numerous, widely distributed, and difficult to deal with various options proposed to limit the impact of biting flies are application of chemicals like malathion or sumithion to stable walls or/and managing the grazing periods for stock at peak period of biting activity of the flies since they are most active in the middle of the day in sunlight; housing animals during the day would offer them protection, allowing animals to have access to field shelters could also help separate hosts from vectors (Coetzer et al., 1994).

Table 1. Prevalence of camel Trypanosomosis in some countries based on serological testes.

Country	Prevalence (%)	Source
Nigeria	27	Losos (1980)
Mauritania	24	Dia et al. (1997)
Niger	29	Pacholek et al. (2001)
Kenya	28	Njiru et al. (2001)
Ethiopia	21	Zeleke and Bekele (2001)
Jordan	33	Alrawashdeh et al. (2000)
India	22	Pathak et al. (1993)
Sudan	33	Elamin et al. (1999)
Iran	10	Zarif-Fard et al. (2001)

Source: Felicia and Anthony. (2005).

EPIDEMIOLGY

Host range and geographic distribution

Although trypanosomiasis is often referred to as African trypanosomiasis, certain trypanosomes do cause infections outside this continent. *T. evansi*, the causative agent of surra occurs not only in Africa, but also in Central and South America, the Middle East, and Asia. Surra has a wide host spectrum, the main host species varies with the geographical region. In Africa, beyond the northernmost limits of the tsetse fly belt, and in parts of East Africa, camels are the most important host, whilst in Central and South America the horse is principally affected (Dia et al., 1997). In Asia, a much wider range of hosts is involved, including the Bactrian camel and dromedaries, cattle, buffalo, horses and pigs (Pacholek et al., 2001). This is contrary to observations in Africa and South America, where there is little evidence to suggest that domesticated livestock other than camels and horses, respectively, are clinically affected or infected with *T. evansi* (El-Sawalhy and Seed, 1999).

The disease is most severe in horse, donkeys, mules, camels, dogs and cats. Camels, horses, dogs and Asian elephant are more susceptible than sheep and goat, which are more susceptible than bovines and pigs. Rats and mice are highly susceptible as experimental hosts for detecting subclinical (non patent) infection (Reid and Husein, 2001). It has been suggested that, unlike in tsetse-transmitted trypanosomiasis, wildlife reservoirs of infection are unimportant with *T. evansi*, although it is possible that South American coatis and capybaras are an exception to this (Herrera and Dvila , 2004). The ability to be transmitted by blood-sucking insects other than Glossina, has enabled *T. evansi* to extend its range into African areas north of the Sahara desert, into Asia Minor, Pakistan, India, the USSR, China, Sumatra, Java, the Philippines, Mauritius, Madagascar, and South and Central America. It was introduced by camels into Australia, North America and South-West Africa.

Introduction of the parasite to new areas is generally characterized by a high prevalence of infection, with mortality reaching 30 to 100% (Elamin et al., 1999).

Occurrence and prevalence

Trypanosomes are insect-borne and their occurrence depends on vector dynamics. Majority of camels suffer from trypanosomosis caused by *T. evansi* that is spread mechanically and independently of tsetse flies. Camels are also affected to a lesser extent by the tsetse-transmitted trypanosome species *T. brucei* (Evans et al., 1995). *T. evansi* parasite is cosmopolitan wherever camels are reared and camel trypanosomosis is endemic in most camel herds and 95% of camel trypanosomosis has been associated with *T. evansi* in Africa (Table 1) (Njiru et al., 2000).

Camel trypanosomosis in Ethiopia

T. evansi causing surra in camels is common in the southern and eastern regions of the country (Table 2). In Ethiopia, the distribution of *T. evansi* coincides with the distribution of camels in the semi-desert environment of the country. This trypanosome also occurs in the dry country of the North West near the Sudan border. In Southern Ethiopia (Borena), the disease caused by *T. evansi* is well known to the breeders by the local name "Dhukane" and is given the first priority in its order of importance among camel diseases (Demeke, 1998; Tekle and Abebe, 2001).

Course of infection and risk factors

The sequel to infection with the trypanosomes is not always a disease, some may affect self cure, but some individual animals may come down with the disease of

Table 2. Prevalence of *T. evansi* in camel by parasitological method in Ethiopia.

Region	Location	Sample size	Prevalence (%)	Sources
Oromia	Borena	391	10.9	Tekle and Abebe (2001)
	Yabello	294	31.9	Lakew (1993)
	Dello-Mena and Sawena	619	12.12	Hagos et al. (2009)
	-	-	24.88*	-
Somali	Ogaden	321	6.5	Wossene (1988)
	Somali	336	7.7	Issa (1998)
Tigrai	-	280	5	Hailu (2000)
Afar	Issa	327	0.3	Tefera (1985)

*CATT/T.evansi. Source: Hagos et al. (2009) and Alekaw (2004).

different stage. In camel trypanosomosis, the period between initial infection and the onset of clinical signs is extremely variable, but generally ranges between 5 and 60 days - although longer periods (such as 3 months) have been recorded. The interval between infection and the demonstration of parasites in the blood is usually less than 14 days (AHA, 2005). Factors that affect the incubation period include the initial infective dose (equivalent to the number of infective insect bites), and stress. Stress occurs in late pregnancy and early in lactation in animals that are more susceptible (Getahun and Demeke, 1998). Inter-current infections (helminthosis), also stressful, may accentuate the severity of the disease. Trypanotolerance may also be reduced by low plane of nutrition or when animals have to trek for long distances in search of water and pasture in the dry season. This is especially common in the nomadic pastoral communities. Surra affects camels of all ages with a higher incidence of disease in sub-adult camels shortly after weaning (Evans et al., 1995). There is usually a build-up of fly vector populations (*Tabanids, Hippoboscids, Stomoxys*) during the rains due to a good humid environment for breeding hence resulting in increase of new infections. During the dry season, pastoralists usually take their animals to riverine or swampy areas, which are also favourable grounds for these flies. The degree of risk depends on the challenge, that is, the number of vector fly bites that an animal experiences in a given time. *T. evansi* has adapted to an entirely mechanical, non-cyclical mode of transmission by bloodsucking flies other than tsetse and infects a wide range of animal hosts compared to cyclically transmitted trypanosomes (Evans et al., 1995).

HOST RESPONSES

Pathology and pathogenesis

The earliest clinical sign of infection with *T. evansi* in any

host is the development at the fly bite of a chancre: a cutaneous swelling in which the first trypanosomes multiply (Luckins et al., 992). This initial replication increases the establishment of infection, while at this spot also the first interactions take place between the host immune system and the trypanosomes. After formation of a chancre, trypanosomes invade the blood stream, which is accompanied by pyrexia. The parasitaemia may remain high for 4 to 6 days after which it declines with remission of the temperature (Murray et al., 1998). Anaemia is a major component of the pathology of surra and of African trypanosomosis, generally the degree of anaemia might be considered as an indicator of the disease severity. The parasitaemia causes a large number of red blood cells (RBCs) to be removed from circulation by cells of the mononuclear phagocytic system (MPS) in the spleen, bone marrow, and haemal lymph nodes. The removal of a large number of RBCs leads to a fall in packed red cell volume (PCV) to below 25% or even to as low as 10%. This results in affecting animal camel with anaemia and it became dull, anorexic, listless, with ocular discharges, and loss of body condition (Evans et al., 1995).

In the late stages, anaemia continues to be a major factor, with probably additional causes. However, irrespective of the cause of anaemia the primary abnormality of function are the anoxic conditions created by the persistent anaemia tissue anoxia, which results in a fall in tissue pH and vascular damage (Connor, 1994). Following this are signs of dysfunction which appear in the various organs. An increase in cardiac output due to increases in stroke volume and heart rate and a decrease in circulation time are obvious manifestations. The central nervous system is reported to be most susceptible to anoxia with consequent development of cerebral anoxia (FAO, 2000). In camels suffering from surra on postmortem, the carcass is generally emaciated, pale and may be icteric sometimes. The lymph nodes are enlarged and oedematous on incision. There is hydrothorax, hydropericardium and ascites. In acute

cases, the spleen is enlarged but in chronic cases, it is atrophic, but these changes are not considered patognomonic for disease (Dargantes et al., 2005).

It is known that *T. evansi is* a member of the Brucei group of trypanosomes, which have a known preference for connective tissues of a host, where they disrupt the collagen bundles and destroy the fibroblasts which produce and maintain the collagen (Boid, 1980). This disruption of host connective tissues, along with the vascular damage attributable to brucei group trypanosomes, would be expected to release large quantities of cytoplasmic and mitochondrial enzymes into the serum, thereby causing further tissue damage. The fever characterized by high temperature might be due to the effects of toxic metabolites produced by dying trypanosomes (Wellde et al., 1989). In addition, the oedema reported in the dependant parts of the body during the chronic stage could be due to a significant decrease in the albumin levels, resulting in alterations in osmotic pressure of the blood (Dargantes et al., 2005).

Immune response

Trypanosomiasis is a disease affecting the immune system of the host animal (Lutje and Mertens, 1995). Although the immune system is designed to protect a host from pathogens, it can sometimes be overwhelmed, respond inappropriately or result in immune mediated disease with clinical signs (Stijlemans et al., 2007). Circulating trypanosomes are rarely observed in individuals suffering from chronic disease and studies have failed to show a correlation between the intensity of inflammation and the level of parasitaemia (Olivares-Villagomez et al., 1998). This may be because the immune response is directed against both parasites and self antigens. The parasites might achieve this through molecular mimicry or inflammation and tissue damage leading to the release of tissue proteins which stimulates formation of self antigens (Soares and Santos, 1999). *T. evansi* as purely extracellular parasites survives, multiply and differentiates in extracellular fluids of the mammalian host including the aggressive vascular environment. Thus, these parasites are permanently confronted with the multiple components of the host's immune system ranging from innate to adaptive immune defences. Among many molecules, the trypanosomal DNA and the GPI anchor of the VSG that might be released from the dead trypanosomes has been shown to activate macrophages to secrete proinflammatory molecules like TNF -, IL-6, IL-1, IL-10 and NO as the first response of the host immune system that are involved in the control of the first peak of parasitemia by the toxic nature of TNF and NO for both the host cell and the parasite (Stijlemans et al., 2007).

However as a prototype of extracellular parasites, these pathogens defy humoral immunity through a subtle mechanism of antigenic variation whereby they sporadically vary their main exposed membrane surface glycoprotein (termed variable surface glycoprotein or VSG) to elude antibody (Ab) recognition. IL-6 (secrated by activated macrophages) resptors are only present on directly activated B-cells which result in an increase in IgM and IgG antibodies (Pays, 2006).

The polyclonal B cell activation induced by *T. evansi* infections is characterised by a predominantly IgM response with limited IgG production (Sacks et al., 1980). Sacks et al. (1980) hypothesized that penetration of IgM into tissues where trypanosomes replicate may be impeded because it is a larger molecule compared to IgG and that this may lead to chronic infections, because of the presence of tissue reservoirs, whilst preventing uncontrolled growth by the parasite in the circulation. IgM is detectable during parasitaemia but IgG levels are detectable only after remission of parasitaemia (De-Aquino et al., 1999). Therefore elimination of the infecting VAT appears to be associated mainly with an IgM response, although both IgM and IgG responses to the variable surface glycoproteins (VSG) occur during infection. The antibodies directed against the specific surface exposed epitopes of the VSG coat opsonize the parasites and the immune complexes are efficiently phagocytosed and destroyed, mainly in the liver, by the macrophages. A role for complement-mediated lysis in parasite clearance has been proposed but could not be confirmed because *T. evansi*-infected complement (C5)-deficient AKR mice control successive parasitaemia waves as efficiently as complement-competent strains (Vincendeau and Bouteille, 2006) .

An increase in gamma-globulin (IgM) during both acute and chronic *T. evansi* infections in camels has been reported (Naessens, 2006) but this is not protective, as the majority of the antibodies are auto antibodies. In the acute phase of the disease, lymph nodes and spleen are remarkably reactive. This may account for the generalized lymphoid tissue hyperplasia characteristic of *T. evansi* infections, while in the late stages the immune system becomes depleted of lymphoid cells (Raes et al., 2002).

Antigenic variation and immune evasion

The blood stream form of African trypanosomes are entirely covered by 5 × 106 dimers of variable surface glycoproteins (VSG), which is the most abundant surface protein in the blood stream form of the trypanosomes. It forms a dense surface coat of 12 to 15 nm over the entire surface of the trypanosome and accounts for about 15 to 20% of the total protein content of the bloodstream form of the parasite (Field and Carrington, 2009). This surface coat is attached to the outer membrane of the trypanosomes by glycosylphosphatid linositol (GPI) anchors, which make the variable surface antigen water-

insoluble and may contribute to the host's immune response to trypanosome infection (Pays and Nolan, 1998). It is likely that the VSG repertoire of *T. evansi* is smaller than that of trypanosomes with a tsetse fly intermediate host because exchange of genetic information and rearrangement of VSG repertoires occurs in this vector (Engstler et al., 2007). During the ascending phase of the parasitemia, the majority of parasites are of the same antigenic type (called homotype). The host immune system recognizes this homotype and makes antibodies against it. As the parasites of the major variable antigenic type (VAT) are eliminated the parasitemia goes in descending phase but at the same time, the parasites expressing the heterotype or the minor VATs are multiplying and one of them overgrows others. As a result, this one becomes the new homotype, leading to a new wave of parasitemia and resulting in a long-lasting chronic infection. So expression of the VSG is central in the antigenic variation process and eventually for exhausting the host immune system in the benefit of the parasite (Field et al., 2009).

Immunosuppression

Pathogenic trypanosomes induce a generalized immuno-suppression of both humoral antibody response and T-cell-mediated immune responses. As a result, in the long term, the host's immune responses fail and it succumbs to either the overwhelming parasite load or to secondary infection, consequently leading to occurrence of the trypanosome-induced immunopathology. Various studies have shown that polyclonal B cell activation, generation of suppressor T-cells and macrophages and altered antigen handling and presentation are all mechanisms that could be involved in trypanosome mediated immuno-suppression (Sileghem and Flynn, 1994). It seems that macrophages are central to immunosuppression and that upon activation of these cells a variety of factors and cytokines are released which cause a range of effects such as B-cell activation and T-cell suppression. During trypanosome infections, TNF which are secreted by classically activated macrophages are involved both in parasitemia control and infection associated pathology like anemia, organ lesion and fever. Trypanosome-induced immunosuppression is also appeared to be due to the action of trypanosome enzymes. Trypanosome enzymes, such as phospholipases, neuraminidases and proteases have all been implicated in membrane fluidity and cellular damage (Fung et al., 2007).

Current alternative anti disease strategy

Beside treatment, effective vaccination strategy is a second approach for the control of any infectious diseases. In the case of trypanosomiasis, all conventional anti-parasitic vaccination efforts undertaken so far, that used dominant surface protein, have failed due to the antigenic variation of the trypanosomes surface coat. Therefore, an alternative strategy of the vaccination is demanding. As alternative vaccination approaches, different parasitic molecules have been attempted (Fung et al., 2001). The GPI-anchor of the VSG as one of the major parasitic components causing the inflammatory response associated to the infection has been identified (Taylor et al., 1999). In one of the studies, this information has been used to evaluate GPI based vaccination as an alternative strategy with antidisease potential. Using liposomes as slow delivery system, the GPI administered prior to the infection had been shown to result in a better control of the parasitemia and a longer lifespan of the infected mice. These trials were successful in reducing weight loss, liver damage, acidosis and anemia during *T. brucei* and *T. evansi* infection models; this reduction in pathology was associated with a reduced TNF production and an increased level of IL-10, along with the expression of alternatively activated macro-phage. Due to increased level of IL-10, CD4/Th-cells activated and secrete IL-4, IL-10 and IL-13 which are responsible for T-cell dependant B-cells activation (Naessens, 2006).

CONCLUSION AND RECOMMENDATIONS

Camel trypanosomosis is a disease of major economic importance in many countries of Africa, Asia and South America. Because of the wide geographic range of surra, its control has attracted international attention, vector control seems not the solution for surra as a range of non-related biting flies should be targeted, each with its own biology, while unlike tsetse flies most other flies are proliferate breeders, and as such vector populations are difficult to control. Anaemia is a major component of the pathology of surra and of African trypanosomosis. Trypanosomiasis is a disease affecting the immune system of the host animal. *T. evansi* as purely extracellular parasites are permanently confronted with the multiple components of the host's immune system ranging from innate to adaptive immune defences. Among many molecules, the trypanosomal DNA and the GPI anchor of the VSG that might be released from the dead trypanosomes has been shown to activate macrophages to secrete proinflammatory molecules as the first response of the host immune system. However as a prototype of extracellular parasites, these pathogens defy humoral immunity through a subtle mechanism of antigenic variation.

The polyclonal B cell activation induced by *T. evansi* infections is characterised by a predominantly IgM response with limited IgG production. The vaccination approaches by using dominant surface proteins have not been successful, mainly due to antigenic variation of the

parasite surface coat. On the other hand, the chemo-therapeutic drugs in current use for the treatment of surra are toxic and problems of resistance are increasing. Therefore, there is an argent need for alternative control approaches against camel trypanosomiasis. Therefore, the following points are recommended:

1. Biology of the parasite as well as the host-pathogen interaction needs to be studied for each specific geographical area as there might be variations in the strains of the parasites and the responses of camels to the disease
2. The dynamics of mechanical transmission of camel trypanosomosis in endemic areas has to be thoroughly studied by including those factors contributing to occasional outbreaks.

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